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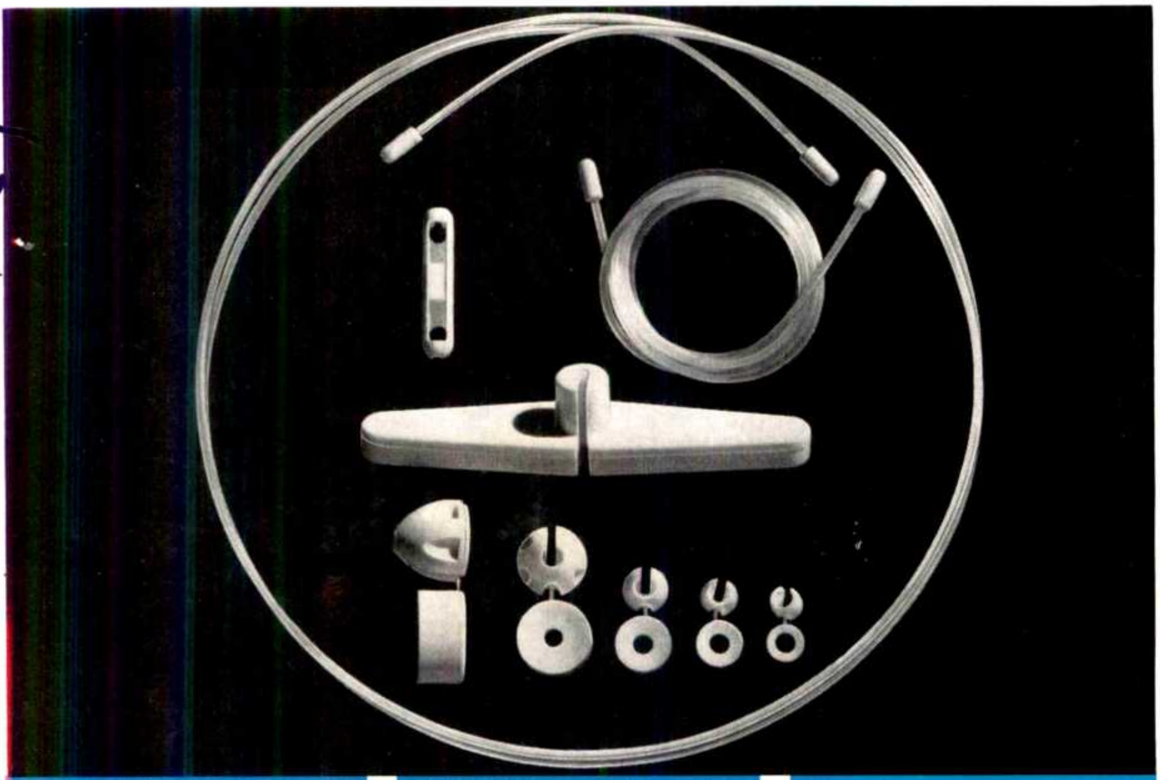

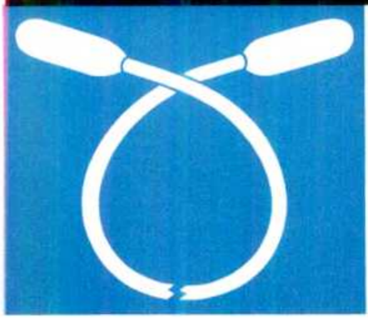

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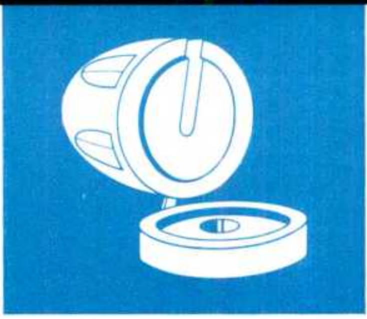

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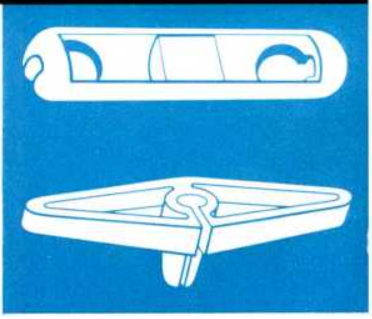

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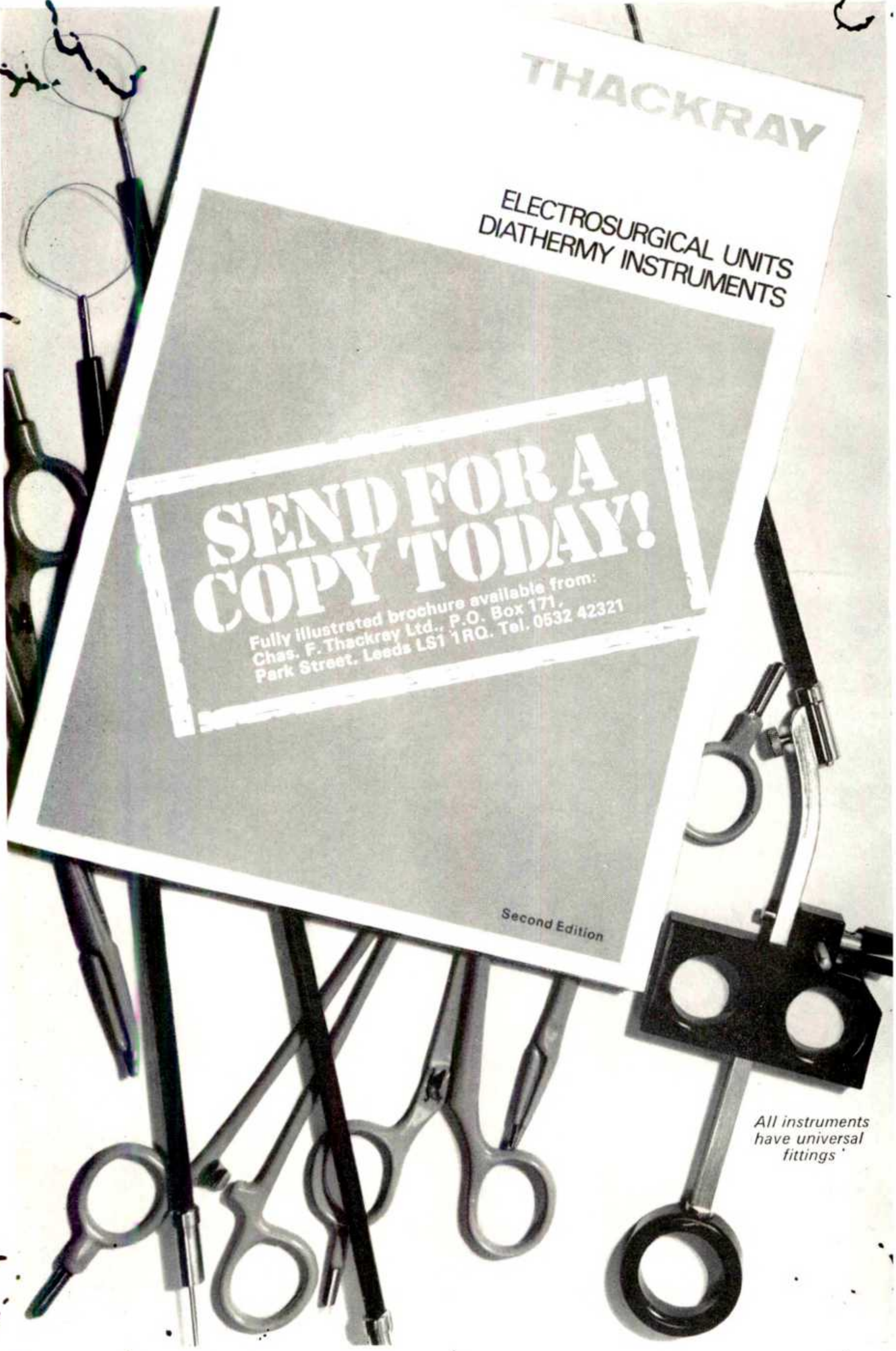

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CONTENTS

PAGE

ORIGINAL PAPERS

OPERATIVE TREATMENT OF HIGH GASTRIC ULCER WITH SPECIAL REFERENCE TO PAUCHET'S METHOD *Adam Lewis and George Qvist* 1

EROSIVE GASTRITIS: ITS DIAGNOSIS, MANAGEMENT, AND SURGICAL TREATMENT *A. M. Desmond and K. W. Reynolds* 5

THE REVERSIBILITY OF POSTGASTRECTOMY ALKALINE REFLUX GASTRITIS BY A ROUX-EN-Y LOOP *H. H. Lawson* 13

THE LESION OF THE SECOND CANCER OF THE LARGE BOWEL - *R. J. Heald and H. E. Lockhart-Mummery* 16

HIRSCHSPRUNG'S DISEASE - - - - - - - - *P. W. Davis and D. B. E. Foster* 19

PYLORUS-PRESERVING GASTRECTOMY IN THE TREATMENT OF DUODENAL ULCER *T. P. J. Hennessy, D. G. Weir, and D. D'Auria* 27

PERIMUSCULAR EXCISION OF THE RECTUM FOR CROHN'S DISEASE AND ULCERATIVE COLITIS *E. C. G. Lee and B. L. Dowling* 29

VESICO-URETERIC REFLUX FOLLOWING RENAL TRANSPLANTATION *R. V. S. Yadav, W. Johnson, P. J. Morris, P. Sprague, D. Yoffa, and V. C. Marshall* 33

LYMPHANGIOGRAPHY AND SURGERY IN LYMPHANGIOMA OF THE SKIN *J. M. Edwards, R. D. G. Peachey, and J. B. Kinmonth* 36

THE BOERHAAVE SYNDROME - - - - - - - - - - *Joseph Callaghan* 41

THE EFFECTS OF CALCULI ON URETERAL FUNCTION - - - - - *J. A. Ross and P. Edmond* 45

CARCINOMA OF THE DUODENUM - - - - - - - - - *John S. Kenefick* 50

BILATERAL DOUBLE NIPPLES - - - - - - - - - - *Terence Brightmore* 55

SOME CLINICAL ASPECTS OF IDIOPATHIC RETROPERITONEAL FIBROSIS - - - - *M. J. Mitchinson* 58

PLATELET ADHESIVENESS AND LIPOPROTEIN LIPASE ACTIVITY IN PATIENTS WITH BENIGN AND MALIGNANT DISEASE OF THE PROSTATE - - - - - - - - *J. M. Ham, M. Jones, and D. Kemp* 60

RETICULO-ENDOTHELIAL SYSTEM ACTIVITY DURING HOMOGRAFT REJECTION AND IMMUNOSUPPRESSION *R. W. Blamey, Jane M. Baker, and D. L. Crosby* 62

THE EFFECT OF ELECTRICAL STIMULATION OF THE LEGS ON POSTOPERATIVE THROMBOSIS *G. E. Moloney, M. Tessa Morrell, and R. H. Fell* 65

SHORT NOTES OF RARE OR OBSCURE CASES

BILATERAL URETERIC OBSTRUCTION CAUSED BY BENIGN PELVIC LIPOMATOSIS *P. L. Golding, M. Singh, and B. Worthington* 69

HYDROPNEUMOTHORAX COMPLICATING PERFORATED PEPTIC ULCER - *J. W. P. Bradley and L. P. Fielding* 72

A CASE OF RETROPERITONEAL HAEMANGIOMA - - - - - *S. J. A. Powis and D. I. Rushton* 74

A SINGLE CONGENITAL ARTERIOVENOUS FISTULA OF THE HAND *R. M. Greenhalgh, D. S. Rosengarten, and J. S. Calnan* 76

SPONTANEOUS RUPTURE OF THE STOMACH IN AN ADULT - - - - - *Christopher D. Jefferiss* 79

REVIEWS AND NOTICES OF BOOKS

Frozen Section in Surgical Diagnosis—*Andrew A. Shivas and Suzanne G. Fraser.* Hepatic Encephalopathy—*Frederick Steigmann and Bernard F. Clowdus.* Orthopädische Therapie—*G. Chapchal and D. Waigand.* Principles of Medical Statistics—*Sir Austin Bradford Hill.* Les Analgésiques et la Douleur—*G. Vourc'h, J. de Castro, P. Gauthier-Lafaye, J. F. Giudicelli, and P. Viars.* Anaesthetics, Resuscitation and Intensive Care—*Walter Norriss and Donald Campbell.* Recent Advances in Haematology—ed. *A. Goldberg and M. C. Brain.* Pathologie du Pied—*Jean Lelièvre.* Technique des Plâtres et Corsets de Scolioses—*Marc Ollier.* The Continuing Education of the Surgeon—ed. *Harold G. Barker.* Surgical Anatomy—*B. J. Anson and C. B. McVay.* Cardiovascular Surgery, 1969—ed. *Earle B. Mahoney.* Urology and Renal Medicine—*J. E. Newsam and J. J. B. Petrie.* Handbuch der Experimentelle Pharmakologie. Anticoagulantien—ed. *F. Markwardt.* Venous Thrombosis and Pulmonary Embolism—*Michael Hume, Simon Sevitt, and Duncan P. Thomas.* Shaw's Textbook of Gynaecology—*John Hawkins and Gordon Bourne.* Simultaneous Prostatectomy and Inguinal Herniorrhaphy—*Sidney R. Weinberg, Albert Kovetiz, and Stephen M. Lazarus.* Orthopédie Traumatologie—*Société Française de Chirurgie Orthopédique et Traumatologie.* The Scientific Basis of Medicine. Annual Reviews, 1971—ed. *Ian Gilliland and Jill Francis.* Human Organ Support and Replacement—ed. *James D. Hardy.* Myoplastic Amputation, Immediate Prosthesis and Early Amputation—*Marian Weiss.* International Encyclopedia of Pharmacology and Therapeutics, Section 8: Local Anaesthetics—ed. *P. Lechat.* Surgical Treatment of Coronary Arteriosclerosis—*Rene G. Favaloro.* 81

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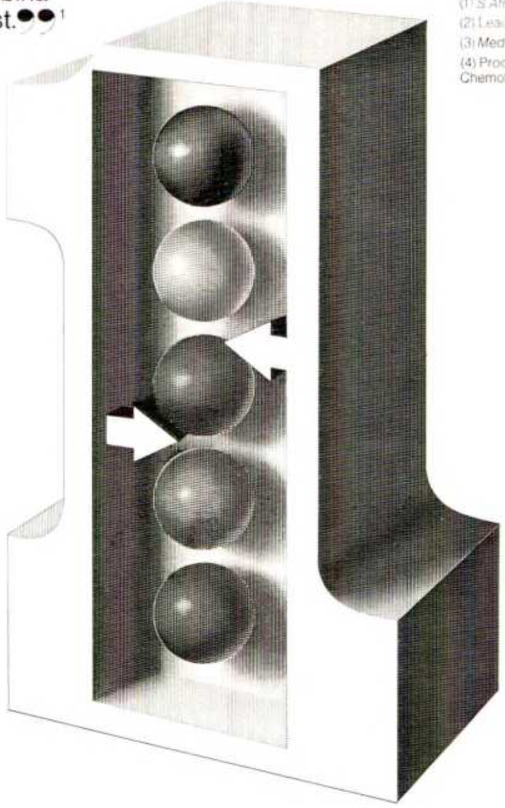

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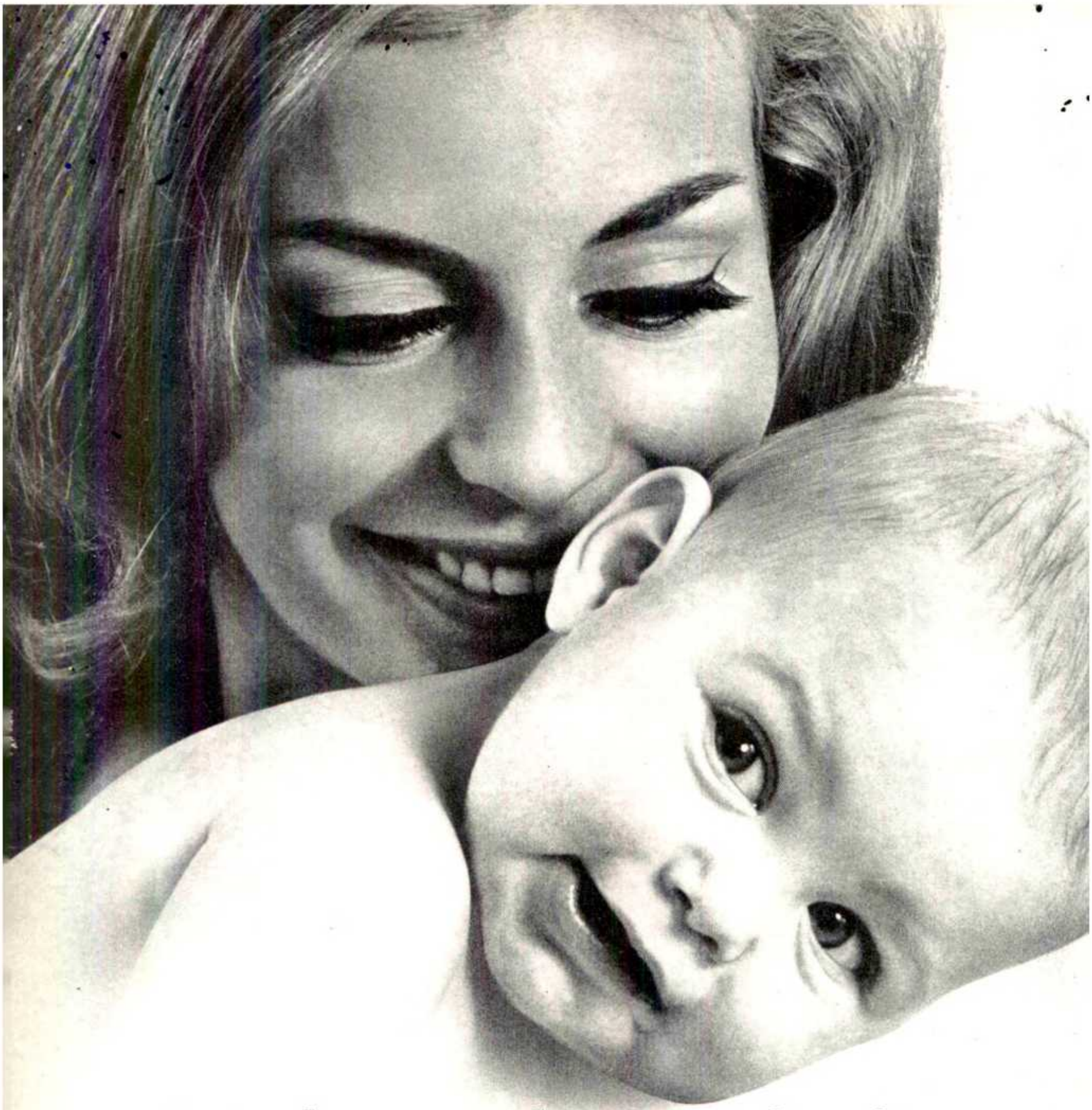

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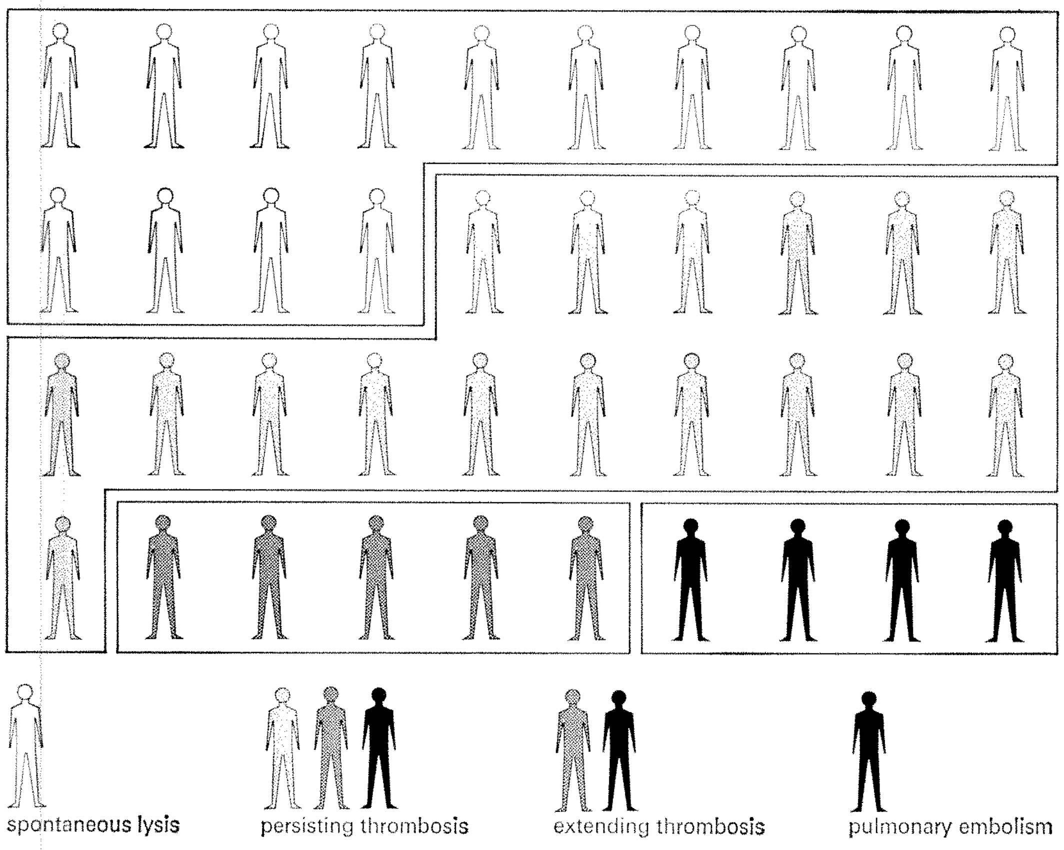

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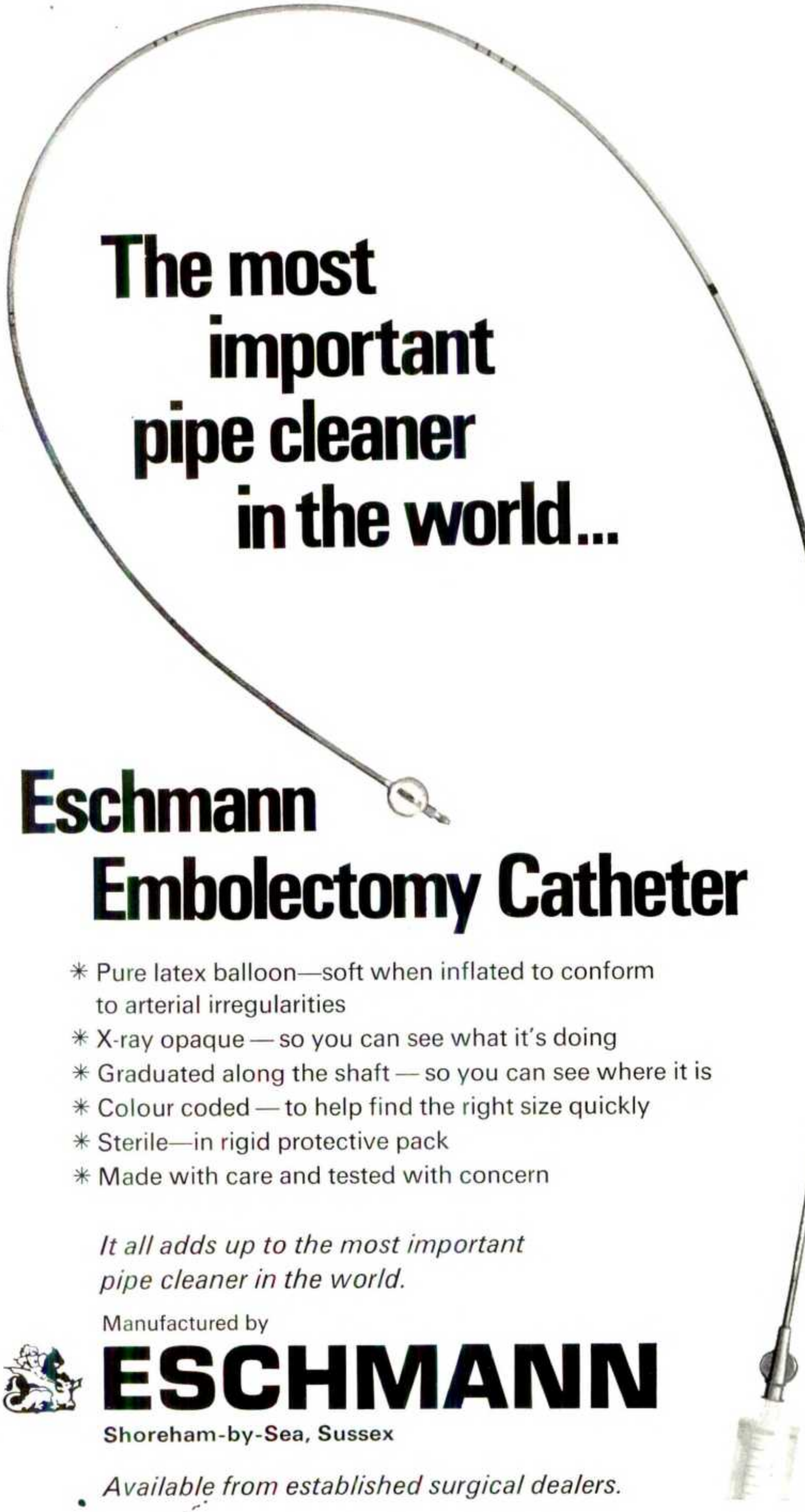

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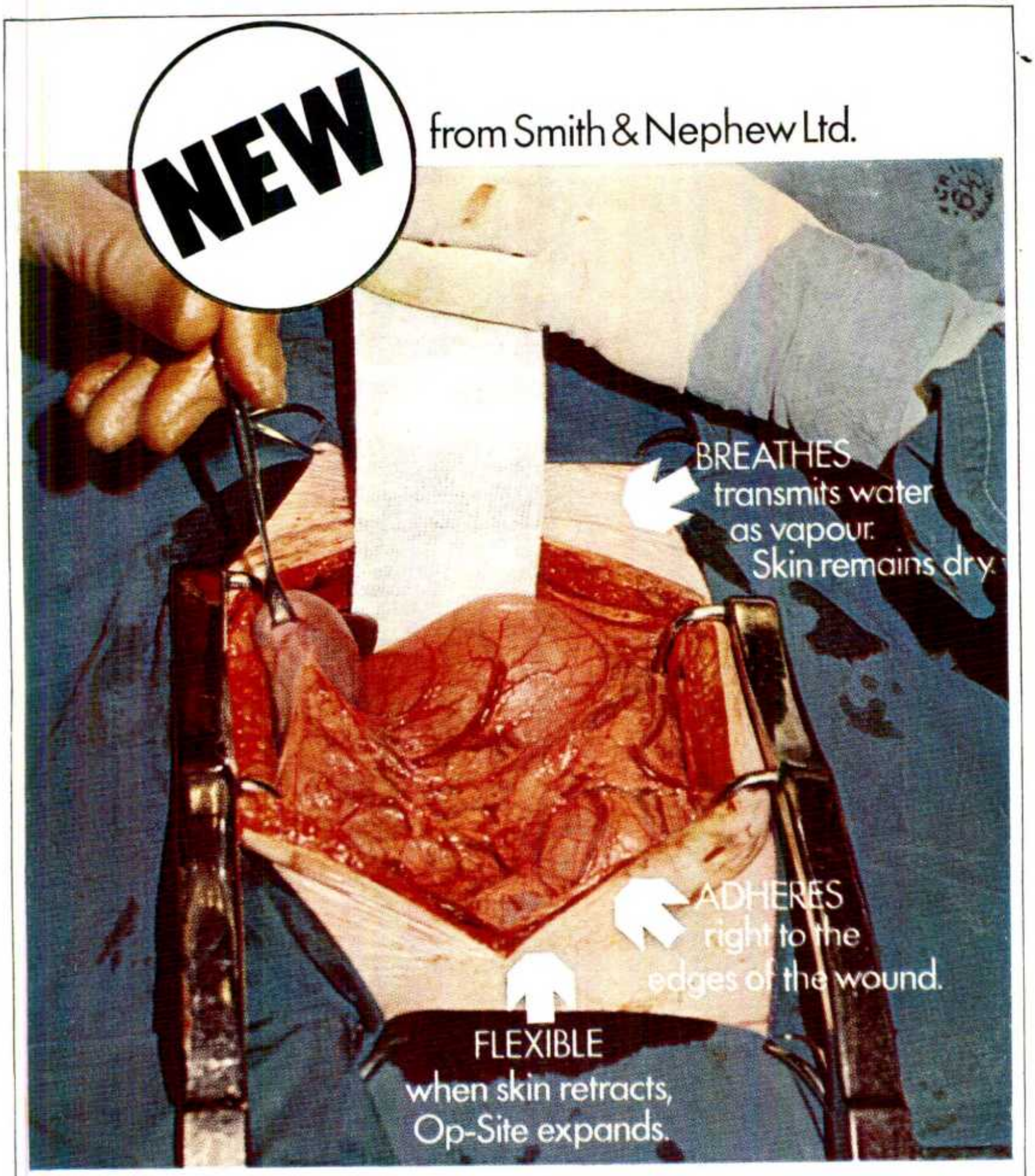

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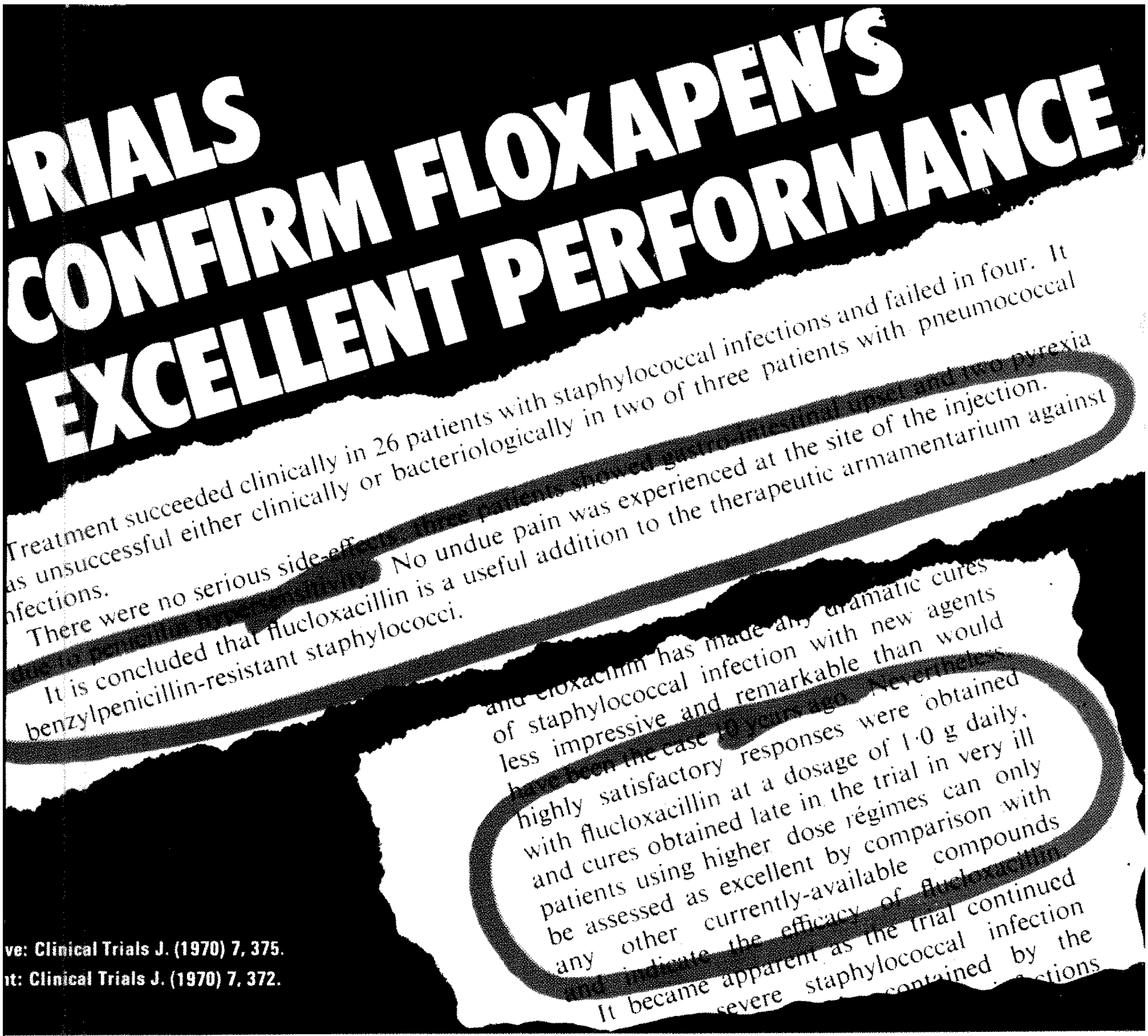

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ORIGINAL PAPERS

OPERATIVE TREATMENT OF HIGH GASTRIC ULCER WITH SPECIAL REFERENCE TO PAUCHET'S METHOD

By ADAM LEWIS AND GEORGE QVIST

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SUMMARY

A high gastric ulcer may be treated by excision, or the ulcer may be retained and healing encouraged by other means. If the ulcer is retained there is a small but definite risk of malignancy. Neither gastric drainage, nor the Kelling–Madlener operation, nor vagotomy and pyloroplasty ensures healing in a high gastric ulcer. Local wedge resection of the ulcer is attended by very poor results, and a high mortality and morbidity preclude the use of subtotal or total gastrectomy. Pauchet's procedure combines the advantages of limited gastrectomy and gastroduodenal anastomosis with complete removal of the ulcer. It is the recommended operation for high gastric ulcers.

BENIGN gastric ulcers situated high on the lesser curvature tend to occur in elderly patients (Veselý, Kubíčkova, and Dvořáková, 1968) with achlorhydria (Baron, 1963) who possess a hereditary predisposition to this type of ulcer (Johnson, 1965). Operations for high gastric ulcer comprise those in which the ulcer is removed and those in which the ulcer is left in situ. Removal of a high gastric ulcer may involve a difficult juxta-oesophageal dissection and thus result in a higher mortality and morbidity than those procedures that avoid this manœuvre. On the other hand, ulcers left in situ may not heal (Levin, Palmer, and Kirsner, 1954; Shipman, 1965; Woodward, Eisenberg, and Dragstedt, 1967), and despite an apparently adequate biopsy may later prove to be malignant. The choice of operation for high gastric ulcer thus involves balancing the risk of a difficult subdiaphragmatic dissection in an often elderly patient against the risk of recurrence or malignancy in a retained ulcer.

PROCEDURES WHICH DO NOT INVOLVE THE REMOVAL OF THE HIGH ULCER

Gastric Drainage.—Results are poor whether drainage is achieved by pyloroplasty (Kennedy and George, 1967; Woodward and others, 1967) or by gastro-enterostomy (Maingot, 1969). There is no doubt that gastric ulcers may remain unhealed or may recur in patients with an entirely adequate pyloroplasty (Qvist and Fox, 1969) or gastro-enterostomy (Tanner, 1964), and therefore these procedures are rarely, if ever, indicated for high ulcers.

Vagotomy and Gastric Drainage.—Conservative surgery by vagotomy and pyloroplasty has been strongly advocated by some surgeons (Hendry, 1961; Weinberg, 1961; Burge, Gill, and Lewis, 1963; Farris and Smith, 1963; Dorton, 1964; Wasuna, Kennedy, Gillespie, and Kay, 1971), but ulcers in the region of the cardia often remain unhealed or recur (Colp and Druckerman, 1946; Lewis and Qvist, 1971). Ulcers that fail to respond to vagotomy and drainage do particularly badly on medical treatment (Bank, Marks, Louw, and Brom, 1969), and although occasionally silent (Qvist, Davis, and Fox, 1969) they remain liable to complications. In a poor-risk patient with an uncomplicated high gastric ulcer, the risk of recurrence may be worth accepting, but, in general, vagotomy with drainage is not recommended for high ulcers.

Kelling-Madlener Operation.—This operation (Kelling, 1918, 1938; Madlener, 1923) leaves the ulcer in situ and entails a gastric resection below it (*Fig.* 1). A relatively modest gastrectomy is feasible and a difficult juxta-oesophageal dissection is avoided. Excellent results have been claimed for this operation (Madlener, 1923; Zukschwerdt and Horstmann, 1936; Kelling, 1938; Colp and Druckerman, 1946; Finsterer, 1954), which must be preceded by a biopsy of the ulcer in order to exclude malignancy. The technique of the Kelling-Madlener operation is similar to that of standard partial gastrectomy, the operation being completed by gastrojejunal or gastroduodenal anastomosis. Although vagotomy may be added to this procedure (Zollinger, 1958), it is of doubtful value. The resection of variable amounts of stomach has been recommended, from a pylorectomy (Smoler, 1934) to a three-quarters gastrectomy (Maingot, 1969), but the efficacy of this operation appears to be more dependent on the provision of adequate drainage than on the amount of stomach resected (Burge, 1966). The operation involves more extensive surgery than other procedures in this group and by no means do all the ulcers heal (Colp and Druckerman, 1946; Levin and others, 1954). Many surgeons (Lewisohn, 1947; Marshall, Jensen, and Davison, 1961; Maingot, 1969) avoid the Kelling-Madlener operation altogether, and others reserve it for those patients who are not considered likely to survive a difficult subdiaphragmatic dissection (Tanner, 1952; Wells, 1960).

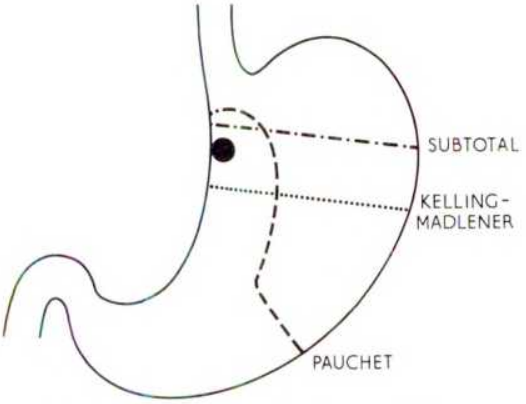


FIG. 1.—Types of gastrectomy for high gastric ulcer.

PROCEDURES WHICH INVOLVE THE REMOVAL OF THE HIGH ULCER

Wedge Resection.—The results of wedge resection alone are very poor (Judd and Rankin, 1923), and the technical difficulties of a high dissection still largely remain. Even when combined with vagotomy and pyloroplasty a wedge resection does not prevent recurrence of a high gastric ulcer (Lewis and Qvist, 1971), and thus cannot be recommended for routine use. It may, however, be the only practicable course available for a bleeding ulcer in a poor-risk patient.

Partial Gastrectomy.—Partial gastrectomy, preferably the Billroth-I operation, is generally accepted to be the best operation available for chronic gastric ulcer (Tanner, 1967; Maingot, 1969). In the case of a high gastric ulcer, subtotal resection may be necessary (*Fig.* 1), and gastrojejunal rather than gastroduodenal anastomosis is then required. The main technical difficulty in gastrectomy for high gastric ulcer is experienced in the resection of the stomach without endangering the cardia. The procedure may be facilitated and major gastric resection avoided by the methods of Tanner or of Pauchet.

Tanner's Rotation Manœuvre (Tanner, 1952, 1969).—Tanner's rotation manœuvre may be performed for high posterior gastric ulcer if the ulcer is not too high for clamps to be applied above it. The ulcer is rotated from its posterior position and held as if on the lesser curve. The true lesser curve now lies anteriorly and the greater curve posteriorly, and the ulcer is clearly exposed below the cardia. Clamps are applied as for Billroth-I gastrectomy, and transection distal to these clamps allows the specimen to be removed together with a tongue of posterior gastric wall which includes the ulcer. Having reconstructed the 'lesser curve' and released the clamps, the upper end of the suture line will rotate back to the posterior wall. Depending on the amount of stomach removed, gastroduodenal or gastrojejunal anastomosis may then be performed.

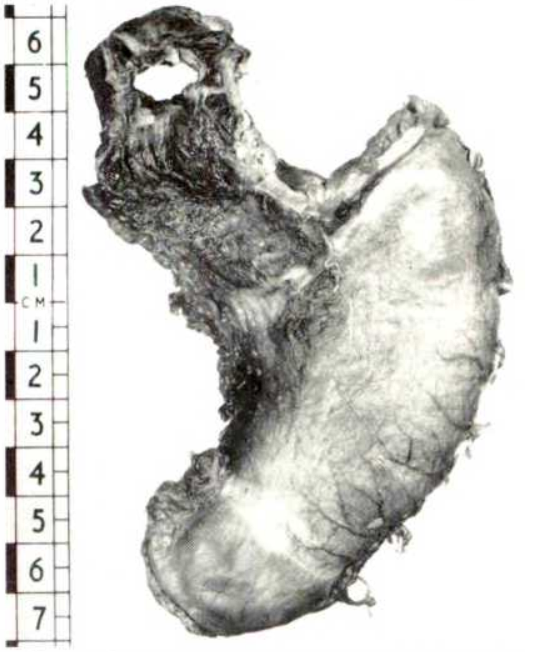
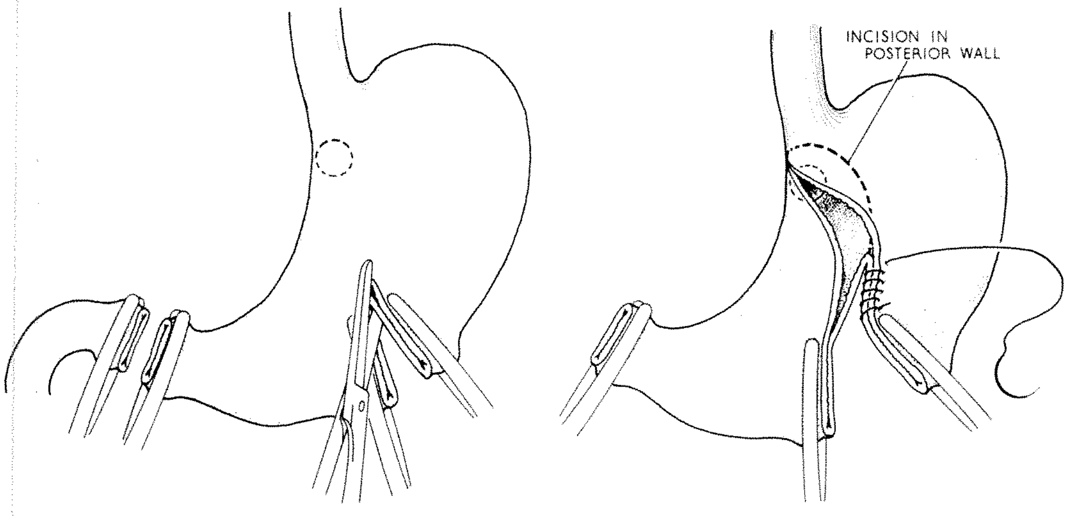


FIG. 2.—Gastrectomy specimen excised by Pauchet's method.

Pauchet's Procedure (*Fig.* 1).—Pauchet's procedure facilitates the safe resection of lesser-curve gastric ulcers that are too high for clamps to be placed above them. The method was first described by Victor Pauchet, a Paris surgeon, in 1924 (Pauchet, 1924), an English translation of his work appearing a year later (Pauchet, 1925). The method is a modification of the Schoemaker procedure (Schoemaker, 1911) and consists of a lower gastrectomy which is extended to include a rim of lesser curve up to and including the ulcer (*Fig.* 2). In his original description Pauchet advocated preliminary transection of the stomach between the clamps below the ulcer. The upper clamp is then removed and the tongue of the lesser curve containing the ulcer is excised separately with scissors. Pauchet's method of excising a high gastric ulcer has been applied to modern gastrectomy technique (Maingot, 1969; Tanner, 1969), and the essential steps in the operation are as follows (*Fig.* 3).

The stomach is mobilized in the usual manner and the duodenum is divided between clamps. The lesser omentum is divided from below upwards to free the lesser curvature of the stomach.

Ligation of the left gastric artery or its branches at this stage may be difficult in the case of a very chronic high gastric ulcer, and it is often necessary to complete the division of the upper end of the lesser omentum later on, *pari passu* with excision of the upper end of the lesser curvature, at which stage the forward and upward displacement of the stomach gives an excellent exposure of the left gastric vessels *Fig.* 3 C).



A B

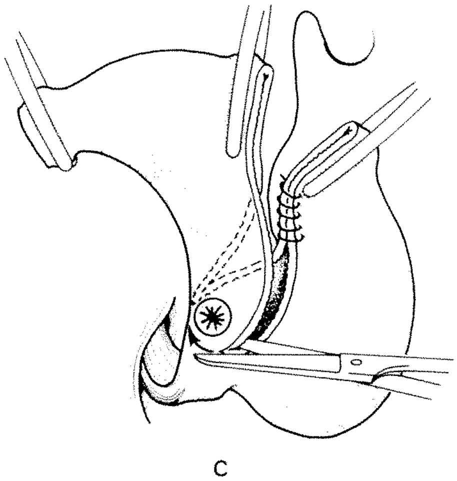
FIG. 3.—Stages of Pauchet's operation.

Two small Payr clamps are now placed side by side horizontally across the stomach at the junction between the antrum and the body and with their tips just short of the lesser curve. The stomach between these two clamps is incised with a knife and the clamps are widely separated (*Fig.* 3 A). Using scissors, the anterior and posterior walls of the stomach are now divided from the tips of the Payr clamps towards the ulcer, thus removing a strip of the lesser curve *Fig.* 3 B). When the ulcer is reached the excision is continued on to the anterior or posterior wall, according to the position of the lesion, and the ulcer is emoved in continuity (*Fig.* 3 C). Care should be taken to confine the upper part of the excision strictly o the margin of the ulcer. In this way a flap of the opposite gastric wall will remain and may be used to epair the defect left by the excision of the ulcer. Bleeding is greatly reduced if the lesser curve is esected bit by bit, a continuous 0 chromic catgut uture being inserted to reconstruct the lesser curve after each short segment is removed. The lesser curve s then reinforced with a layer of interrupted 0 chromic catgut, and the operation is completed by a gastroduodenal anastomosis.

Total Gastrectomy.—This procedure is attended by a high mortality and morbidity (Armstrong and Denick, 1960) and, except in cases of repeated ecurrence (Wells, 1960), is unjustifiable when dealing with benign ulcers (Tanner, 1952; Maingot, 969).

DISCUSSION

Before deciding on the correct procedure to adopt or the treatment of a high gastric ulcer, it is clearly ssential to establish the benign nature of the ulcer. There seems little doubt that the higher a gastric ulcer occurs on the lesser curve the more likely it is to be malignant (Jordan, 1958; Glassman, 1970). If, therefore, it is proposed to leave the ulcer in situ, an adequate four-quadrant biopsy (Zollinger, 1958) should be undertaken. Unfortunately, even a carefully performed biopsy is not infallible (Farris and Smith, 1963), and thus only total removal of the ulcer will ensure that a malignant lesion has not been missed.



C

There has been much difference of opinion in the past concerning the incidence of malignant change in a previously benign ulcer (Wilson and MacCarty, 1909; Mallory, 1940). Publications to date (Glassman, 1970) indicate that malignancy may occur in between 2 and 8 per cent of gastric ulcers, although there is no absolute proof on this point. Whichever figure is accepted, the prognosis of carcinoma of the stomach is extremely poor, and it seems reasonable to eliminate the risk of this complication by excision of the ulcer whenever possible.

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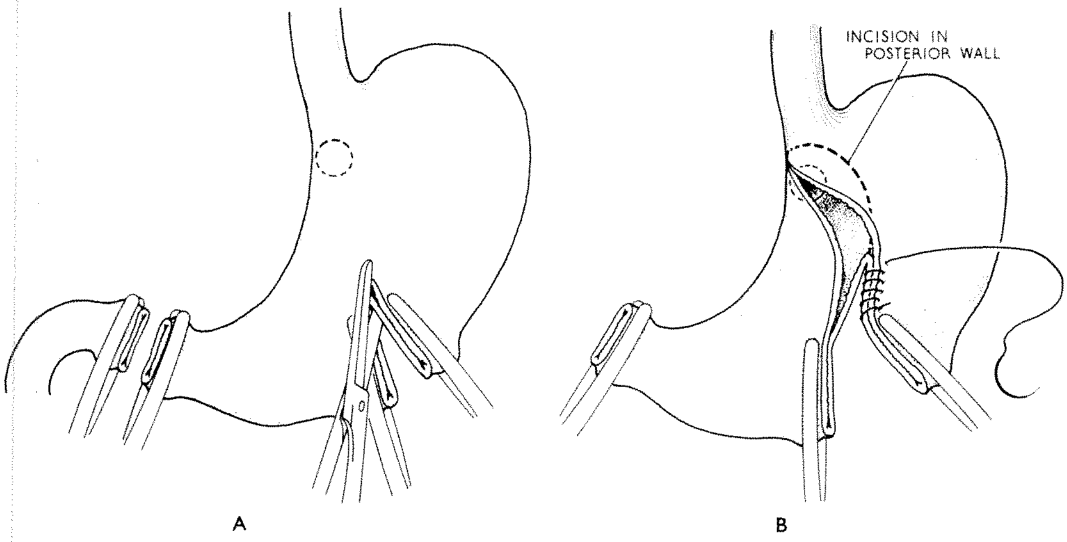

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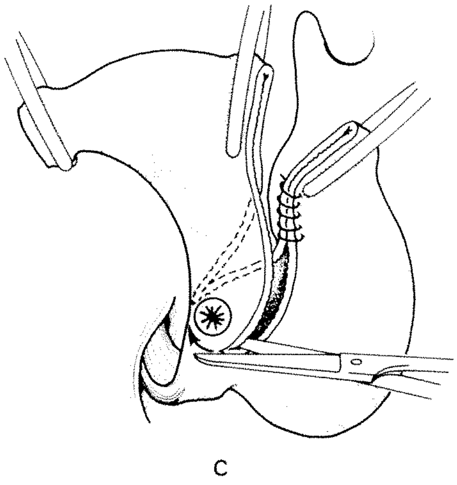

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EROSIVE GASTRITIS: ITS DIAGNOSIS, MANAGEMENT, AND SURGICAL TREATMENT

By A. M. DESMOND and K. W. REYNOLDS
ST. JAMES'S HOSPITAL, BALHAM, LONDON

SUMMARY

Three hundred and thirty-one patients with severe haemorrhage resulting from erosive gastritis, representing 10 per cent of 3938 patients admitted with severe gastroduodenal bleeding during the past 30 years, are presented. The problems of diagnosis and management are discussed; particularly, the role of immediate gastroscopy, and the indications for surgical treatment and the surgical procedure best designed to control the haemorrhage.

Forty-seven patients required 51 emergency surgical procedures, and it was found that the Billroth-I gastrectomy was far superior to any other operation. Polya gastrectomy, vagotomy, and gastric vasoligation were used, with a high incidence of recurrent bleeding and often necessitating a further emergency surgical operation—usually total gastrectomy. It is suggested that a possible explanation of this is the prevention of biliary reflux into the stomach, which is what the Billroth-I gastrectomy seems to achieve. In 1 case presented, a patient with a Polya gastrectomy and erosions who had severe haemorrhage, bleeding was controlled by conversion to a Billroth-I anastomosis.

BETWEEN 1940 and 1970, 3938 patients with gastroduodenal haemorrhage were admitted to the Gastroenterological Unit at St. James's Hospital, Balham. The purpose of this communication is to present some conclusions which were reached as a result of a study of these cases. Particular attention is paid to the problem of diagnosis and management of severe haemorrhage resulting from erosive gastritis.

Table I.—THE DIAGNOSIS IN CASES OF MASSIVE GASTRODUODENAL HAEMORRHAGE, 1940–70

Diagnosis	*No. of Cases*
Gastric ulcer	1407
Duodenal ulcer	1438
Anastomotic ulcer	157
Oesophageal ulcer	10
Erosive gastritis	331
Hiatus hernia	131
Portal hypertension	110
Carcinoma of the stomach	103
Other gastric neoplastic growths	12
Mallory-Weiss syndrome	37
Carcinoma of the pancreas or bile-ducts	9
Aortoduodenal fistula	2
Pancreatitis	2
Retrograde jejunal intussusception	2
Carcinoma of the oesophagus	2
Miscellaneous	16
Unknown	169
Total	3938

Table I lists the diagnosis in 3938 patients. Three hundred and thirty-one cases, or approximately 10 per cent of all admissions with gastroduodenal haemorrhage, were due to erosive gastritis.

Surgeons are primarily concerned with the place of emergency surgery in gastroduodenal haemorrhage. The role of surgery in the management of haemorrhage from erosive gastritis has latterly been our interest.

Much has been written concerning the emergency surgery of bleeding peptic ulcers, and in most centres today the indications for surgery are more or less stereotyped. Our experience of this problem will be discussed briefly.

Since 1953 it has been our policy to select for emergency surgery those cases who are likely to continue bleeding or to have recurrent haemorrhage. Thereby we hope to reduce mortality.

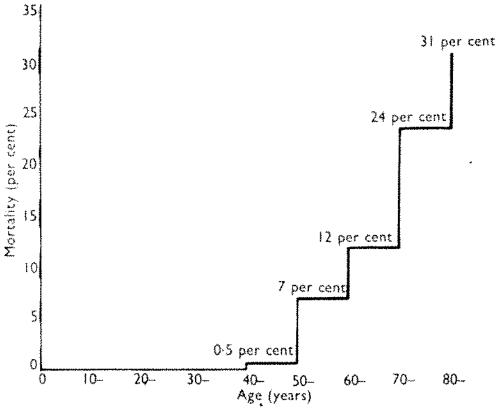

FIG. 1.—The relationship between age and mortality of patients with gastroduodenal haemorrhage.

Table II.—RELATIONSHIP OF SEVERITY OF FIRST HAEMORRHAGE TO MORTALITY IN 200 CONSECUTIVE CASES

HAEMORRHAGE	NO. OF CASES	MORTALITY (per cent)
Initial haemorrhage		
Severe	82	21·0
Mild	118	7·6
Total	200	13·0
Died at first haemorrhage	3	11·5*
Died at repeat bleed	23	88·5*

* Expressed as a percentage of the total number of deaths.

It is generally accepted that mortality is increased in the following circumstances:—

1. In patients over 50 years of age. This is confirmed by our series (*Fig.* 1).
2. When the initial haemorrhage is severe enough to cause oligaemic shock (*Table II*).

3. When pain persists after the initial haemorrhage despite bed-rest.

4. When haemorrhage is associated with steroids, anticoagulants, or anti-inflammatory drugs such as aspirin, indomethacin, or butazoladin.

5. When haemorrhage persists or recurs after 48 hours. Mortality increases with delay in treatment, as shown in *Fig. 2*.

Table III outlines the policy of this unit towards severe gastro-intestinal haemorrhage secondary to peptic ulceration. We believe, contrary to many, that a similar aggressive approach must be made when dealing with bleeding erosive gastritis. The current practice of this unit is to perform a 50 per cent Billroth-I operation for all bleeding chronic gastric ulcers. The ulcer is always removed, high lesser-curve ulcers being removed by the Pauchet manœuvre, thus obviating the need for very high gastric resections.

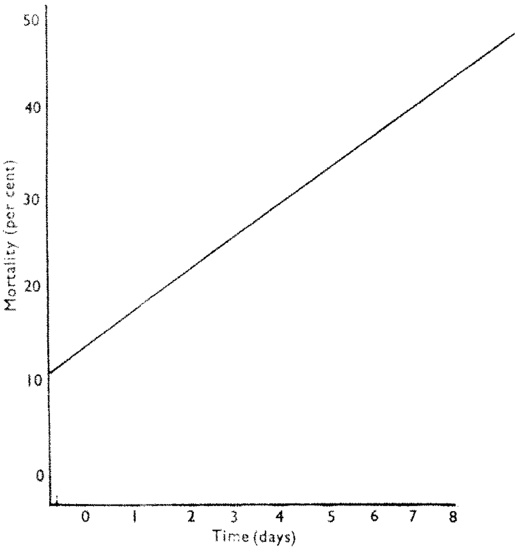

FIG. 2.—The relationship between mortality and the period from admission to operation.

Chronic duodenal ulcers are treated by a standard two-thirds partial gastrectomy, valved with an antecolic gastrojejunal anastomosis. Conservative surgery in the form of vagotomy and drainage together with oversewing of the bleeding point has been used in small or acute duodenal ulcers, but in a callous penetrating ulcer with a large vessel in its base we perform a Polya gastrectomy.

There still remain those cases in whom thorough laparotomy including Kocher mobilization of the duodenum fails to reveal a source of haemorrhage. In the past these have been managed by closure of the abdomen or by blind gastrectomy (Gray, 1953), or by the addition of vagotomy to both these procedures. It is our opinion that none of these procedures is entirely satisfactory. There is a high incidence of continuing haemorrhage after any of the above procedures. If the stomach is opened widely by a gastrotomy, inspection and palpation of the interior wall will, in many instances, reveal an acute mucosal lesion. These lesions are often high on the lesser curve, and if solitary can be under-run, as described by Markby (1965) and Banning, Baron, Kopelman, Lam, and Warren (1965).

Diffuse mucosal lesions in the form of acute gastric erosions do not respond to this simple procedure. We believe that a 50 per cent Billroth-I partial gastrectomy is the treatment of choice in these cases.

MATERIALS AND METHODS

The series consists of 331 cases of erosive gastritis. Forty-eight patients required emergency surgical procedures, and 57 operations were performed. The age and sex distributions of erosive gastritis are analysed. The improved diagnostic rate with the introduction of certain diagnostic criteria is considered. Finally, an analysis of surgical procedures and the results between 1940 and 1970 are given.

In 1969 we introduced the following diagnostic criteria: (1) associated aetiological factors, (2) immediate gastroscopy, (3) a normal barium meal, and (4) cases diagnosed by exclusion of other causes of gastroduodenal haemorrhage. The results of these are analysed in order to establish how they apply to our cases, and they are compared with similar data which were retrospectively collected prior to 1969.

We have defined immediate gastroscopy as gastroscopy between 0 and 12 hours after admission, and for this the fibre-optic gastroscope and duodenoscope have been used, often at the bedside. Prior to this the practice had been to use the rigid Hermon–Taylor gastroscope when the haemorrhage had subsided or at a convenient time. Consequently, the investigation was often delayed for 48 hours or more,

Table III.—OUTLINE OF THE MANAGEMENT OF HAEMORRHAGE FROM PEPTIC ULCERATION

Age	*Evidence of Ulcer*	*Severity of Bleed*	*Time of Surgery**
Over 50	Good evidence of presence of an ulcer	Severe bleed	Emergency surgery probable
		Non-severe bleed	Consider if bleeding recurs
	Insufficient evidence of presence of an ulcer	Severe bleed	Consider if bleeding recurs
		Non-severe bleed	Emergency surgery if medical treatment fails
Under 50	Good evidence of presence of an ulcer	Severe bleed	Consider if bleeding recurs
		Non-severe bleed	Emergency surgery if medical treatment fails
	Insufficient evidence of presence of an ulcer	Severe bleed	
		Non-severe bleed	

* Absolute indications for emergency surgery:—
1. With perforation in most cases.
2. With pyloric stenosis.
3. Continuous bleeding.

* Added incentives for emergency surgery:—
1. Persistence of severe ulcer pain after bleed.
2. Severe pain radiating to back.
3. Patients with ulcers and taking cortisone.
4. Patients using anticoagulants.

by which time acute mucosal lesions had often healed and the gastroscopy was normal.

Apart from local abnormalities of the oropharynx or oesophagus there are no contra-indications to fibre-optic endoscopy. Failure to obtain good views of the stomach occur when it is filled with blood-clot which cannot be removed by gentle lavage. It is our experience that when this latter state of affairs exists emergency surgery is nearly always indicated.

Table IV.—COMPARISON OF IDIOPATHIC AND DRUG-ASSOCIATED EROSIVE GASTRITIS, 1966–70, AND THEIR ASSOCIATION WITH SURGERY

TYPE OF EROSIVE GASTRITIS	1966	1967	1968	1969	1970	TOTAL
No. of drug-associated erosions	6 out of 14	7 out of 14	7 out of 23	3 out of 19	9 out of 13	32 out of 83
No. of drug-associated erosions coming to surgery	2 out of 6	1 out of 7	1 out of 7	0 out of 3	3 out of 9	7 out of 32
No. of idiopathic erosions	1 out of 14	5 out of 14	15 out of 23	16 out of 19	4 out of 13	41 out of 83
No. of idiopathic erosions coming to surgery	0 out of 1	0 out of 5	3 out of 15	2 out of 16	1 out of 4	6 out of 41

Table V.—ANALYSIS OF 'EARLY' AND 'LATE' POSTOPERATIVE CASES OF EROSIVE GASTRITIS

YEAR	NO. OF CASES	DETAILS
1966	2	1. Early: associated with septicaemia 1. Late: following previous Polya operation
1967	3	All immediately after prostatectomy. All massively transfused
1968	1	Early: postappendicectomy and advanced renal failure
1969	3	1. Early: postprostatectomy 2. Late: both following previous Polya operations
1970	5	1. Early: following abdominoperineal excision of rectum 4. Late: All following previous Polya operations

Prior to the introduction of the diagnostic criteria, many cases had been diagnosed as erosive gastritis by exclusion of other lesions in the stomach or duodenum. The effect of the diagnostic criteria, and particularly immediate gastroscopy, in decreasing the number of cases diagnosed by this means is analysed.

RESULTS

Age and Sex Distribution.—Analysis of 147 patients admitted between 1960 and 1967 shows a peak incidence in the fifth, sixth, and seventh decades, with 65 per cent of the series being over 50 years of age (*Fig.* 3). Sixty-one per cent of the series were male, but the age distribution was similar for both sexes. Similar figures are found for patients admitted between 1968 and 1970.

On reviewing the series as a whole, 60 per cent of the patients who required emergency surgery for uncontrolled or continuing postoperative bleeding were over the age of 60 years.

Aetiological Factors.—Careful retrospective study of the case histories between 1940 and 1960 reveals very little detail of associated aetiological factors such as recent drug ingestion.

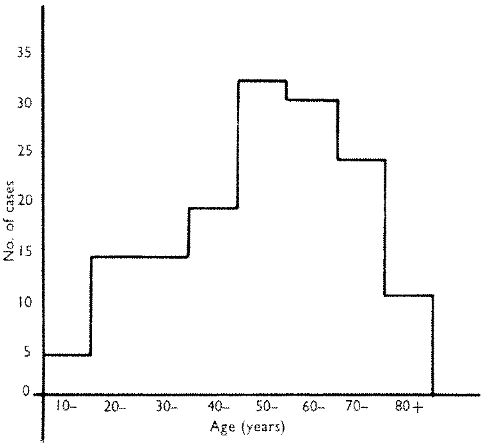

FIG. 3.—The age distribution of 147 cases of erosive gastritis, 1960–6.

Table VI.—THE DIAGNOSTIC CRITERIA USED IN ESTABLISHING THE DIAGNOSIS OF EROSIVE GASTRITIS, 1966–70

DIAGNOSTIC CRITERIA	1966	1967	1968	1969	1970	TOTAL
Ingestion of known associated factor	13	11	8	11	11	54
Positive fibroscopy	2	6	6	5	11	30
Negative fibroscopy	1	1	6	9	2	19
Negative barium meal	9	11	21	19	12	72
Operative diagnosis and post-mortem diagnosis	5	3	4	2	5	19
Diagnosis by clinical methods and exclusion	8	6	14	14	2	44
Total No. of cases	14	14	23	19	13	83

Since 1967 a careful record has been made during history-taking of all possible associated factors, including a detailed history of all the drugs which were taken. On reviewing the case notes the incidence of associated factors in the 1960–6 group was 26 per cent, but from 1967 to 1969 the incidence rose to 55 per cent and to 85 per cent in 1970. Cases where no associated factors are known are termed 'idiopathic'. Analysing the cases from 1967 to 1970 we found that emergency surgery was indicated more frequently in the group with associated factors than in the idiopathic group (*Table IV*). Twenty-five per cent of the group with associated factors came to emergency surgery, and 14 of these cases had had previous surgery. These are divided further into 'early' and 'late' postoperative cases (*Table V*). 'Early' signifies haemorrhage due to erosive gastritis occurring during the immediate postoperative phase, following surgery for diseases other than those of the gastroduodenal system. The 'late' group had had previous gastroduodenal surgery, often many years previously. There were no patients who had previously had Billroth-I operations in this group.

The Diagnostic Criteria.—The results of the diagnostic criteria are shown in *Table VI*. The data for the period 1966–8 were retrospectively extracted from the notes. Between 1969 and 1970, however, with these criteria in mind, searching histories and immediate gastroscopy have decreased the number of cases diagnosed by exclusion of other lesions causing gastroduodenal haemorrhage. This greatly improved diagnostic rate is shown in *Table VII*. The data for the two periods, 1960–6 and 1967–9, are compared with those obtained in 1970.

Table VII.—COMPARISON OF THE DIAGNOSTIC CRITERIA BETWEEN THREE PERIODS OF TIME

DIAGNOSTIC CRITERIA	1960–6 (87 cases)		1967–9 (56 cases)		1970 (13 cases)	
	No.	Per cent	No.	Per cent	No.	Per cent
Ingestion of a known associated factor	—	—	43	76	11	85
Erosions confirmed by gastroscopy	14	16	19	33	11	85
Negative gastroscopy	21	24	16	28	2	15
Normal barium meals	65	74	52	93	12	92
Diagnosis confirmed at operation	10	—	9	—	5	—
Diagnosis by exclusion*	44	50	35	62	2	15

* Factors excluded included positive ingestion history, negative late gastroscopy, normal barium meal, and no dyspeptic history.

In 1960–6 and 1967–9 immediate gastroscopy was not performed, but in 1970 every case had immediate gastroscopy. Immediate gastroscopy resulted in an 85 per cent positive diagnosis rate for erosive gastritis.

Analysis of Emergency Surgical Procedures for Erosive Gastritis, 1940–70.—Forty-eight patients required emergency surgery. This represents 14 per cent of the series. A total of 57 operative procedures were performed (*Table VIII*).

The mortality rate for those patients requiring emergency surgery was 16 per cent. The overall mortality of the series was 7 per cent. This compares with a mortality of 7 per cent in cases admitted during the same period with gastroduodenal haemorrhage from causes other than erosive gastritis (*Table IX*). The mortality of cases requiring emergency surgery in the latter group was 20 per cent.

Table X shows the surgical mortality of erosive gastritis in the three periods which were studied. The causes of death in 8 cases are shown in *Table XI*, and can be compared with the causes of 14 operative deaths (representing a 20 per cent mortality) between 1966 and 1969 in cases of massive haemorrhage not due to erosive gastritis (*Table XII*).

Table VIII analyses the 48 cases requiring emergency surgery and their final outcome.

Commentary on the Surgical Procedures.—Reference to *Table VIII* shows that 9 cases were treated by vasoligation (that is, ligation of the right and left gastric arteries and the right and left gastro-epiploic arteries). Five suffered continuing haemorrhage. This procedure was used extensively in the early 1940's in an attempt to control bleeding in patients in whom thorough laparotomy revealed no lesions. It was subsequently abandoned because of the high rate of continuing haemorrhage. It is of interest to note, however, that there was only 1 case which required further surgery, all the other cases being eventually controlled by conservative measures. There were no deaths in this group.

Table VIII.—ANALYSIS OF SURGICAL PROCEDURES, 1940–70

OPERATION	NO. OF OPERATIONS	CONTINUING OR RECURRENT BLEEDING	TYPE OF FURTHER SURGERY	OUTCOME
Laparotomy alone	1	1	Billroth-I partial gastrectomy	Bleeding controlled
Vagotomy + pyloroplasty	1	1	None	Controlled after prolonged transfusion
Vasoligation	9	5	Billroth-I partial gastrectomy in 1 case	All eventually controlled
Billroth-I partial gastrectomy	28	1	Total abdominal gastrectomy	Died septicaemia; 4 deaths in controlled cases
Polya gastrectomy	8	4	1. Vagotomy, higher gastrectomy, total gastrectomy 2. Total gastrectomy 3. Higher gastrectomy 4. Total gastrectomy	Controlled eventually Controlled Rebleed; death Controlled 2 deaths in the 4 cases originally controlled
Roux gastrectomy	1	—	None	Controlled
Total	48	12	9 operations in 7 cases	8 deaths (16 per cent)

In this series the Billroth-I 50 per cent partial gastrectomy emerges as the operation of choice. A total of 30 operations was performed, 28 as primary procedures and 2 for recurrent haemorrhage following other forms of emergency surgery. Only 1 case continued to bleed postoperatively, and this was associated with a Gram-negative septicaemia and peritonitis. The patient eventually died. There were 4 other postoperative deaths, giving a mortality of 16 per cent. Of these 4 cases, continuing haemorrhage was not a cause of death in any. One died of a leaking anastomosis and was thus a technical fault. The other 3 deaths occurred in patients all over 70 years of age.

The causes of death are shown in *Table XI*. Although the operative mortality of 16 per cent is high, it compares with the mortality of 20 per cent for emergency surgery for gastroduodenal haemorrhage due to other causes (*Table IX*).

Table IX.—COMPARATIVE MORTALITY OF MASSIVE HAEMORRHAGE DUE TO EROSIVE GASTRITIS AND ALL OTHER CAUSES OF HAEMORRHAGE, 1967–70

CAUSE OF HAEMORRHAGE	NO. OF CASES	MORTALITY	
		No.	Per cent
All haematemesis and melaena cases admitted as emergencies excluding erosive gastritis	537	38	7
Emergency surgical procedures in haematemesis and melaena cases excluding erosive gastritis	104	21	20
Erosive gastritis cases admitted as emergencies	69	5	7
Emergency surgical procedures in erosive gastritis cases	14	2	14

Table X.—MORTALITY OF EMERGENCY SURGICAL TREATMENT OF EROSIVE GASTRITIS

PERIOD	TOTAL NO. OF CASES	NO. OF EMERGENCY SURGICAL PROCEDURES	OPERATIVE MORTALITY	
			No.	Per cent
1940–59	175	24	6	25
1960–6	87	10	—	—
1967–70	69	14	2	14
Total	331	48	8	16

Table XI.—ANALYSIS OF CAUSES OF DEATH IN 8 CASES OF EROSIVE GASTRITIS (1940–70)

OPERATION	AGE (years)	FURTHER SURGERY	CAUSE OF DEATH
Billroth-I	43	Total gastrectomy	Leaking anastomosis
Higher partial gastrectomy for rebleed	69	None	Continued haemorrhage
Billroth-I	71	None	Coronary
Billroth-I	81	None	Cardiovascular accident
Polya	65	None	Intestinal obstruction
Billroth-I	74	None	Bronchopneumonia
Polya	80	None	Renal failure
Billroth-I	72	None	Peritonitis; leaking anastomosis

One of the last cases to be included in the Billroth-I series was a patient with a long-standing Polya gastrectomy who developed severe bleeding from erosions following aspirin ingestion. Haemorrhage was controlled by conversion to a Billroth-I type of anastomosis without further gastric resection.

CASE REPORT

E. S., aged 64 years, was admitted as an emergency on 17 Sept., 1970, with melaena. He had had a partial gastrectomy in 1942 for chronic duodenal ulcer. During the week before his present admission he had taken 2–3 Anadin tablets daily. He had no history of dyspepsia since his operation in 1942.

On admission, his haemoglobin was 8 g., electrolytes were normal, and urea was 20 mg. per cent. He was treated by sedation, bed-rest, milk, and transfusion. Twenty-four hours after admission he collapsed with further melaena. He continued to bleed slowly during the next 48 hours and then he had a massive haematemesis and again collapsed. By this time he had received 17 units of blood.

The patient underwent laparotomy on 21 September through an upper midline incision. The previous Polya–Hofmeister partial gastrectomy was noted to be normal, with no evidence of gastric or stomal ulceration. The duodenal stump was normal. A wide gastrotomy revealed diffuse bleeding erosive gastritis. The Polya anastomosis was dismantled and converted to a Billroth-I gastroduodenal anastomosis without any further resection. This procedure brought about control of the haemorrhage.

Table XII.—ANALYSIS OF CAUSES OF DEATH IN 14 CASES OF GASTRODUODENAL HAEMORRHAGE DUE TO LESIONS OTHER THAN EROSIVE GASTRITIS, 1966–9

OPERATION	AGE (years)	FURTHER SURGERY	CAUSES OF DEATH
Polya	61	None	Coronary thrombosis
Billroth-I	67	None	Pulmonary embolus
Billroth-I	69	None	Small-bowel obstruction
Polya	73	None	Bronchopneumonia
Polya	73	None	Bronchopneumonia
Radical Polya	73	None	Bronchopneumonia
Billroth-I	73	None	Congestive cardiac failure and bronchopneumonia
Polya	53	None	Septicaemia
Polya	83	None	Bronchopneumonia
Polya	82	None	Congestive cardiac failure
Radical Polya	46	None	Bronchopneumonia; renal failure
Billroth-I	82	None	Congestive cardiac failure
Billroth-I	80	None	Haemorrhage
Radical Polya	76	None	Hepatic failure
Billroth-I	80	None	Bronchopneumonia

The number of operations during this period was 70, the number of operative deaths was 14, and the mortality was 20 per cent.

Of the patients treated by Polya gastrectomy, 3 out of 8 cases died, a mortality of 37 per cent. Of the 8 cases, 4 suffered continuing haemorrhage, and 3 of these were eventually controlled by total abdominal gastrectomy. All 3 cases survived, but this operation is a very serious and major undertaking with a high mortality and morbidity. The other patient died of recurrent haemorrhage from the gastric remnant after a higher gastrectomy. Considering these facts it is surprising that the mortality was not greater. It can be seen from *Table VIII* that neither the addition of vagotomy nor of higher gastrectomy has any place in the treatment of continued haemorrhage after a Polya partial gastrectomy. Roux gastrectomy as advocated by other surgical centres, notably Bristol, has been used once in this series. This was a patient who many years previously had had a retrocolic gastrojejunostomy for a duodenal ulcer. For technical reasons a Roux gastrectomy was performed, with no postoperative bleeding.

DISCUSSION

The Diagnosis of Erosive Gastritis.—In agreement with the reports from many other centres we have found that erosive gastritis is the third commonest condition requiring emergency admission to hospital with massive gastro-intestinal haemorrhage. In 89 unselected cases of upper gastro-intestinal bleeding analysed by Mailer, Goldberg, Harden, Grey-Thomas, and Burnett (1965) the three main causes were peptic ulcers, acute erosions, and oesophageal varices. Obviously the number of gastric and duodenal ulcers far outnumber that of acute erosive gastritis in our series. The latter, however, constitutes approximately 10 per cent of the admissions. Undoubtedly in this and other published series many cases of erosions were lost to the 'miscellaneous' group of causes of haematemesis and melaena.

Because of the difficulty in diagnosing erosive gastritis we introduced the diagnostic criteria mentioned earlier. The results of these criteria are shown in *Table VII* and we would like to consider them here in more detail.

Associated Aetiological Factors.—A detailed history of all the drugs taken by the patient is essential in all cases of haematemesis and melaena, and it is necessary to check this again when the patient has been resuscitated. Careful retrospective review of case histories between 1940 and 1960 reveals very little detail of associated aetiological factors such as recent drug ingestion. Between 1960 and 1966 such associated factors were found in 26 per cent of cases. In 1967 we started to record all the drugs which had been taken by patients who were admitted with gastroduodenal haemorrhage in an attempt to establish drug-associated acute mucosal lesions as a cause of haemorrhage.

Table VII compares these three periods in the series and shows the effect of the introduction of the diagnostic criteria in 1969. In the period 1969–70, 85 per cent of cases of proved erosive gastritis gave a history of ingesting a known associated aetiological factor.

Banning and others (1965), in a 5-year follow-up study of gastroduodenal haemorrhage, found aspirin-associated bleeding in 33 per cent of the whole series. It should be noted, however, that 40 per cent of their cases were acute ulcers, a higher percentage than in most published series. Mailer and others (1965) obtained a history of aspirin ingestion in 5 out of 7 cases of gastric erosions in a series of 89 unselected cases. Between 1967 and 1970 we have found aspirin-associated bleeding in 20 per cent of all the patients who were admitted with haematemesis and melaena. We have also seen acute gastric erosions in patients who were known previously to have peptic ulcers. Neither a previous Polya gastrectomy nor vagotomy and drainage protects the patient. This has also been the experience of Bartlett and Ottinger (1966) and Croft and Wood (1967). We have not, however, seen erosive gastritis develop in the gastric remnant of a patient who had had a previous Billroth-I partial gastrectomy.

Immediate Gastroscopy.—The position of gastroscopy in the diagnosis of gastric lesions is clearly established. Mailer and others (1965) showed that gastroscopy gave a 57 per cent correct diagnosis in both acute and chronic ulcers and was the only way of diagnosing acute gastric erosions. Bartlett and Ottinger (1966) obtained a positive endoscopic diagnosis in 8 out of 9 cases of bleeding gastritis.

The introduction of fibre-optic endoscopy and its subsequent developments have made the direct visualization of the digestive tract from the crico-pharyngeal sphincter to the ampulla of Vater both safe and comparatively easy. Reference to *Table VII* shows that between 1960 and 1966, 16 per cent of cases who were subsequently proved to have acute erosions had positive gastroscopies, while between 1967 and 1969, 33 per cent had positive gastroscopies. However, many cases did not have a gastroscopy until 48–72 hours after admission, and others were unsuitable for the procedure with the rigid Herman–Taylor type of gastroscope.

In 1969 immediate gastroscopy was introduced. With the fibre-optic instrument, gastroscopy is easy to perform and can be done at the bedside with topical oropharyngeal anaesthesia. With immediate gastroscopy the diagnostic accuracy in the acute gastric mucosal lesion has risen to 85 per cent. We believe that immediate gastroscopy is essential in the diagnosis of erosive gastritis, as these lesions often heal in 48 hours with bed-rest. Subsequent gastroscopy is then essentially normal. For this reason we have included a negative, often late gastroscopy in the diagnostic criteria. Unheralded haemorrhage associated with drug ingestion, a normal barium meal, and a normal late gastroscopy strongly suggest acute erosive gastritis. Such cases are included under the designation 'diagnosis by exclusion' and the value of immediate gastroscopy in eliminating this group is shown in *Table VII*.

Barium Studies.—Within the context of the diagnostic criteria a normal barium meal is considered to be one in which there is no radiologically demonstrable lesion of the stomach or duodenum. Patients who have had previous gastroduodenal surgery are regarded as having abnormal barium studies.

Mailer and others (1965), in discussing the use of emergency radiology in the diagnosis of upper gastro-intestinal bleeding, demonstrated lesions in 79 per cent of cases. The results, as would be expected, were best in cases of chronic duodenal and gastric ulceration. They concluded that barium studies were useless in the diagnosis of acute erosions as all cases who were proved endoscopically had normal barium meals. This has also been our experience, but within the context of the diagnostic criteria we consider negative radiology to be of importance.

Surgical Attitudes to Erosive Gastritis.—The management of massive haemorrhage due to peptic ulceration is now standardized in most centres, with an early surgical bias in patients with a good ulcer history who are over 50 years of age. Despite this and improved facilities in resuscitation and anaesthesia the mortality remains high.

During the decade 1960–70, 7 per cent of all the cases who were admitted to our specialized gastric unit died. Of these bleeding peptic ulcer admissions, 20 per cent required emergency surgery, and this was associated with a mortality of 20 per cent. There was a similar mortality for the cases of erosive gastritis over the same period (*Table IX*). Despite these figures there appears to be, even in specialized units, considerable variation in the selection of patients for surgical treatment of erosive gastritis, and in the procedures used to control the haemorrhage. The current trend, if any, is towards more conservative operations, such as vagotomy and drainage. Carruthers, Giles, and Clark (1967), in discussing conservative surgery for bleeding peptic ulcers, had 13 cases of acute erosions in a series of 117 patients who were treated by emergency surgery. Of these 13 patients with erosions, 4 had partial gastrectomies, 3 of which continued to bleed postoperatively, and 1 died. The remaining 9 were treated by vagotomy and pyloroplasty, with a mortality of 33 per cent. These 13 cases represent 11 per cent of the series and their mortality was 30 per cent owing to continuing haemorrhage. Carruthers and others (1969) conclude that the conservative approach, that is, vagotomy and drainage, 'is not entirely satisfactory'. They also point out that continuing haemorrhage was only seen in cases of erosive gastritis and it was this that accounted for the high mortality.

Gray (1953), in the Lahey Clinic series, found that 11 per cent of his cases continued to bleed after blind partial gastrectomy and 63 per cent did so after laparotomy alone. Bartlett and Ottinger (1966) also reported 7 cases of continuing haemorrhage out of 14 cases of erosive gastritis who were treated by the Polya type of partial gastrectomy. The mortality was 28 per cent. Walt (1969) considered the problem of erosive gastritis in relation to hepatic trauma. Gastric erosions frequently complicate severe hepatic trauma and 7 out of 30 cases in his series did so. Five patients required emergency vagotomy and drainage procedures and 3 of these (60 per cent) suffered fatal continuing haemorrhage. Katz and Siegel (1968) stated: 'Gastroscopically proven acute mucosal lesions are generally amenable to conservative therapy', and of their series, 9 per cent required emergency surgery, with a mortality of 45 per cent; all the cases were treated by vagotomy and drainage. In their discussion these authors related their mortality to hepatic decompensation in cirrhotic patients. All the fatal cases, however, died from active haemorrhage due to the erosions. Erosive gastritis frequently complicates severe burns, and Foley (1969) found that 51 per cent of a series of 335 autopsy cases had acute erosions and that 41 (25 per cent) died of haemorrhage from these. He urges that the management of haemorrhage in a burned patient should closely parallel that in a non-burned patient.

The most conservative attitude is put forward by Banning and others (1965) and Markby (1965), who consider oversewing the bleeding point to be the operation of choice. However, these authors described solitary, or at the most two, high lesser-curve lesions.

We have always regarded erosive gastritis as a multifocal pathology in the gastric mucosa, and we have purposely excluded from this series of erosive gastritis the solitary, localized, acute, high lesser-curve lesions.

From the work so far quoted two facts emerge:—

1. The management of erosive gastritis lacks uniformity both in indications for and technique of surgical intervention.

2. The mortality in most published series owing to continuing haemorrhage is unacceptably high.

We believe that the management of erosive gastritis should parallel that of haemorrhage from peptic ulcers, with the same bias towards early surgery in patients over 50 years of age.

We believe that the results in *Table VIII* indicate that early aggressive surgery in the form of the Billroth-I partial gastrectomy would largely eliminate the problem of continuing haemorrhage. It would also appear that any lesser procedure than a total gastrectomy for continuing haemorrhage after a vagotomy or Polya gastrectomy is associated with a prohibitive mortality. Total gastrectomy itself is a formidable surgical procedure with a high intrinsic mortality. Recent personal experience with 1 case of converting a Polya to a Billroth-I type of anastomosis with dramatic control of haemorrhage introduces the possibility of a procedure with a lesser mortality in continuing haemorrhage.

Aetiological Concepts of Erosive Gastritis.— The association of aspirin ingestion and both occult and massive gastro-intestinal bleeding was first recognized by Douthwaite and Lintott (1938). Parry and Wood (1967) have shown that the tendency to overt bleeding bears no relationship to the tendency to occult bleeding. Croft and Wood (1967) suggest that the two disorders should be considered separately. In their series 78 per cent of the cases suffered occult bleeding when given aspirin and these results were reproducible 6–8 weeks later. They also studied the effect of repeated doses of aspirin on the gastric mucosa in 5 cases who were subsequently to undergo partial gastrectomy. The stomachs were studied immediately on removal and all the cases receiving aspirin had lesser-curve erosions. These authors suggested that aspirin may cause excessive exfoliation of gastric epithelial cells. To test this hypothesis they studied the rates of accumulation of DNA in gastric washings. In all the cases who had initially bled when given aspirin there was a significant increase in the rates of DNA accumulation when aspirin was given again. Patients who had not bled when first given aspirin did not show this increase in DNA accumulation in the gastric washings. As a result of these studies they proposed that aspirin stimulated epithelial shedding in excess of the ability of the mucosa to replace the surface cells. To support this hypothesis further they pointed out that cases of atrophic gastritis who never bled when given aspirin had a higher surface-cell turnover than normal. Neither vagotomy nor partial gastrectomy affected the susceptibility to bleed.

Anatomically, the majority of erosions occur in the upper stomach in the region of the high lesser curve. This predilection has been studied by Markby (1965), who considers the distribution of erosions to be related to the vascular anatomy in the region. Barlow, Bentley, and Walder (1951) studied the mucosal arteries in this region and showed that they differed from all the other areas of the stomach. In the upper lesser curvature there is no submucosal arterial plexus, the mucosal arteries arising as branches from the left gastric artery at the point where it divides into ascending and descending branches. The mucosal capillaries join to form veins which run vertically through the mucosa and pierce the muscularis to form large veins which accompany the mucosal arteries. They postulated that a local impairment of the mucous barrier is responsible for acute erosions and that the haemorrhage is of venous origin owing to the vascular anatomy in this area.

Much work has been done to support the concept of systemic as opposed to local factors in the causation of drug-associated gastro-intestinal haemorrhage. Wolf and Wolff (1947), in their classic work on their subject, Tom and his gastric fistula, were not able to injure his exposed mucosa by the direct application of aspirin. They were, however, able to produce mucosal erosions with topical irritants, including hydrochloric acid, after they had wiped or washed away the protective mucous layer.

Menguy and Masters (1965, 1967) and Menguy and Desbaillets (1967) have been responsible for much of the research on gastric mucus and its modification, both quantitatively and qualitatively, by drugs such as aspirin, phenylbutazone, and indomethacin. Gastric mucus is secreted by the surface cells and foveola of the gastric glands and is particularly abundant in the glands of the prepyloric region. Native mucus is thick, highly viscous, and cohesive, with a high pH. It can be separated into: a mucoid fraction consisting of polymers of glycoprotein molecules, a protein fraction immunologically identical with serum proteins, and a third fraction of as yet unidentified polypeptides.

The glycoprotein polymers consist of long filaments which have a polypeptide backbone to which are attached oligosaccharide side-chains. Normal glycoproteins are only slowly hydrolysed by proteolytic enzymes such as pepsin. This resistance to proteolysis is due to the spatial configuration of the oligosaccharide side-chains. Menguy and Masters (1965, 1967) and Menguy and Desbaillets (1967) have extensively studied the effect of acute inflammatory drugs on gastric mucus and basically two facts emerge:—

1. Inflammatory drugs decrease the rate of secretion of gastric mucus and therefore the rate of renewal of the mucous barrier.
2. The mucus which is secreted is chemically altered. Particularly, the carbohydrate content of the glycoproteins is reduced.

It has been shown experimentally that if the carbohydrate side-chains are removed by appropriate chemical means, then mucoproteins are readily hydrolysed by trypsin or pepsin (Menguy and Masters, 1965). The anti-inflammatory drugs all reduce the carbohydrate content of gastric mucus, particularly I-fucose and hexosamine. A possible hypothesis is that the drug-modified gastric mucus is hydrolysed by refluxed bile and pancreatic juices, thus removing the normal protective mucous barrier and exposing the mucosa to endogenous acid, resulting in the production of erosions. Kowalewski, Schier, and Koheil (1970) have studied the response of canine gastric mucosa to histamine after experimental impairment of the mucous barrier. They removed the mucous barrier by instilling 2 N saline into fundic pouches. Histamine infusion then produced maximal acid peptic activity in a gastric mucosa which was not protected by the normal mucous barrier. Numerous acute mucosal lesions resulted.

Can the efficiency of the Billroth-I partial gastrectomy in controlling haemorrhage be explained by this hypothesis? The poor results obtained by the Polya gastrectomy may be due to the fact that tryptic digestion of mucoprotein by refluxed bile and pancreatic juices continues in the gastric remnant postoperatively. In addition, because of the nature of the Polya anastomosis the normal mechanism for the inhibition of acid production is lost. Sokolov (1904) noted that acid in either the antrum or the duodenum caused inhibition of further acid production. With the Polya gastrectomy the antrum is removed and the duodenum is by-passed.

Du Plessis (1960, 1962) and Lawson (1964) have studied regurgitant gastritis in detail. Reflux of the duodenal contents into the stomach under experimental conditions produces a chronic gastritis. Changes in the mucosa are maximal when both bile and pancreatic juices are refluxed, and least with pancreatic juices alone (Lawson, 1964). Lawson (1964) also studied reflux following both the Polya anastomosis and the Billroth-I procedure. Microscopical changes of gastritis were limited to a 2-cm. area from the anastomosis in the Billroth-I type of partial gastrectomy. The stomach proximal to this area was entirely normal. By comparison the changes following the Polya anastomosis extended over halfway up the gastric remnant. Lawson (1964) confirmed that these changes were due to reflux into the gastric remnant and were not due to operative trauma by use of the Roux gastrectomy. From this work we may conclude that pancreaticobiliary reflux into the gastric remnant is less after the Billroth-I operation than after the Polya anastomosis.

In addition, it is a clinical observation that the Billroth-I gastrectomy is often slower to drain postoperatively than the Polya procedure. We believe that pancreaticobiliary secretions do not enter the gastric remnant for 48–72 hours postoperatively following the Billroth-I gastrectomy. This allows residual erosions to heal, and in the absence of further enzymatic mucoproteolysis the protective mucous barrier is re-established. It would also seem logical to assume that once the stimulus that originally altered the glycoprotein fraction is removed the mucus would return to normal.

The case against vagotomy and drainage is less clear. All such series which have been considered in this discussion, however, were associated with a high rate of continuing haemorrhage and therefore mortality. We have been unable to find any comparable work on reflux following vagotomy and drainage to that on the Polya and Billroth-I gastrectomies. Biliary reflux is said to occur more frequently with a gastro-enterostomy than with a pyloroplasty, and gastritis is frequently seen endoscopically after both operations. Normally, antral acidification results in an increase in mucous secretion and an increase in its carbohydrate content. This is abolished by vagotomy. Emas and Grossman (1967), in studies on dogs, have shown that there is no change in maximal acid output in response to gastrin after vagotomy and drainage. The presence of gastrin-induced acid plus the inability following vagotomy to increase mucous production may explain the high rate of continuing haemorrhage from erosive gastritis with this operation. The role of biliary reflux in these cases needs further investigation.

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THE REVERSIBILITY OF POSTGASTRECTOMY ALKALINE REFLUX GASTRITIS BY A ROUX-EN-Y LOOP

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SUMMARY

Partial gastrectomies were carried out in 6 dogs. All developed stomal gastritis. Prevention of reflux by a Roux-en-Y loop allowed the mucosa to return to histological normality. These findings support the use of this procedure for the condition of postgastrectomy reflux gastritis in human subjects, and explain the need for a vagotomy at the same operation.

CHRONIC gastritis has been shown to be present in the majority of stomachs after partial gastrectomy (Palmer, 1954). Subsequently, du Plessis (1962) described a clinical syndrome which he attributed to gastritis caused by unregulated reflux of bile and pancreatic juice into the stomach through the new stoma. The same author reported good results in human subjects with postgastrectomy alkaline gastritis when bile and pancreatic juice were excluded from the stomach by a Roux-en-Y loop. Van Heerden, Priestley, Farrour, and Phillips (1969) also recorded good results in human subjects after the same procedure.

Although the clinical evidence suggests that gastritis is reversible when reflux is prevented, there appears to be no recorded experimental work that has examined this hypothesis. For this reason the present investigation was undertaken.

MATERIALS AND METHODS

A Polya partial gastrectomy was carried out in 6 unselected mongrel dogs. As far as could be judged, the whole antrum was removed and a control biopsy was taken from the cut end of the stomach.

At a variable time after the partial gastrectomy a second operation was performed on the same animal. A 5-cm. incision was made through the anterior wall of the stomach and a biopsy was taken from both the anterior and posterior walls of the gastrojejunal junction. The gastrectomy wound was closed and the proximal or afferent loop was disconnected from the stomach. The site of the disconnexion was closed and the proximal loop containing bile and pancreatic juice was anastomosed to the side of the jejunum at least 60 cm. from the duodenojejunal junction in order to be sure that reflux did not occur. No vagotomy was added.

Table I.—THE TIMING OF THE PROCEDURES

DOG NO.	DURATION OF PARTIAL GASTRECTOMY	DURATION OF ROUX-EN-Y LOOP
1	6 months	6 months
2	6 months	1 year
3	6 months	2 years
4	1 year	2 years
5	2 years	6 months
6	2 years	6 months

When the dog was subsequently killed, the gastric remnant was opened along the greater curvature and rolls of mucosa were prepared for histology as described by Stein (1937). It was then possible to observe in the same animal the normal stomach, the stomach after gastrectomy, and the postgastrectomy stomach after a Roux-en-Y loop.

Table I summarizes the timing of these procedures.

RESULTS

The results were remarkably constant in the 6 animals.

In all cases the control biopsy from the cut end of the gastric remnant showed fundic tissue, indicating that the whole antrum had been removed. The

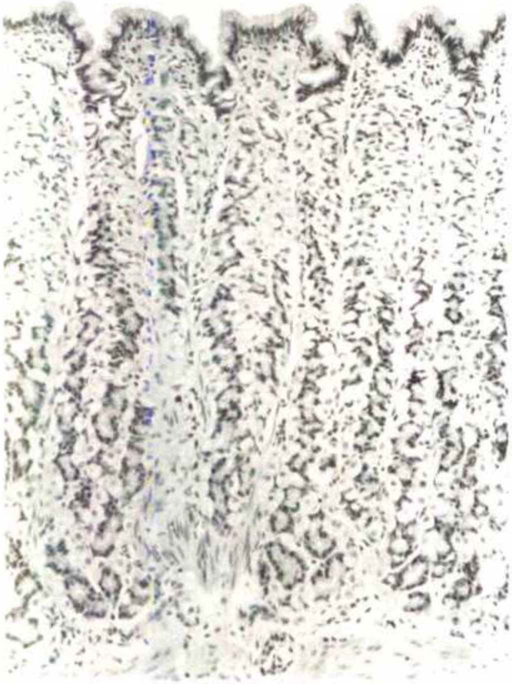

FIG. 1.—Normal fundic mucosa. Note the shallow foveolae and the wide layer of chief and parietal cells. (× 150.)

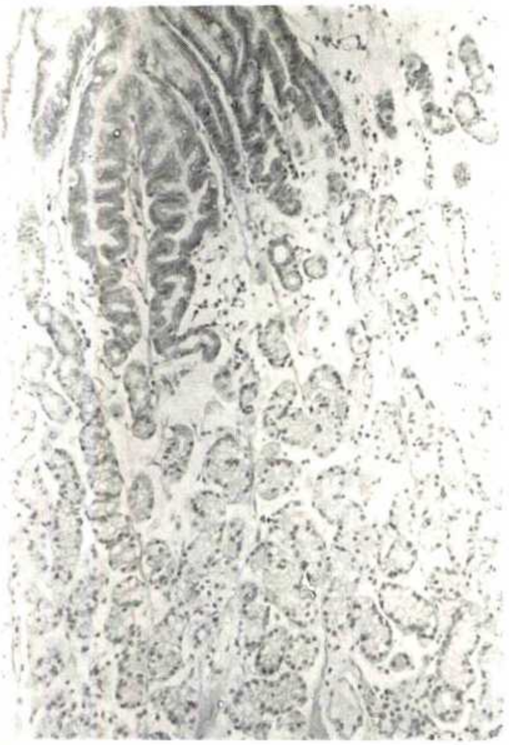

FIG. 2.—The 'corkscrew' appearance of chronic gastritis with deep foveolae and loss of chief and parietal cells. (× 150.)

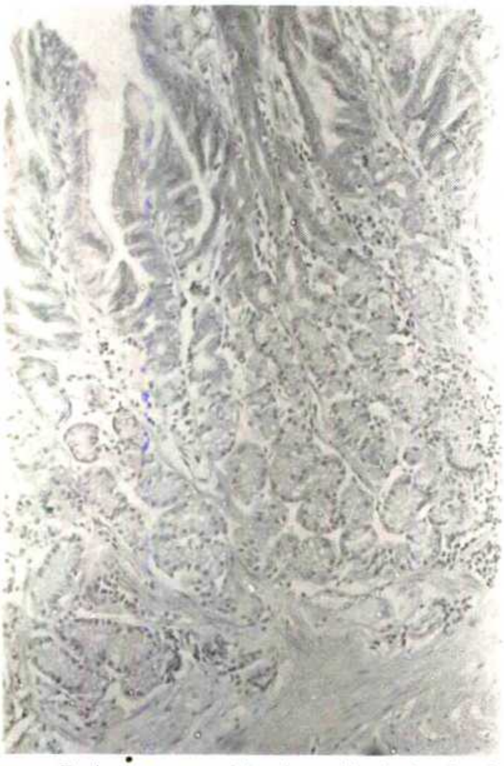

FIG. 3.—Further appearance of chronic gastritis. An intrafoveolar papilla can be seen. (× 150.)

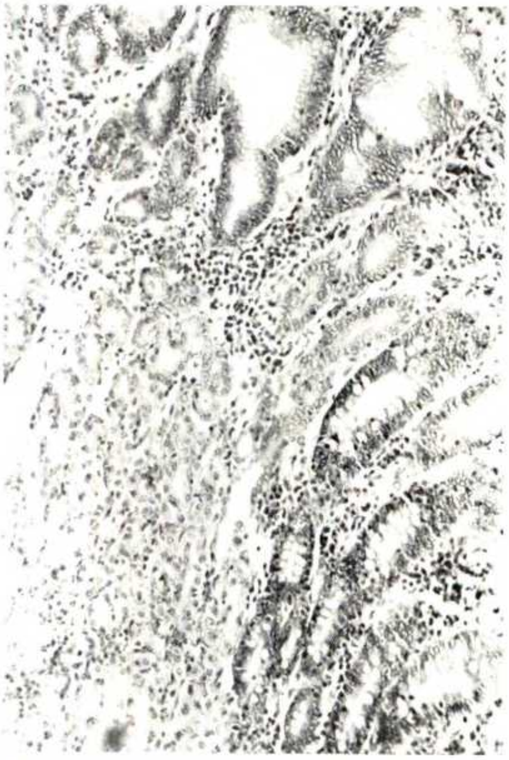

FIG. 4.—The stomal mucosa after a Roux-en-Y loop. The normal jejunum can be identified by the goblet cells. The adjacent normal fundus has chief and parietal cells. (× 150.)

appearance of the normal fundus is shown in *Fig.* 1, nd has been well described elsewhere (Palmer, 954). The points of special significance are the foveolar depth, which is only one-sixth of the total width of the mucosa, the orderly layers of parietal cells near the lumen with chief cells on the lamina muscularis mucosa, and the normal mitotic activity.

In all cases the mucosa after gastrectomy showed severe gastritis. No obvious difference was seen either in the type of gastritis or in the extent of gastritis relative to the duration of the gastrectomy. n all cases the gastritis extended throughout the length of the biopsy specimen, although there were healthy areas between the areas of gastritis.

The changes seen are illustrated in *Figs.* 2 and 3. In *Fig.* 2 there is the typical 'corkscrew' appearance of the foveolae owing to elongation downwards towards the lamina muscularis mucosa. The foveolar depth is therefore considerably increased with a corresponding decrease in the numbers of chief and parietal cells. *Fig.* 3 illustrates another characteristic feature of gastritis, where a papilla of surface epithelium may be seen in the depth of a foveola. There was a marked increase in the mitotic activity, as has been previously described in this type of gastritis Lawson, 1964).

When the animals were sacrificed after reflux had been prevented by a Roux-en-Y loop, the mucosa at the gastrojejunal junction had returned to histological normality in all 6 dogs. This is shown in *Fig.* 4, where jejunal mucosa can be identified by the large number of goblet cells in the surface epithelium, and adjacent fundic mucosa can be recognized by the parietal cells. In the fundus the depth of the foveolae was normal, and the corkscrew appearance had disappeared. The mitotic activity was normal.

DISCUSSION

In the present investigation gastric mucosa which was shown to be normal histologically became grossly abnormal after a Polya gastrectomy. When reflux was prevented by a Roux-en-Y loop the mucosa returned to histological normality. The deduction from this observation is that refluxing alkaline juice is a factor in the production of gastritis, and this is supported by other experimental evidence which has shown that bile and pancreatic juice cause chronic gastritis in the dog (Lawson, 1964; Menguy and Max, 1970).

Gastritis has been shown to be present in 50 per cent of postgastrectomy patients (Palmer, 1954) and in many normal human subjects (Hebbel, 1949). Both these observations could be explained by unregulated reflux of duodenal contents.

The mechanism by which bile acts is probably through interference with the permeability of surface mucin so that H^+ ions leave the stomach and diffuse into the mucosa, which is then damaged (Davenport, 1968; Geal, Phillips, and Summerskill, 1970).

In the series of dogs reported here it was not possible to relate the duration of the gastrectomy to the extent of the gastritis, as biopsies were limited to the area of the stoma. The full extent of the gastritis could only be assessed by the examination of the whole stomach. However, the type of gastritis appeared to be the same regardless of the duration of the gastrectomy. It seems that protection from reflux for 6 months is sufficient to reverse gastritis, which may have been present for up to 2 years. It is possible that a shorter period of protection from reflux may also be effective. Within the limitation of this experiment it may also be said that even if gastritis is present for 2 years it is worth while preventing reflux as a return to histological normality does occur.

Lambley (1962) described anastomotic ulceration following the Roux-en-Y loop procedure. Because of the reappearance of chief and parietal cells after this operation it is likely that acid secretion will increase. Therefore a vagotomy would be an essential part of the procedure in human subjects (du Plessis, 1962).

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THE LESION OF THE SECOND CANCER OF THE LARGE BOWEL

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SUMMARY

A survey is presented of the clinical experience at St. Mark's Hospital with 83 patients suffering from metachronous cancer of the large intestine. It was found that there was a much improved chance of cure in those who were attending the follow-up clinic at the time of the occurrence of their second growth. The reasons for this and the implications in cancer prophylaxis are discussed.

It is now well known that primary cancers of the large intestine may be multiple (Ginzburg and Dreiling, 1955; Moertel, Bargen, and Docherty, 1958; Bussey, Wallace, and Morson, 1967). If two or more are present at the same time they are described as 'synchronous'. If the second cancer develops later, usually after the first has been cured by surgery, then the term 'metachronous' is generally applied to it. The records of St. Mark's Hospital contain details of 4884 survivors from operations for cancer of the colon or rectum between the years 1928 and 1970. Of these, 83 patients (1·6 per cent) had had operations for second or metachronous cancers. This paper is a clinical study of the presentation, pathology, and management of these second or subsequent growths.

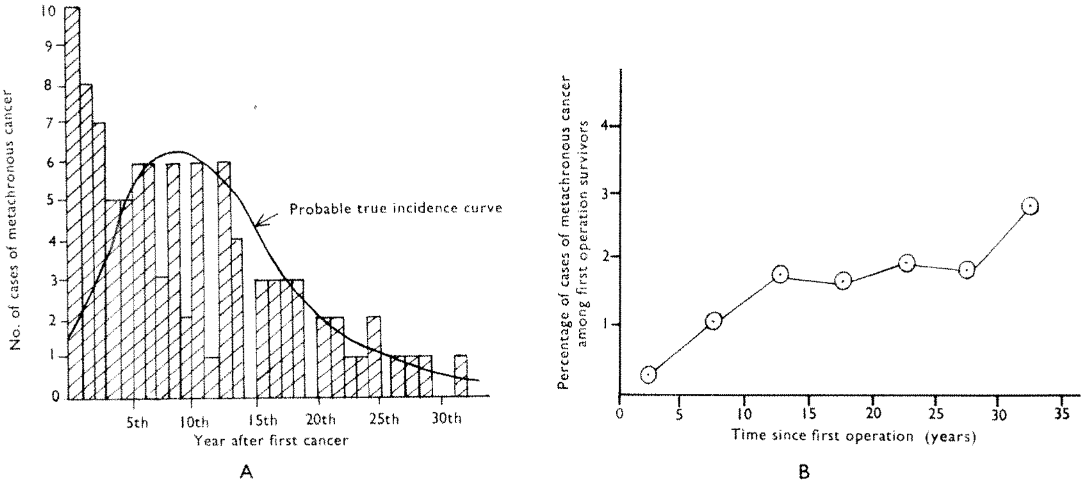

FIG. 1.—A, Incidence of metachronous cancers. B, Incidence of metachronous cancers as a percentage of patients who were alive and at risk.

Since their occurrence is a rare event many clinicians expect unusual cancers. Often they are viewed with inordinate gloom and are regarded as the harbingers of doom. Conversely, some authorities (Gruber, Schein, and Gliedman, 1970) have claimed that they are more benign than other cancers and that cure rates are unexpectedly high. We have therefore listed the features of these second growths to see if they differ in any way from other large-bowel cancers. We have then tried to assess how th diagnosis was made, whether it could or should hav been made earlier, and whether routine visits by th patient to the follow-up clinic had been of value Finally, we have tried to draw some conclusion which may be of value in the future management o patients with large-bowel cancers.

PATIENTS STUDIED

The patients who were studied were divided int two groups:—

Group A included 56 cases in whom both operations were performed at St. Mark's Hospital.

Group B comprised 27 cases in whom the firs growth had been operated on elsewhere.

Care has been taken to exclude patients in who cancer supervened on familial adenomatosis or o ulcerative colitis. In addition, local recurrences an implantations were excluded in the manner describe by Bussey and others (1967).

RESULTS

Timing of the Second Growth.—*Fig.* 1 A show the actual number of cases of second cancer each yea after the first operation. It seemed very likely tha the apparent high incidence of second growths in th first 2 years was artificial, and that many of thes must have been synchronous growths which ha been missed at the first operation. We looked carefully into the notes of these patients and found tha this was indeed the case. The reasons for missin these synchronous cancers are considered in detai later. However, it is probable that the true incidenc of metachronous cancer follows the corrected line o the histogram. Using this correction the averag nterval between first and second operations was just ver 11 years.

Fig. 1 B shows the incidence of subsequent cancers s a percentage of the patients at risk. The low ncidence in the first 5 years probably reflects the election of patients with a 'clean colon' by the first peration and by the exclusion of the 'missed ynchronous' cancers. The subsequent tendency for he incidence to rise may simply be the result of the creasing age of the survivors.

able I.—Association of Benign Tumours in Group A

Total No. of patients	56
No. with adenomas	29
No. with villous papilloma	6
Total No. with benign tumours (1 patient had both types)	34 (60 per cent)

Table II.—Site of Metachronous Cancers

Site	*No.*
Caecum and right colon	23
Transverse colon	9
Descending colon	7
Sigmoid colon	27
Rectum	24

Table III.—Pathological Features of Second or Subsequent Growths

Pathological Features	*Occurrence* (per cent)
Histological grade	
Low	29
Average	53
High	18
Dukes staging or degree of spread	
'A'	24
'B'	36
'C'	20
Inoperable	20

Association with Benign Tumours.—A full tatistical review of this important subject is in reparation. It is complicated by variations throughut the world in the definition of the words 'polyp' nd 'adenoma'. Applying the St. Mark's criteria it as previously been emphasized that the incidence of econd cancers is doubled in those patients whose irst operation specimen also contained adenomas. n group A (both operations at St. Mark's), where he chance of their discovery was greatest, benign umours were extremely common (*Table I*). They vere discovered at some stage (i.e., on one or other peration specimen or during follow-up) in almost wo-thirds of the patients, which is over double the ncidence in patients with one cancer and over ten imes that in the population as a whole. In 7 cases ocal carcinoma was actually shown to be present in a enign lesion.

Site.—The site of second or subsequent cancers is hown in *Table II*. This is a fairly normal pattern of istribution if one takes into consideration the fact hat the majority of first cancers had been in the ectum or sigmoid area. There is a slight preonderance of right-sided lesions but the figures are oo small to be significant.

Pathological Features.—Bussey and others 1967) showed that the stage and grade of the first rowth tended to be unusually favourable. This is robably because there are more long-term survivors rom operations for less malignant and less advanced growths. It does not imply an intrinsic tendency for multiple growths to be more benign.

The stage and grade of the second or subsequent growths are shown in *Table III*. The distribution of low, average, and high grades of malignancy is not significantly different from that found in most large series. However, the discovery of 24 per cent of the growths at stage 'A' and 36 per cent at stage 'B' is a significant improvement upon the staging usually found.

Table IV.—Stage of the Growth in Relation to Follow-up

Stage of Growth	Patients attending Follow-up Clinic (per cent)	Patients not attending Follow-up Clinic (per cent)
'A'	27	17
'B'	42	24
'C'	22	12
Inoperable	9	47
'A' and 'B' together (a good chance of cure)	70	40
'C' and inoperable (probably incurable)	30	60

Table V.—Stage of the Growth related to the Method of making the Diagnosis

'Primary' Diagnosis	Stage of Growth			
	'A'	'B'	'C'	Inoperable
No symptoms and sigmoidoscopy	9	3	—	—
Symptoms and sigmoidoscopy	10	6	2	3
Symptoms and barium enema	2	12	3	1
Signs, i.e., mass felt	1	12	9	6
Laparotomy diagnosis	0	0	1	2

The Value of Follow-up.—The figures for the stage and grade of the growths show that metachronous growths have the usual distribution of malignant potential but are found at a more favourable stage. The inference is that the second growths are being diagnosed earlier. We wondered if this improvement reflected the efforts of the follow-up clinic. We therefore divided group A into two subgroups: (1) those who were attending the follow-up clinic at the time when the second growth developed, and (2) those who had defaulted or had been discharged. The results are shown in *Table IV*. The control group is small (17 patients), but the 41 growths in the 'follow-up' group have been diagnosed at an appreciably earlier stage than is found in most series. Conversely, no less than 8 of the 17 patients who were not attending the clinic had inoperable growths, which is five times the incidence in those patients who attended a follow-up clinic.

The Method of making an Earlier Diagnosis.—*Table V* shows the way in which the diagnosis was arrived at. A small group of patients had no symptoms and the growth was detected entirely by follow-up sigmoidoscopy. The great majority, however, whether attending the clinic or not, did have symptoms which led on to investigation. These were essentially the same symptoms as those produced by any large-bowel cancer. Pain and bleeding each occurred in about half of the patients, but bowel upsets and more general symptoms were also common. In some of the patients a mass was detectable in the abdomen or on rectal examination, i.e., the diagnosis was made on physical signs. Finally, a small number defied all investigations and the diagnosis was made only by laparotomy. Clearly, in many patients the various examinations were complementary, but it was generally clear that the decision to operate depended on one critical discovery and only this is listed in *Table V* (e.g., if a mass was found and investigations confirmed its nature it is only listed in the 'mass' column). *Table VI* shows a marked deterioration in the staging when a growth produces symptoms, and a further deterioration when it has become palpable. These findings argue strongly for early sigmoidoscopy and barium enema in the diagnosis of large-bowel cancer.

Table VI.—STAGE OF THE GROWTH RELATED TO THE CLINICAL PRESENTATION

CLINICAL PRESENTATION	STAGE OF GROWTH		
	'A' (per cent)	'B' (per cent)	'C' AND INOPERABLE (per cent)
No symptoms or signs	75	25	0
Symptoms but no signs	30	45	25
Signs	4	40	56

Particular Pitfalls.—As the clinical history of the patients was studied it became apparent that growths in certain sites were especially liable to cause difficulty.

The Distal Limb after Perineal Excision.—There were 7 patients in this group. They all presented with discharge or with pain in the perineum. Diagnosis was often delayed because the distal limb was forgotten or because technical difficulties prevented the passage of the sigmoidoscope.

The Stump after Hartmann's Operation.—Two patients had growths in this site and both growths were missed for long periods, despite discharge from the stump through the anus.

Cancer of the Caecum.—This notoriously elusive diagnosis was a constantly recurring problem, with frequent failure of the barium enema to reveal the lesion. More recently the double-contrast enema has improved the radiological results, though failures do still occur.

Missed Synchronous Cancer.—On 23 occasions (in 21 patients) a second or third operation was performed within 2 years of the first. Consideration of the clinical details leads us to believe that 18 of the growths were present at the first operation but were not detected at that time. These patients have been discussed previously because they were removed from the figures to produce the 'corrected incidence' curve in *Fig.* 1. We thought it would be instructive to investigate the reasons for these synchronous lesions being missed. *Table VII* shows that in 12 of the 18 patients the relevant investigation had not been performed. In some this was because pain prevented instrumentation, but in most it was because attention was focused on the first lesion and further diagnostic activities were forgotten.

We believe that it is wrong to operate on any part of the large bowel for cancer without a full investigation of the remainder of the bowel. In particular the following individual cases underline some specia dangers.

1. *Resection of the colon without prior sigmoidoscopy* In 1 patient a total colectomy and ileorectal anastomosis for a second cancer plus polyps were performed above a third (rectal) cancer. Sigmoidoscopy had been deferred because of local pain. In another patient a transverse colectomy elsewhere was completed without detecting a second (rectosigmoid) carcinoma. No sigmoidoscopy had been performed, although the lesion was later seen and biopsied through the sigmoidoscope.

Table VII.—REASONS FOR MISSING SYNCHRONOUS CANCER IN 18 PATIENTS

Reason	*No. of Patients*
Sigmoidoscopy relevant but omitted	5
Sigmoidoscopy performed but lesion missed	1
Barium enema relevant but omitted	7
Barium enema performed but lesion missed	3
No details available	2

2. *Excision of the rectum without both a barium enema and a thorough palpation of the colon*: In 1 patient a carcinoma of the splenic flexure was missed when a sigmoid lesion was resected. In another patient a caecal cancer, the patient's third, was missed at operation for a growth in the sigmoid. The patient died of obstruction from the missed lesion 3 weeks later.

In yet another patient a recurrent growth was seen on sigmoidoscopy, but a different growth (the second primary) was removed and the recurrence was left in the upper rectum.

In none of these cases had a barium enema been performed.

3. *Failure to consider the possibility of metachronous colon cancer at laparotomy for some other pathology* In 1 female patient a carcinoma of the ovary was removed, but a second colonic cancer (at the splenic flexture) was missed.

DISCUSSION

A second cancer of the large bowel is unlikely to occur many times in the experience of any one surgeon. For this reason, with his attention focused on one lesion, he is in particular danger of missing the second growth. Our experiences with the 'missed synchronous' group emphasize the importance of a fixed routine which leaves nothing to chance. No resection of colon should ever be undertaken without an adequate preoperative sigmoidoscopy, as it is all too easy to miss a small polypoid lesion in the rectum or rectosigmoid which may be impalpable from the abdomen. Further, no resection or excision of the rectum should be done without a good double-contrast enema to demonstrate the rest of the large bowel. Even if the surgeon palpates the colon carefully at laparotomy it is all too easy to miss the presence of a small polyp or carcinoma, particularly in a fat patient; the surgeon who claims he can feel any polyp in the colon at laparotomy is deceiving himself. With good preparation and modern techniques a double-contrast enema is nearly always possible, even if the rectal growth is somewhat obstructive.

Another important feature of this series is that it contains a group of patients who were attending a follow-up clinic at the time when their second cancer developed. The histological grading of the metachronous growths is certainly no worse than other large-bowel cancers, and we have shown that the diagnosis was made at a much earlier stage in those who were attending the clinic. This is due in part to the discovery of some symptomless growths by sigmoidoscopy or barium enema—a group in which at least 90 per cent of the patients can expect to be cured by surgery. Another factor, however, which is difficult to quantify but in our view important is the early questioning of the patient about symptoms which might otherwise have been overlooked. It is one of the main aims of this paper to draw attention to the possibility of a second cancer developing, and to emphasize the value of investigating suspicious symptoms at an early stage.

We believe that all patients who have had a colonic or rectal cancer removed, particularly if there have been associated adenomas, should be followed up for life. It is difficult, however, to decide how frequently the various investigations should be performed. Regular sigmoidoscopy is mandatory, and perhaps the fibre-optic colonoscope will make a real impact in the future. It is our personal view, however, that a good radiology department can produce more comprehensive pictures of the colonic mucosa with greater certainty than the colonoscope. We believe that the purchase of good machinery for preparing the colon, if combined with enthusiastic radiological co-operation, is a better investment than the expensive colonoscope. If time is available, a double-contrast enema every 2 years combined with sigmoidoscopy every 6 months will yield a modest harvest of polyps and an occasional but consolingly curable cancer. This is perhaps an ideal which will not be widely realized, but at least both doctor and patient must be aware that any new bowel symptoms still demand investigation and cannot be shrugged off because of the previous operation.

Finally, our experience with this series suggests that our attitude to the diagnosis of cancer of the colon and rectum should change. Morson (1971) has produced evidence that the evolution of cancer of the colon and rectum is relatively slow. The fact that follow-up has proved of such value accords with this idea, and implies that growths of the large intestine are amongst the most suitable for prevention by regular clinical investigation, perhaps as a part of 'executive checks'.

Furthermore, the series has demonstrated the value of making the diagnosis before the growth has become palpable, and preferably before it has become symptomatic. It is apparent, therefore, that the knowing hand upon the abdomen and the passage of the informed rectal digit are no longer enough. Rather, the colon at risk must be patrolled with the sigmoidoscope and the double-contrast enema, and our efforts should be directed towards improving still further the quality of colon radiology.

Acknowledgements.—We are indebted to the surgeons of St. Mark's Hospital whose patients have been studied, and to Dr. B. C. Morson and Dr. H. J. R. Bussey for their assistance. The expenses of this investigation were met out of a grant from the Cancer Campaign.

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HIRSCHSPRUNG'S DISEASE

A CLINICAL REVIEW

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SUMMARY

1. Experience with 38 cases of Hirschsprung's lisease seen over a 20-year period is described.

2. Only 24 per cent of cases presented with a combination of symptoms and signs such as to suggest the correct diagnosis on clinical grounds.

3. Barium-enema examination carries a high true-positive' rate, but cases reported as negative must be viewed critically. A radiological diagnosis of diopathic megacolon should not be accepted without supplementary rectal biopsy and/or anorectal pressure studies.

4. Survival without surgery is compatible with Hirschsprung's disease, but the dangers of enterocolitis nust be acknowledged.

5. Rectosigmoidectomy, which includes resection to an area of normal innervation proximally and excision of part of the internal sphincter of the rectum distally, produces a satisfactory late functional result at an acceptable mortality-rate.

6. A colostomy prior to rectosigmoidectomy is advisable when there is a history of repeated attacks of subacute obstruction and one or more episodes of enterocolitis. A colostomy after rectosigmoidectomy is advisable in those cases which are submitted to laparotomy for intestinal obstruction in the period following operation, even when no mechanical cause for obstruction is demonstrable.

7. Patients with problems relating to coprostasis following treatment of congenital anorectal disorders

should be submitted to rectal biopsy, since a proportion of these patients reveal a deficiency of innervation of the distal large bowel which approximates to that seen in Hirschsprung's disease.

ALTHOUGH paediatric surgical practice has come to be concentrated in special centres, and this evolution in the pattern of treatment will continue, there will remain regions in which this branch of surgery is undertaken by general surgeons with a special interest in paediatric surgical problems. In this context we have thought it useful to assess our experience with Hirschsprung's disease over the past 20 years to enable comparison with experience in other centres and, since different types of operation have been proposed in recent years, to evaluate the need for changing our operative technique.

FIG. 1.—Harald Hirschsprung (1830–1916), Professor of Paediatrics, Copenhagen.

Harald Hirschsprung (*Fig.* 1), Professor of Paediatrics, Copenhagen, first published a description of the disease which bears his name in 1888. He reported 2 children aged 11 months and 7 months respectively, giving a full clinical history of each patient to the time of death and describing in detail the post-mortem macroscopic appearance of the dilated colon. However, Tittel (1901) was the first person to draw attention to the absence of ganglion cells in the narrow distal segment of the bowel.

In Hirschsprung's disease the infant or child commonly presents with symptoms and signs of large-bowel obstruction. This obstruction is fu
tional and is associated with an absence of gangli
cells between the muscle coats and between the in
muscle layer and the mucosa. Large irregular ner
fibres are seen in the same area. There is a transitio
zone showing a tendency to a more normal pattern
innervation before normally innervated bowel
reached. The process may be confined to the m
distal part of the rectum where it necessarily invol
the internal sphincter mechanism. However, t
aganglionosis may spread far proximally and invol
small bowel. No good evidence of 'skip' lesi
exists.

A simple explanation of the disease may be t
since the parasympathetic component of bo
innervation is lacking, a functional state of sympathe
overactivity, or muscle spasm, exists and hence th
is a functional obstruction. In the past both sym
thetic blockade and lumbar sympathectomy have be
used and abandoned because of poor results.

Gannon, Noblet, and Burnstock (1969) investigat
by a fluorescent technique the adrenergic innervati
of normal and aganglionic regions of bowel fr
patients with Hirschsprung's disease. In nor
bowel the adrenergic nerves end around intramu
ganglion cells. In aganglionic bowel the adrener
nerves form dense varicose plexuses in both muscula
externa and muscularis mucosae. Gannon and oth
(1969) suggested that the cause of megacolon
Hirschsprung's disease is a lack of nervous pathwa
controlling the *intrinsic* reflexes which is proba
congenital in origin. In a normal person, filling t
rectal ampulla beyond a critical pressure results
internal sphincter relaxation. The response in
patient with Hirschsprung's disease is a further rise
internal sphincter contraction (Howard, 1969). T
response to some extent explains the functional cau
of coprostasis in these patients, and it can be used al
as the basis of a test which aids the different
diagnosis of megacolon.

For the present some form of surgical treatme
remains necessary for the infant or child with acute
recurrent intestinal obstruction caused by Hirsc
sprung's disease. Sir Frederick Treves published
report in 1898 of a rectosigmoidectomy performed
a 6-year-old girl with Hirschsprung's disease.
laid emphasis on the narrow distal segment and i
probable origin as a congenital defect. The patie
was treated by rectosigmoidectomy and was left with
colo-anal anastomosis. She was reported on 59 yea
later by Daintree Johnson, Davis, and Evans (195
At that time she led an active life with two bow
actions daily and satisfactory voluntary contr
Surgical treatment was established on a firm bas
with the publication of the work of Swenson and B
(1948), who described a technique of rectosi
moidectomy which was evolved initially on a laborato
and subsequently on a clinical basis. Swenson h
continued to make contributions to the technique
this operation, particularly in emphasizing t
necessity for low-oblique section of the rectum
include the posterior half of the internal sphinct
mechanism (Swenson and Donnellan, 1969). In
effort to avoid the difficulties related to pelv
dissection and anastomotic problems in infants, and
retain rectal sensation, alternative techniques ha
been devised, most of them based on the retrorect

pull-through technique of Duhamel (1960) and the endorectal pull-through technique of Soave (1964).

In the United Cardiff Hospitals the procedure of choice has been rectosigmoidectomy, and the results will show that there is no compelling reason to change this. One still awaits for convincing evidence that the alternative methods produce better results. It is worth noting that Swenson and Donnellan (1969) have now followed up patients for up to 20 years and claim good results in more than 95 per cent of cases; this includes not only faecal continence and rectal sensation but also normal bladder and ejaculatory function.

Table I.—NUMBERS, SEX, AND MORTALITY OF PATIENTS WITH HIRSCHSPRUNG'S DISEASE

SURVIVAL	NO. OF PATIENTS		
	Male	Female	Total
Alive	21	7	28
Dead	9	1	10
Total	30	8	38

Table II.—SYMPTOMS AND SIGNS OF PATIENTS WITH HIRSCHSPRUNG'S DISEASE

SYMPTOM	NO. OF PATIENTS	PERCENTAGE
Distension	35	92
Constipation or diarrhoea	32	84
Vomiting	29	76
All combined	22	58
Positive rectal findings	16	42
Diagnostic combination	9	24
Total No. of patients	38	100

MATERIALS AND METHODS

A review of cases seen in the United Cardiff Hospitals in the 20 years from 1950 to 1969 is presented. Some cases have been discarded because of the absence of post-mortem histological proof of Hirschsprung's disease, though one cannot always be sure that post-mortem material has included the anorectal region. On the other hand, if a case has behaved in every way, clinically and radiologically, as Hirschsprung's disease it has been included although a post-mortem examination has not been obtained. Thirty-eight cases of Hirschsprung's disease have been traced and their sex and mortality are indicated in *Table I*.

Symptoms and Signs (*Table II*).—With regard to clinical diagnosis the most common *single* feature was abdominal distension (35 out of 38 cases), but just over half of the patients had a background of vomiting combined either with abdominal distension or with an abnormal bowel habit, the latter varying from absolute constipation to intermittent constipation or occasional watery stools. Less than half had noteworthy rectal findings, varying from a definite stricture to a so-called 'tight' sphincter, and in some instances the sudden expulsion of meconium or faeces on withdrawal of the finger. Only one-quarter of the 38 patients had a combination of symptoms and signs which strongly suggested a diagnosis of Hirschsprung's disease on clinical grounds.

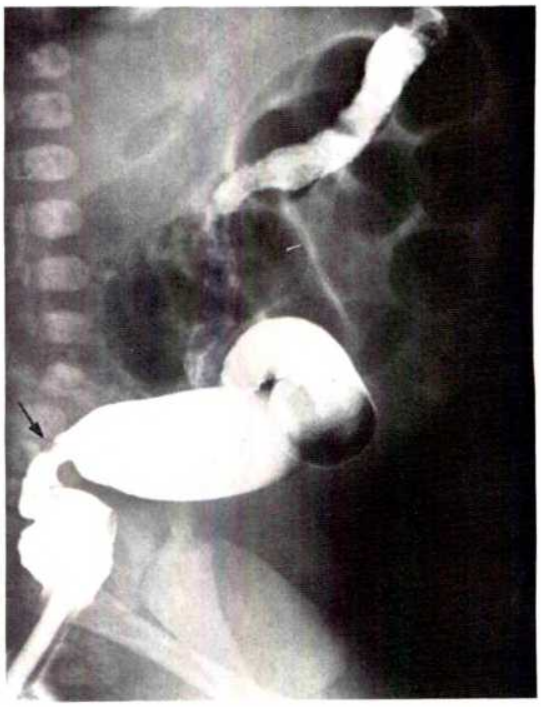

FIG. 2.—Barium enema (lateral view) of a neonate showing dilatation of the sigmoid colon proximal to the narrow segment, which is clearly seen at the rectosigmoid junction.

Radiology (*Fig. 2*).—Plain films of the abdomen are not helpful in the specific diagnosis of Hirschsprung's disease, but a barium enema is essential, and a 24–48-hour post-evacuation film is considered to be particularly useful in demonstrating the characteristic retention. Twenty-eight patients with subsequent histological proof of Hirschsprung's disease had barium-enema examinations. The results were categorized in the usual way and the findings summarized. In 22 patients (77 per cent) the diagnosis of Hirschsprung's disease was offered and this was proved to be correct. However, the passage of time or previous surgery involving the bowel may be associated with an erroneous radiological interpretation. Thus, 1 patient with a 'true positive' had had a rectosigmoidectomy performed elsewhere, and when admitted 3 years later for revision rectosigmoidectomy owing to a residual aganglionic segment, the barium enema was reported as showing idiopathic megacolon. A second patient, radiologically a 'true positive' at $3\frac{1}{2}$ years of age, which was proved by rectal biopsy, had a repeat barium enema 6 years later and this was reported as showing idiopathic megacolon.

The 6 'false negatives' were all proved subsequently to be Hirschsprung's disease. Two patients, both 3 years of age, were diagnosed as having idiopathic megacolon. One died 9 years later with enterocolitis, and the other died after rectosigmoidectomy, either from enterocolitis or from the effects of pelvic sepsis. One 6-year-old infant and one 11-day-old infant had long-segment Hirschsprung's disease, in 1 case extending high up the descending colon, and in the other extending up into the ileum. The barium

P, 25, 351

enemas of both these patients were reported as normal. One 2-day-old infant and one 5-day-infant had repeated enemas for up to 2 years before a diagnostic picture could be demonstrated.

From our experience with radiology in the diagnosis of Hirschsprung's disease the following conclusions can be drawn:—

1. A negative barium enema in a neonate cannot be taken to exclude Hirschsprung's disease and repeated examinations are justified.
2. A negative barium enema will not exclude a long-segment Hirschsprung's disease.
3. In 4 out of 28 patients (14 per cent) a radiological diagnosis of idiopathic megacolon has been offered at some time. Such a diagnosis cannot be accepted without a rectal biopsy.

Table III.—Treatment of 38 Patients with Hirschsprung's Disease

Treatment	*No. of Patients*
Conservative	6
Colostomy	6
Definitive surgery	26
Total	38

Table IV.—Details of Colostomy in 20 Patients

Procedure	No. performed	No. died	Average Age	Percentage Mortality
Emergency (neonates)	12	4	8 days	33
Emergency (infants)	7*	2	10 wk.	29
Elective	1	—	12 yr. 7 mth.	—
Total	20	6	30 days†	30

* Including 1 ileostomy for long-segment disease.

† Excluding the child of 12 years and 7 months.

Bowel Biopsy.—Nine formal rectal biopsies were performed without complications. One showed a 'false negative' because it was taken from the distal to the anorectal junction. Six bowel biopsies were performed in conjunction with laparotomy for diagnosis and colostomy. There was 1 'false negative'. No death was attributable to either of these methods of biopsy.

Outcome in 38 Patients (*Table III*).—Six of the 38 patients have been treated conservatively, either by choice or necessity, 6 were treated by a colostomy in the first place but did not survive long enough for further action, and 26 patients underwent elective surgery with or without a prior colostomy.

Conservative Treatment.—Six patients 'settled' on a conservative régime based on simple measures including rectal wash-outs and bowel stimulants. Subsequently 1 patient has been lost to follow-up. Two patients have died. The first, diagnosed as having Hirschsprung's disease at 3 weeks of age, was treated conservatively and died at 6 months as a result of advanced large-bowel obstruction and a bleeding diathesis associated with intravenous sulphadiazine. The second child was diagnosed as having idiopathic megacolon at 3 years of age and died at 12 years, having been admitted to hospital in peripheral circulatory failure, associated with enterocolitis. A post-mortem examination confirmed the diagnosis of Hirschsprung's disease.

Of the 3 survivors who were followed up, the first remains well at 8 years, following diagnosis at 7 days of age, and has recently been discharged from hospita surveillance. The second is 9 years old, and 4 years after diagnosis maintains normal bowel actions with laxatives, though suffering occasional episodes o pain and distension. The third is 10 years old, and 6 years after diagnosis, though well developed, gets occasional episodes of abdominal distension and fou diarrhoea. A recent barium enema was said to show idiopathic megacolon although a rectal biopsy 6 years ago established the diagnosis of Hirschsprung's disease. All these children must be considered at risk from enterocolitis.

Colostomy.—Six infants had a colostomy per- formed because of intestinal obstruction. In 5 this was carried out in conjunction with laparotomy to exclude an associated intestinal anomaly, although in no case was this found. The fact that these 6 infant did not survive beyond this stage of treatment must be seen in perspective since 20 colostomies have been performed as the first line of surgical treatment in thi series (*Table IV*). There is a high morbidity-rat associated with colostomy in the newly born infant relating to wound dehiscence, prolapse of colonic mucosa, stenosis of the colostomy opening, and bleeding from the bowel surface. Nineteen neonate and infants had an emergency colostomy performed the average age at the time of operation being 30 day (range, 2 days to 17 weeks). Of the 6 patients who died 2 died from complications directly referable to surgery—1 developed a small-bowel fistula and th other suffered a wound dehiscence. The remaining deaths were from a combination of associated diseas or gross congenital disorders. The overall mortality rate in relation to the total number of colostomie performed was 30 per cent.

Table V.—Details of Definitive Surgery for Hirschsprung's Disease

No. of Patients	Type of Operation	No. of Deaths	Percentage Mortality
25	Rectosigmoidectomy	1	4
25	All types	2	8

Definitive Surgery (*Table V*).—Twenty-six patients underwent definitive surgery for Hirsch sprung's disease. One patient has been excluded from further consideration because following colostomy h underwent definitive surgery elsewhere. Recto sigmoidectomy, following the Swenson technique, ha been the procedure of choice, and 26 such operation have been performed in this centre on 25 patients with 1 death, giving a mortality-rate of 4 per cent. This figure includes 2 rectosigmoidectomies performed in 1 patient. The one death in this series occurred month after rectosigmoidectomy and after normal bowel actions had commenced. Whether this death occurred from enterocolitis or from the effects o pelvic sepsis is not clear. A second child, who had been left with a colostomy following a poor result after rectosigmoidectomy performed 5 years previously died following a Soave procedure. This gives mortality-rate of 8 per cent for definitive surgery fo all types of procedures.

The youngest patient operated on was 4 months old and the oldest 13 years and 4 months. When there is an element of choice in timing definitive surgery it is our practice to undertake rectosigmoidectomy at about 7 months when the child has grown beyond the neonatal period and has established a good feeding pattern. At this time there are no behaviour problems, and infectious diseases, skin sepsis, and upper respiratory-tract infections which complicate or delay major surgery are not obtrusive (*Fig.* 3).

Morbidity.—In assessing the results of major elective surgery in infants and children a consideration of the complications is most important. As a group of patients they are not easy to handle or to assess and active intervention is sooner resorted to in the early days after operation in the hope of avoiding a situation which might become irremediable.

Taking the problems occurring in the period following operation ('early') together with those arising some time following discharge from hospital ('late'), we have found that 13 out of 25 patients had some complication. Of these 13 patients, 2 who suffered 'early' complications also suffered 'late' complications. The overall morbidity-rate was 52 per cent (*Table VI*).

Table VI.—THE MORBIDITY IN 25 PATIENTS

COMPLICATION	TIME OF OCCURRENCE	
	Early	Late
Intestinal obstruction	4	6*
Stenosis	3	—
Enterocolitis	2	—

* Includes 2 patients who also had early complications.

Table VII.—LATE RESULTS OF RECTOSIGMOIDECTOMY IN 25 PATIENTS

CATEGORY	NO. OF PATIENTS	PERCENTAGE
Good	12	48
Intermediate	5	20
Poor	3	12
Died	1	4
Lost	4	16
Total	25	100

1. *Early.*—Four patients required laparotomy for postoperative intestinal obstruction, including 1 patient who suffered a volvulus which was corrected surgically. Two of these patients showed no obvious cause for obstruction at laparotomy but both required subsequent hospitalization for subacute intestinal obstruction, 1 on three occasions. In all instances the problem resolved with conservative treatment. A third patient had no obvious cause for obstruction at the time of laparotomy but subsequently developed a rectovaginal fistula.

Three patients developed 'stenosis' in the region of the anastomosis. In 2 instances this stenosis has been attributed to anastomotic stricture; 1 patient was submitted to revision surgery and the other awaits further surgery. The third patient had a stenosis which was due to a residual aganglionic or transitional segment and this was excised at a second rectosigmoidectomy.

Two patients developed evidence of enterocolitis following operation. One responded to treatment following isolation of a pathogenic *Escherichia coli* organism. The second patient had a similar organism isolated prior to operation but not subsequently. This patient died, but whether from the effects of enterocolitis or from pelvic sepsis is not clear.

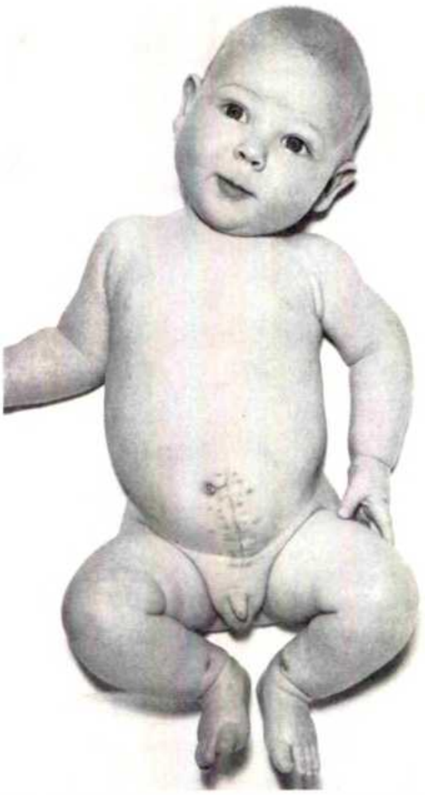

FIG. 3.—M. T., 10 days following rectosigmoidectomy at 4 months.

2. *Late.*—The late morbidity has been manifested in all instances as episodes of subacute intestinal obstruction which always responded to conservative measures. Two of these patients, who had had a laparotomy performed in the 'early' phase when no cause for obstruction was found, have required multiple admissions, and although neither has been readmitted to hospital for as long as 3 years in 1 instance the presence of a residual aganglionic segment has been proved histologically. A third patient who presents approximately every 6 months with subacute obstructive symptoms, which resolve without the need for hospitalization, has been shown to have a residual aganglionic segment.

Late Results of Rectosigmoidectomy (*Table VII*).—Follow-up data are available for 21 out of 25 patients (83 per cent). Assessment has been made between 1 and 15 years following operation, with a mean follow-up time of 6·3 years. The follow-up has been carried out by means of personal interviews, examinations of recent hospital patient notes, and postal inquiry via the patients' general practitioners and parents. Three categories of result have been defined:—

1. *Good*: No further treatment required.
2. *Intermediate*: Episodic abdominal pain and distension with constipation and/or diarrhoea. The patient may have required single or multiple hospital admissions for observation or conservative treatment. The patient may in time move into either of the other two categories, 1 or 3.
3. *Poor*: The patient will require further major surgery.

Good (12 patients).—All patients have normal bowel actions with no obstructive episodes or incontinence. They lead normal healthy lives.

Intermediate (5 patients).—Two patients, who have had multiple hospital readmissions for subacute obstructive episodes, have required no further treatment for the past 3 years. Two other patients require out-patient surveillance for intermittent abdominal distension associated with constipation. One patient is fit and well but suffers bowel incontinence once daily.

Poor (3 patients).—Two patients developed anastomotic stenosis requiring revision surgery. One awaits surgery, and the other had a Soave procedure 5 years after rectosigmoidectomy. The third patient had a functional stricture treated by a second rectosigmoidectomy.

Died (1 patient).—Death in this patient, which occurred about 4 weeks following rectosigmoidectomy, was from the effects either of enterocolitis or of pelvic sepsis. A post-mortem examination was not obtained.

Lost (4 patients).—One patient was fit with normal bowel function at the time of discharge from hospital. A second patient was seen 6 months following discharge from hospital and was free of complaints at that time. There was no information on the 2 other patients whom it was not possible to trace.

Revision Surgery.—Following definitive surgery a second operation is made necessary by any operative technique which allows development of a mechanical stricture at the site of anastomosis. Revision surgery may also be necessary when a functional stricture becomes evident. This may be due to abnormal bowel being left in the colon immediately proximal to the anastomosis, a situation avoided by the use of frozen-section control. The abnormal bowel may show the typical features of aganglionosis with abnormal large nerve-trunks, or there may be a number of immature ganglion cells without abnormal nerve-trunks, representing an approximation to the normal pattern of innervation and often referred to as the 'transitional zone'. A similar functional problem will occur if distal resection of the large bowel is made cephalad to the anorectal junction rather than in that region. The histological features of the bowel distal to the line of anastomosis will be those typical of Hirschsprung's disease, i.e., complete aganglionosis with abnormal nerve-trunks.

Three patients in this series have required revision surgery. One patient had a rectosigmoidectomy performed elsewhere and 3 years later (aged 4 years) required a second rectosigmoidectomy when the presence of residual aganglionic bowel was proved histologically. Six months following discharge from the hospital she was free from complaints. The second patient developed a stricture following rectosigmoidectomy. This responded to dilatation, although function was not satisfactory. The patient made a good recovery following a second rectosigmoidectomy 6 months later, and the histological features suggested the problem was related to a residual transitional zone. This patient was well with normal bowel function 6 weeks after operation, but was lost to subsequent follow-up. The third patient, aged 18 months, developed anastomotic stenosis following rectosigmoidectomy and remained with a colostomy until revision surgery 5 years later. This patient died from pelvic sepsis following a Soave procedure (*Table V*).

Colostomy in Relation to Rectosigmoidectomy (*Table VIII*).—Thirteen patients had a colostomy in place at the time of rectosigmoidectomy.

Table VIII.—COLOSTOMY IN RELATION TO RECTOSIGMOIDECTOMY

PROCEDURE	NO. OF PATIENTS	COMPLICATIONS	NO. OF DEATHS
Prior colostomy	13*	4†	0
No colostomy	12	3	1
Total	25	7	1

* Includes 1 ileostomy for long-segment disease.

† One patient had his colostomy resected during rectosigmoidectomy.

Excluding 1 patient who was over 12 years old at the time of definitive surgery and exceptional in this respect, the mean age for this group at the time of rectosigmoidectomy was 10·5 months (range, 5 to 18 months). Following rectosigmoidectomy, which included resection of the colostomy, 1 patient required laparotomy for 'obstruction'; no cause for this was found and a colostomy was not re-established. The child recovered but developed episodes of abdominal distension with diarrhoea which eventually settled down. A second patient required revision surgery for a stricture which was probably functional in so far as the bowel resected at the second operation showed the features of incomplete innervation, i.e., a transitional zone. Another patient awaits revision surgery for a stricture of surgical origin. A fourth patient had a rectosigmoidectomy performed at 18 months after a neonatal period complicated by gross pelvis sepsis and multiple fistula formation *prior* to establishment of a colostomy. Recovery from the rectosigmoidectomy was smooth although associated with stenosis which required revision surgery at 5 years.

Twelve patients did not have a colostomy established prior to rectosigmoidectomy, which was performed at a mean age of 18 months (range, 4 months to 4·5 years). Two subsequently required laparotomy for intestinal 'obstruction', though no definite cause for this was established at operation. One had a colostomy performed and afterwards recovered satisfactorily. The other did not have a colostomy performed and subsequently developed a rectovaginal fistula. A third patient died from either enterocolitis or pelvic sepsis before a colostomy could be established.

Leaving aside the infant for whom colostomy is essential for the relief of acute large-bowel obstruction, it would seem reasonable to state that a colostomy should be performed before rectosigmoidectomy where repeated episodes of subacute large-bowel obstruction or any single episode of enterocolitis are a feature of the history. This is best performed as a proximal transverse colostomy so that it does not have to be dismantled, as does a left iliac colostomy, during the course of rectosigmoidectomy. This might not be applicable to the occasional case of long-segment disease. Prior to rectosigmoidectomy the anorectal canal should be dilated at regular intervals to avoid the tendency to functional narrowing of the bowel owing to the absence of faecal passage and the intrinsic nature of the deficiency in the innervation of the bowel. Such dilatations will then render anastomosis in this region somewhat easier and help to avoid a stricture of surgical origin. The colostomy can be closed with safety about 3 weeks after rectosigmoidectomy and after digital examination of the anastomosis. In the absence of a colostomy and following rectosigmoidectomy, if indications should arise for exploration of the abdomen on the supposition of obstruction, for which no obvious cause can be found at laparotomy, it is probably wise to perform a proximal colostomy, since both pelvic sepsis and enterocolitis can present in this way and much will have been gained by diverting the faecal stream.

DISCUSSION

The diagnosis of Hirschsprung's disease can be made sufficiently early in life to hold out good prospects of cure. If intestinal obstruction is not so far advanced as to warrant immediate laparotomy and colostomy a barium enema is particularly helpful in establishing a diagnosis. This is best followed at a suitable point in time by rectal biopsy, particularly if the radiology is inconclusive or suggests idiopathic megacolon in an older child. With regard to adjuvant methods of diagnosis we have no experience at this time of anorectal pressure studies (Lawson and Nixon, 1967), but we believe that these will help greatly, particularly in helping to sort out the older child with chronic constipation and in salvaging those with Hirschsprung's disease which has been diagnosed as idiopathic megacolon on clinical and/or radiological grounds. At present we rely on rectal biopsy alone to help us in this problem.

We believe that Swenson's technique of rectosigmoidectomy, if carefully followed, should produce acceptable results both in respect of mortality and late bowel function, and we await the production of convincing comparative data from larger centres before we intend to change our method. Certain details are worth emphasis. A colostomy is not always essential prior to elective operation, but even in the absence of specific indications the evidence suggests that in a small number of cases problems related to pelvic surgery will be avoided by the presence of a colostomy. The anorectal region should be dilated regularly prior to operation, and rectosigmoidectomy should be performed with facilities available for frozen section. Both these precautions will help to prevent an unsatisfactory result owing to either anastomotic stenosis or functional stenosis associated with a residual segment of bowel which does not show the normal pattern of innervation. In this connexion Swenson's own teaching should be followed carefully, viz., a section of the posterior circumference of the internal sphincter should be included by oblique resection of the bowel in the anorectal region, if problems related to distal hold-up of faeces are to be avoided despite an adequate clearance proximally of abnormal bowel. Faecal incontinence owing to removal of the rectum and its sensory modality has not been a feature in the late follow-up of our patients. Others have put this forward as an argument for retaining the rectum—a feature of the Duhamel and Soave procedures. We have 1 patient who had had an ileo-anal anastomosis performed at 9 months and when reviewed at 11 years had one or two bowel actions daily. He has developed normally (*Fig.* 4). This patient was the most extreme example of proximal extension of Hirschsprung's disease in our series. In 1 other case aganglionosis extended to the mid-transverse colon, while in the remainder it has involved the large bowel up to the sigmoid

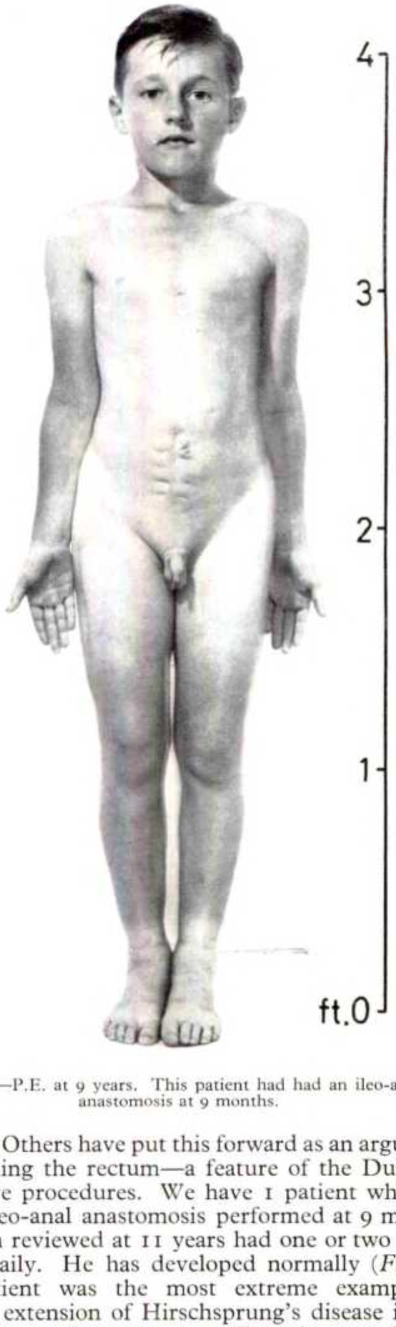

FIG. 4.—P.E. at 9 years. This patient had had an ileo-anal anastomosis at 9 months.

colon region or the lower rectum only. We have not found evidence for 'skip' lesions in any case. The age range of our patients has not demanded an inquiry into ejaculatory function at this point in time, but Swenson has found that this and bladder continence have been retained fully in his patients.

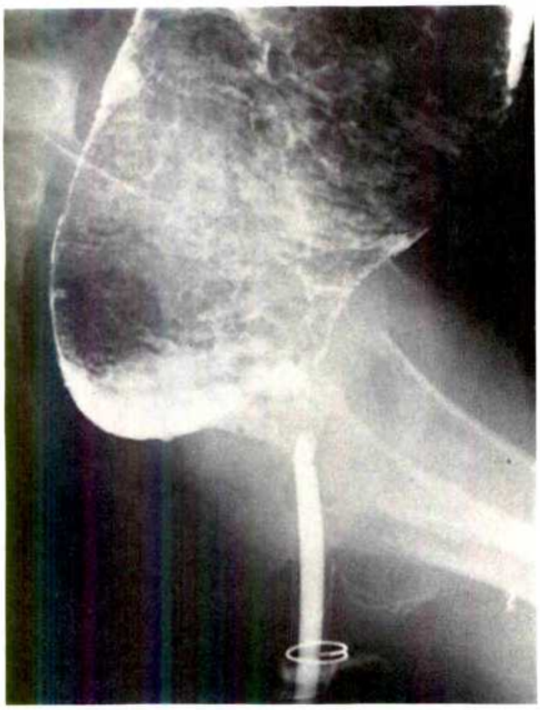

FIG. 5.—M. B. Barium enema (lateral view), 4 years after abdomino-anal pull-through for rectal agenesis, shows megacolon associated with distal functional stricture. The metal ring is on the anal skin.

We have no certain experience of hypoganglionosis, as described by Bentley (1964), but we do have 2 patients who have continued to have megacolon and coprostasis following treatment of rectal agenesis and microscopic anus (*Fig.* 5). The actual numbers with such problems in relation to the total treated for these congenital defects have not been worked out precisely, since our experience in this field is the subject of a current review. Rectal biopsy in a male 4 years after abdomino-anal pull-through for rectal agenesis showed scanty Auerbach's plexuses. The original specimen of the blind rectum showed almost complete aganglionosis with hypertrophied nerve-fibres. A 3-year-old girl, born with a microscopic anus in association with sacral agenesis, was submitted to rectal biopsy and this showed hypertrophied nerve-fibres and very scanty ganglion cells, which were small and poorly defined.

The figures given for aganglionosis occurring in association with anorectal abnormalities vary between 3·4 per cent (Kiesewetter, Sukarochana, and Sieber, 1965) and 30 per cent (Parkkulainen, Hjelt, and Sulamaa, 1960). Where distal large-bowel surgery has been performed, particularly if this has involved ligation and division of the inferior mesenteric artery, an ischaemic cause for a deficiency in innervation might be suggested (Ehrenpreis, 1965; Nixon, 1966). However, where surgery has been confined to such a minor operation as a 'cut-back' procedure there would seem to be evidence of a developmental deficiency in innervation. In functional terms both these conditions behave like Hirschsprung's disease. Their problems are complicated by potential deficiencies in the internal and external sphincter mechanisms, but in either case resection of the abnormally innervated bowel to a point where innervation is normal would seem an essential part of their treatment. Apart from simple observations of the external sphincter mechanism by digital examination, anorectal pressure studies combined with electromyometry will represent an advance in predicting the functional outcome of major surgery in such cases.

Acknowledgements.—We would like to take this opportunity to thank our paediatric colleagues, and the pathologists and radiologists, for their close co-operation in the management of these patients. In particular, we express our appreciation of the nursing staff for their skill in looking after these infants and children.

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PYLORUS-PRESERVING GASTRECTOMY IN THE TREATMENT OF DUODENAL ULCER

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SUMMARY

Twenty patients with duodenal ulcer have been treated by a pylorus-preserving gastrectomy. A functioning pyloric sphincter was maintained by retaining a 2-cm. cuff of antrum and carrying out a Billroth-I type of resection proximally. Basal acid output was reduced by 52·4 per cent and maximal acid output by 65 per cent. Gastric emptying time was prolonged, without producing stasis. A provocative test for the presence of dumping produced symptoms in only 1 patient following this operation in comparison with a high incidence of symptoms in patients who had had a Polya gastrectomy or vagotomy and drainage.

The results suggest that the procedure may be of value in the treatment of chronic duodenal ulcer.

The relative merits of partial gastrectomy and vagotomy and drainage in the treatment of duodenal ulcer have been assessed by controlled trials (Cox, 1968; Goligher, 1970). These trials have shown that there is no significant difference between the results of either operation. Although the great majority of patients do well following these conventional procedures, a small number exhibit undesirable sequelae such as dumping, bilious vomiting, diarrhoea, anaemia, and weight-loss. There is evidence to suggest that these side-effects are due, at least in part, to rapid gastric emptying (George, Connell, and Kennedy, 1968; Colmer, Davies, Owen, and Shields, 1969).

In 1967 Maki, Shiratori, Hatafuku, and Sugawara described a procedure which combined gastric resection with the preservation of a functioning pyloric sphincter. By means of manometric and fluoroscopic studies on dogs (Maki and others, 1967) they had found that transection of the stomach 1·5–2 cm. proximal to the pylorus left a functioning pyloric sphincter with normal gastric emptying. A clinical trial of the procedure was carried out on 50 patients, 30 of whom had gastric ulcers while the remainder had adenomatous polyps or other benign gastric lesions. Gastric emptying was found to be normal after operation, none of the patients developed dumping symptoms, and there was a satisfactory reduction in gastric acidity.

In 1969 Goodale, Tsung, Prevost, Edlich, and Wangensteen investigated the possibility of applying the Maki procedure to the treatment of duodenal ulcer. They obtained a 56 per cent reduction in acid secretion from Heidenhain pouches in dogs and complete protection against the stomal ulceration normally produced by the interposition of a loop of terminal ileum in the first part of the duodenum.

This communication reports the preliminary results of a clinical trial of the Maki procedure in 20 patients with duodenal ulcer.

MATERIALS AND METHODS

Patients.—The 20 patients in the trial had the diagnosis of duodenal ulcer made clinically and radiologically. Confirmation of the diagnosis was made at operation in each case. Patients with pyloric stenosis were excluded, but otherwise the series was consecutive. There were 16 male and 4 female patients. Their ages ranged between 20 and 60 years.

Procedure.—The abdomen is opened through a midline epigastric incision and the diagnosis of duodenal ulcer is confirmed. Mobilization of the distal two-thirds of the stomach is carried out in the usual way, with the exception of the distal 2 cm. where the lesser and greater omenta are carefully preserved. The antrum is then transected 2 cm. proximal to the pyloric ring. No clamps are applied distal to the line of transection, and bleeding points are picked up with fine forceps and ligated. The proximal line of transection is oblique and aims at removing approximately two-thirds of the stomach. The proximal cut end of the stomach is closed in two layers for a sufficient length to form a new lesser curvature and to leave a stoma suitable in size for anastomosis to the preserved antrum. This anastomosis is constructed with a continuous catgut suture to the mucosa and a seromuscular layer of interrupted unabsorbable sutures.

Investigations.—

Gastric Secretion.—Gastric acid secretion was measured pre- and postoperatively, using the augmented histamine test of Kay (1953).

Gastric Emptying.—Gastric emptying was measured by serial radiographs following the ingestion of a mixture of barium and gruel in which 100 g. of barium were added to 150 ml. of gruel (Maki and others, 1967). Gastric emptying times were compared with emptying times following partial gastrectomy, and vagotomy and drainage.

Dumping.—The presence of dumping postoperatively was assessed by giving the fasting patient 75 g. of glucose in 300 ml. of water to drink. The patient was then observed for signs of dumping, such as palpitation, weakness, sweating, and dizziness. In addition to these subjective findings, the patient's pulse and blood-pressure were checked at 10-minute intervals. A rise of 10 points in pulse-rate accompanied by a fall in blood-pressure of 10 points was taken as evidence of dumping.

Gastroscopy.—Five patients were submitted to postoperative gastroscopy, using the Olympus E.F.T.

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fibre-optic gastroscope, and the movements of the pylorus were observed.

RESULTS

Clinical.—There was no mortality in this series. Postoperative progress was uneventful in all cases. Patients had nasogastric suction discontinued within 48 hours and had resumed a normal diet within 10 days. At present (from 3 to 9 months postoperatively) all patients are free of symptoms, except for 1 female patient who complains of a feeling of fullness and occasional vomiting.

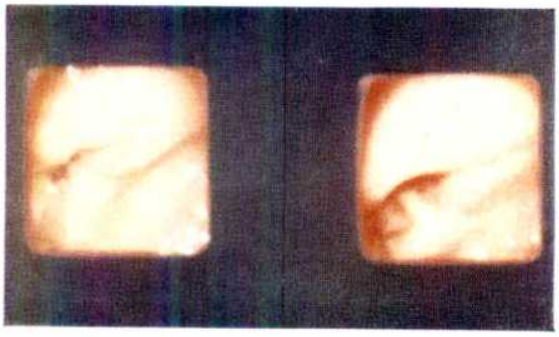

FIG. 1.—Contractions of the pylorus following Maki gastrectomy.

Table I.—BASAL ACID SECRETION (B.S.) BEFORE AND AFTER MAKI GASTRECTOMY

CASE No.	PREOPERATIVE B.S. (mEq.)	POSTOPERATIVE B.S. (mEq.)	REDUCTION IN B.S.	
			mEq.	Per cent
1	4·7	0·2	4·5	95·7
2	8·0	7·7	0·3	2·2
3	2·2	1·4	0·8	36·3
4	1·1	0·2	0·9	82·0
5	0·7	0·4	0·3	42·8
6	5·0	0·5	4·5	90·0
7	4·3	2·8	1·6	37·3
8	8·5	2·0	6·5	76·5
9	0·9	0·5	0·4	44·4
10	12·7	3·2	9·5	74·8
11	1·3	0·2	1·1	84·5
12	0·9	1·5	—	—
13	2·0	0·4	1·6	80·0
14	7·2	0·4	6·8	94·3
15	0·4	0·1	0·3	75·0
16	0·4	2·7	—	—
17	1·5	3·0	—	—
18	2·5	0·6	1·9	76·2
19	3·2	1·4	1·8	56·3
20	0·6	3·7	—	—
Mean	3·4	1·6	1·8	52·4

Mean percentage reduction in B.S. = 52·4 ± 35·6 per cent.

Gastric Secretion.—The mean postoperative reduction in basal acid secretion was 52·4 ± 35·6 per cent (*Table I*). Reduction in maximal acid output, as observed by Kay's augmented histamine test, was 65 ± 18·1 per cent (*Table II*).

Gastric Emptying.—*Table III* shows the emptying rates following the Maki procedure, Polya gastrectomy, and vagotomy and drainage. Only 1 patient in the Maki series emptied in less than 60 minutes. Seven out of 10 patients who had had a Polya gastrectomy emptied in 60 minutes or less. Emptying times following vagotomy and drainage were variable. In 2 of the patients with vagotomy and pyloroplasty who had emptying times of between 150 and 180 minutes there was still some barium mixture in the stomach at 240 minutes. All the patients with a Maki gastrectomy were completely empty at 240 minutes.

Table II.—MAXIMAL ACID OUTPUT (M.A.O.) BEFORE AND AFTER MAKI GASTRECTOMY

CASE No.	PREOPERATIVE M.A.O. (mEq.)	POSTOPERATIVE M.A.O. (mEq.)	REDUCTION IN M.A.O.	
			mEq.	Per cent
1	25·8	2·4	23·4	90·6
2	58·0	22·0	36·0	62·1
3	13·6	5·9	7·7	56·6
4	26·6	9·4	17·2	64·7
5	19·6	8·9	10·7	54·6
6	29·9	5·2	24·7	82·6
7	30·8	10·7	20·1	65·3
8	29·7	15·5	14·2	47·8
9	4·3	1·7	2·6	60·5
10	55·0	10·2	44·8	81·5
11	21·0	2·5	18·5	88·1
12	27·5	8·6	18·9	68·7
13	14·5	2·0	12·5	86·2
14	19·6	6·5	13·1	66·8
15	8·7	2·6	6·1	70·1
16	19·4	2·4	17·0	87·6
17	20·0	16·0	4·0	20·0
18	22·0	13·0	9·0	40·9
19	14·5	6·2	8·3	57·2
20	20·7	10·8	9·9	48·9
Mean	24·0	8·1	15·9	65·0

Percentage reduction in M.A.O. = 65 ± 18·1 per cent.

Table III.—PATTERN OF GASTRIC EMPTYING

OPERATION	TIME		
	30–60 min.	50–120 min.	150–180 min.
Maki	1	6	13
Polya	7	3	0
Vagotomy and P.G.E.	2	2	2
Vagotomy and pyloroplasty	1	2	3

Table IV.—DUMPING SYMPTOMS

NO. OF PATIENTS	OPERATION	SWEATING	WEAKNESS	DIZZINESS	PALPITATION	TACHYCARDIA AND HYPOTENSION	TOTAL NO. OF PATIENTS WITH DUMPING
20	Maki	1	1	1	0	1	1
10	Polya	5	3	5	5	6	6
6	Vagotomy and P.G.E.	1	2	3	2	2	3
6	Vagotomy and pyloroplasty	2	2	2	1	2	3

Dumping.—*Table IV* gives the results of the provocative test for dumping. One patient had symptoms of dumping following pylorus-preserving gastrectomy. Six of the 10 patients who had had a Polya gastrectomy showed evidence of dumping, as did 3 out of 6 patients with vagotomy and pyloroplasty.

Gastroscopy.—The pylorus was visualized postoperatively in 5 patients. In 3, rhythmic contractions of the sphincter were seen (*Fig.* 1). In 2, no sphincter movements were observed.

DISCUSSION

The first criterion of any new surgical treatment for peptic ulceration is that it must prevent the development of recurrent ulceration. The follow-up of this series is too short as yet to say whether this complication will occur. The retention of antral mucosa which is inherent in the preservation of the pylorus raises the possibility that recurrent ulceration could occur. However, a high level of gastrin production from the antral mucosa will be produced if either the acid stream is diverted away from the antral mucosa or gastric retention occurs. In the pylorus-preserving gastrectomy both of these possibilities are avoided. Furthermore, the reduction in gastric acidity provided by this operation is comparable with the reported figures following truncal and selective vagotomy (Jepson, Lari, and Johnston, 1968; Mason, Giles, Graham, Clark, and Goligher, 1968; Dignan, 1970), which have been shown to prevent recurrent ulceration.

The main advantage of the pylorus-preserving gastrectomy lies in its avoidance of the postcibal complications of other gastric operations. By maintaining the reservoir function of the stomach and a normal rate of stomach emptying, dumping symptoms are almost completely avoided. This may be contrasted with the high incidence of such symptoms which occur in association with the rapid rate of gastric emptying following a Polya gastrectomy, and with the variable rates of gastric emptying following vagotomy and drainage operations, which may on occasion be associated with gastric stasis.

The pathway by which the pylorus remains innervated is not known. In highly selective vagotomy (Johnston and Wilkinson, 1970) the nerves of Latarjet passing to the distal antrum are preserved. These nerves are necessarily divided in pylorus-preserving gastrectomy. Maki has suggested that vagal fibres accompany the right gastric artery to the pylorus. The absence of stasis following selective vagotomy without drainage (Burge, McLean, Stedeford, Pinn, and Hollanders, 1969) supports this view.

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PERIMUSCULAR EXCISION OF THE RECTUM FOR CROHN'S DISEASE AND ULCERATIVE COLITIS

A CONSERVATION TECHNIQUE

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Summary

The incidence of abnormalities of micturition and sexual function after removal of the rectum is discussed. It is thought that surgical damage to the autonomic nerves in the pelvis is the main cause of disability in young patients with benign disease. The various modifications of the standard abdominoperineal dissection of the rectum which have been introduced to prevent injury during the operation are described. None has proved entirely successful.

A new technique of rectal dissection, in which two surgeons concentrate on opposite sides of the bowel and carry out the dissection under direct vision in a bloodless field, is described. The results of its use in 24 patients are recorded.

Disorders of micturition and loss of sexual function frequently follow surgical removal of the rectum, especially when the standard abdominoperineal excision is employed to treat a carcinoma (Cooling, 1958; Ceulemans, 1968; Smith and Ballantyne, 1968). As many as one-third of patients may be rendered impotent (Goligher, 1951). Others lose the ability to ejaculate semen (Goligher, de Dombal, Watts, and Watkinson, 1968). Temporary retention of urine is not uncommon, but normal function usually returns by the end of the second week (Smith and Ballantyne, 1968). A small number of patients find it difficult to pass urine satisfactorily for months or years after the operation. Rarely, total incontinence may occur. Complications of this severity may be acceptable when an attempt is being made to eliminate malignant disease. Recently, however, loss of function has been shown to occur in a significant number of patients who have had the rectum excised for ulcerative colitis or Crohn's disease (Stahlgren and Ferguson, 1959). Impotence is often temporary, but in as many as 17 per cent of these patients it may be permanent (May, 1966; Watts, de Dombal, and Goligher, 1966). The patient's age also plays a part. Goligher (1967) found that 6 of 8 patients over the age of 50 were totally impotent although the most careful dissection had been carried out. Only 1 of 33 patients below this age suffered permanent damage. Other authors report similar findings (May, 1966; Daly, 1968).

There are probably numerous causes for the loss of function. These include the psychological problems and general depression of health which may follow major surgery in an elderly patient. It is possible that alteration of the normal pressures in the pelvis resulting from the loss of tissue and muscle may account for some of the disorders of micturition, but the most important single factor in the production of abnormalities of function of the bladder and sex organs is the damage to the autonomic nerves which results from the surgical dissection. This is particularly true of the young patients who are found to have a loss of function after panproctocolectomy.

ANATOMY

Below the peritoneal reflection the rectum is surrounded by fatty tissue. Waldeyer's fascia is a thickened sheet in the retrorectal fat which forms a sling around the rectum and anchors the anorectal junction to the pelvis (Wilson, 1967). This 'suspensory ligament' must be separated from the rectal wall when it is being mobilized (Gabriel, 1963). Within it the autonomic nerves of the pelvis ramify (Ashley and Anson, 1946).

The parasympathetic outflow in the pelvis unites to form a large nerve on each side which runs downwards and forwards until it branches lateral to the rectum (Mitchell, 1953). These nervi erigentes are often clearly visible at operation when the presacral fat is explored. The inferior sympathetic ganglia lie in the same region but are not as easily seen. Branches of both sets of nerves form a plexus in the fat of the side-wall of the rectum before passing forwards to supply the other pelvic structures. This inferior hypogastric plexus is partly fixed to the wall of the rectum by the nerves which supply it. Most attempts to prevent injury have been directed at preserving the nervi erigentes which mediate penile erection and ejaculation as well as effecting bladder contraction. Ejaculation was previously thought to be a function of the sympathetic nervous system (Learmonth, 1931). Both systems play important but controversial roles in the function of pelvic organs (Whitelaw and Smithwick, 1951). Whatever their functions, the peripheral fibres of both cannot be separated during an operative dissection of the rectal attachments.

In order to prevent damage to these nerves various modifications of the standard abdominoperineal dissection have been described. The most important of these are low ligation of the inferior mesenteric vessels (Daly, 1968), careful dissection of the lateral and posterior ligaments (Stahlgren and Ferguson, 1959; May, 1966), retention of the levator ani muscles (Daly, 1968), and preservation of the nervi erigentes in the presacral fat (Watson, 1951; Goligher and others, 1968).

It has been our experience that it is difficult not to enter the presacral pad of fat during the customary manual dissection of the posterior rectal space, however much care is taken. Further, it is even more difficult to prevent damage to the hypogastric plexus of nerves in the lateral perirectal tissue when the rectum is being pulled up and down alternately by the two surgeons, each intent on a concentric dissection. It therefore seemed important to evolve a technique using sharp dissection under direct vision in order to keep as close to the wall of the bowel as possible.

We have devised a technique for synchronous abdominoperineal mobilization of the rectum in this perimuscular plane, using two manœuvres not previously described in this context. A solution of noradrenaline, 1 in 200,000, is injected into the perirectal fat to separate the tissues and to reduce bleeding during the dissection. In order to reduce manipulation and to stay as close to the wall of the bowel as possible the abdominal surgeon concentrates on the posterior plane and the perineal dissector on the anterior one. Lateral dissection is not carried out until these two spaces have been opened and it is then performed under direct vision.

DETAILS OF THE OPERATIVE TECHNIQUE

The standard modified lithotomy position is employed using Lloyd-Davies leg supports, with the operating table angled at a 15–20° head-down tilt. Epidural anaesthesia is an additional help to reduce the bleeding. The operation is described here in the female pelvis because its extra width allows easier visualization, but the technique does not differ significantly in the male.

Pelvic Dissection from Above.—The surgeon operating at the upper end concentrates on the posterior part of the dissection (*Fig.* 1). During panproctocolectomy this stage is reached after the sigmoid colon has been mobilized. An incision is made in the peritoneum covering the mesentery on either side of the sigmoid colon about 1–2 cm. from its wall. The vessels are then divided as close to the bowel as possible, proceeding distally from a point well above the pelvic brim. The ureters may be demonstrated as the peritoneum of the pelvic floor is being approached. By remaining close to the wall of the bowel a low ligation of the terminal branches of the inferior mesenteric vessels is carried out. As the rectum becomes mobilized it can be dislocated forwards until the presacral pad of fat lying below the iliac vessels comes into view. The lateral peritoneum may then be incised close to the bowel wall. Point A in *Fig.* 1 illustrates the start of the posterior plane of dissection just outside the muscle wall of the rectum. By combining the injection of noradrenaline and saline and by using scissors dissection, this perimuscular plane is followed downwards into the pelvis. It is possible to reach as far as the distal sacrum or coccyx under direct vision. Blood-vessels may be ligated if large, or coagulated with a diathermy. No extensive lateral dissection is undertaken at this stage.

Perineal Dissection.—Whilst the abdominal dissector is separating the rectum from the presacral pad of fat (*Fig.* 2, point A) the perineal surgeon concentrates on the mobilization of the anterior part of the rectal wall. An incision is made around the anus after it has been doubly ligated. Sufficient skin should be removed to allow the edges to come together without pitting. The incision is deepened through the external sphincter muscles by cutting with diathermy. These muscles may be removed, but it is possible to retain them. A solution of noradrenaline (1 in 200,000) is injected into the tissues and the tissues are cut until the plane just outside the anterior muscular wall of the rectum is reached (*Fig.* 2). The wall of the rectum (*Fig.* 3, RW) is separated from the vagina without difficulty, using the solution to distend the intervening tissues.

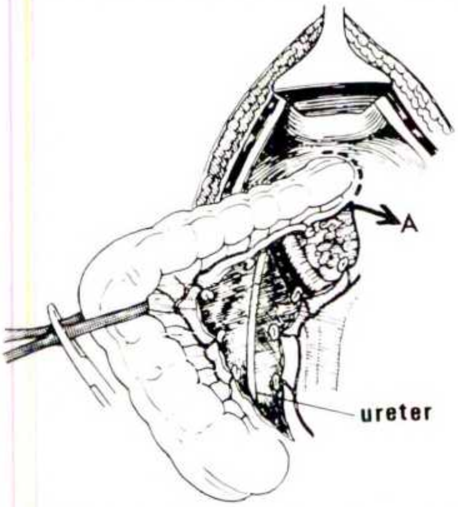

FIG. 1.—Pelvic dissection seen from above. Point A marks the start of the plane between the back of the rectum and the presacral pad of fat.

This sharp dissection in the perimuscular space is continued anteriorly until the peritoneum of the pouch of Douglas becomes visible (*Fig.* 3, P). Using the technique described it is a relatively bloodless procedure. At this stage the posterior plane can be completed by pulling the rectum forwards and dividing the tissues with the scissors after distending with noradrenaline. The colon will now have been freed anteriorly and posteriorly, leaving the lateral attachments.

Lateral Dissection.—Most of the lateral dissection is probably best carried out from above, once again distending the tissues with noradrenaline solution. However, it is surprising how much of the dissection can safely be carried out from below. The haemorrhoidal vessels are ligated close to the rectal wall. When the entire rectum has been freed and the small bowel divided in the abdomen, the colon can be delivered through the perineal wound to prevent soiling of the peritoneal cavity. In a fat patient, or when the pelvis is long and narrow, it has occasionally been found easier to cover the anus with a glove and to pass it into the pelvis so that lateral dissection can be completed under vision from above without pulling excessively on the bowel.

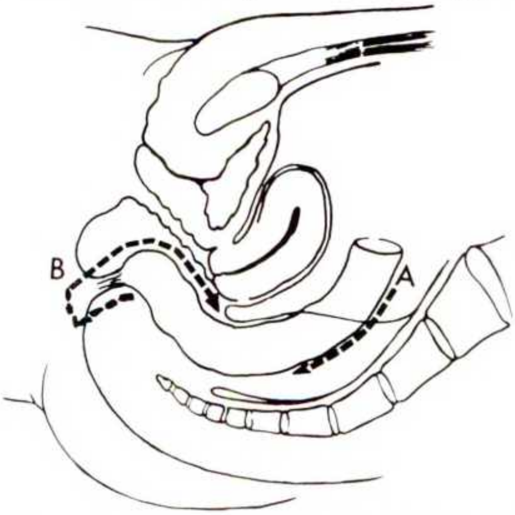

FIG. 2.—Lateral view of the female pelvis. The abdominal dissector concentrates on the retrorectal plane (A) and the perineal dissector on the anterior plane (B).

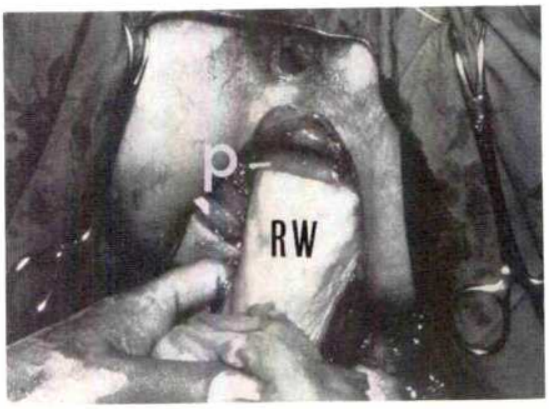

FIG. 3.—Photograph of the perineal dissection, showing the anterior wall of the rectum (RW) having been separated off the vaginal wall until the peritoneum of the pouch of Douglas (P) comes into view.

Closure.—Using this technique the rectum can be removed with little damage to the surrounding pelvic structures. The pelvic peritoneum is closed from above with a layer of fat beneath it, and the levator ani muscles are approximated with interrupted catgut sutures. The fat of the intact ischiorectal fossae can be seen bulging towards each other and they can be approximated with a few interrupted catgut sutures. The tissue spaces of the pelvis below the peritoneum are drained with a central catheter to which low-pressure suction is applied. The skin is closed with interrupted sutures.

DISCUSSION

Most surgeons agree that an attempt should be made to conserve as many of the pelvic structures as possible when operating for benign disease. The various modifications of the standard technique of rectal excision have been described above. Goligher has experimented with a perineal dissection in which the levator ani and sphincter muscles are retained and the dissection is continued by dividing the muscle coat 'all round to enter the plane of the pelvic dissection reached from above' (Goligher, 1967). However, he and others have abandoned the technique in favour of a formal perineal dissection because postoperative convalescence was prolonged in these patients owing to inadequate drainage through the intact sphincters (Lahey, 1952). We have tried a similar dissection in the submucous plane but stopped using the manœuvre after finding that it was seldom possible to avoid opening the lumen of the bowel.

We have employed the technique of perimuscular excision to remove the rectum in 18 patients with ulcerative colitis and in 6 with Crohn's disease who were treated by panproctocolectomy. None of the patients died and no case suffered an extended convalescence due to pelvic infection. The main problem encountered has been the persistence of a sinus in the perineal wound. Five of the 24 patients still retain small sinuses up to 6 months after surgery, and a number of other cases have had delayed healing of the perineal wound. However, the incidence of this complication after the dissection described above is similar to that recorded in the literature by Jalan, Smith, Ruckley, Falconer, Small, and Prescott (1969). A haematoma occurred in 1 patient and minor sepsis of the perineal wound in 5 others. The operation is not technically difficult and has been carried out successfully in a 6-year-old boy with ulcerative colitis.

None of the patients suffered permanent abnormalities of bladder function. In all the patients, indwelling catheters were retained for the first few postoperative days. Two developed infected cystitis. Three others complained of frequency of micturition during the first few weeks. One woman was unable to pass urine when the catheter was removed and it had to be replaced for a further 24 hours. No stress incontinence or total incontinence has been encountered. Of the 11 adult males, all have reported normal erections and 9 have described normal ejaculations.

Contra-indications to Adrenaline or Noradrenaline.—Certain patients are particularly sensitive to the adrenal medullary hormones. Adrenaline may cause abnormalities of cardiac contraction in patients receiving halothane as an anaesthetic (Rosen and Roe, 1963; Katz and Katz, 1966). Hypertensive patients, and in particular those taking drugs which block adrenergic nerves or propanalol, may be hypersensitive to the action of adrenaline and noradrenaline (Meulheims and Entrup, 1964; Smith and Corbascio, 1970). In these it may be possible to use saline alone to distend the perirectal fat during the dissection. In normal individuals it is safe to inject 1 mg. of the hormone over a short period. We have not used more than 60 ml. of the solution during any operation, which corresponds to only one-third of this dose.

CONCLUSION

We have described a technique of dissection which allows the surgeon to remain in a precise plane just outside the muscular wall of the rectum. It prevents damage to the pelvic nerves and does not add to the difficulty or duration of the operation.

The results in the cases described are encouraging. There have been no drawbacks and, in particular, the risk of pelvic infection and sinus formation does not appear to have been enhanced.

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VESICO-URETERIC REFLUX FOLLOWING RENAL TRANSPLANTATION[*]

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SUMMARY

Twenty-eight patients who had received a renal transplant have been studied in order to determine the incidence and significance of vesico-ureteric reflux in association with urinary infection.

The ureters had been anastomosed either by uretero-ureteric or ureterovesical techniques without an anti-reflux procedure.

Ten of the 28 patients had reflux into the transplant and 4 had reflux into a non-functioning ureteric stump. Reflux was significantly more frequent in the ureterovesical group.

Marked reflux in patients with recurrent urinary infections was associated with renal damage. Marked reflux in uninfected patients or mild reflux in patients with recurrent urinary infections was not associated with renal damage.

VESICO-URETERIC reflux has received considerable attention in the general field of urinary-tract infections but little in relation to urinary infections after renal transplantation. There are several reports describing various urinary complications after renal transplantation, such as urinary fistula, ureteric obstruction, and ischaemic necrosis of the ureter, but there is only passing reference to vesico-ureteric reflux in these reports (Starzl, 1964; Prout, Hume, Lee, and Williams, 1967; Murray, Wilson, Tinley, Merril, Cooper, Birtch, Carpenter, Hager, Dammin, and Harrison, 1968; Martin, Mimms, Kaufman, and Goodwin, 1969).

This study of patients with cadaveric renal transplants was undertaken in order to determine the incidence of vesico-ureteric reflux following different techniques of ureteric anastomosis and the relationship of reflux to infection and to renal function. Urinary infection is often a serious problem after transplantation not only because of its possible role in producing septicaemia but also with regard to its effect on renal function.

MATERIALS AND METHODS

Twenty-eight patients with functioning cadaveric renal transplants were studied at periods ranging from 8 to 60 months following transplantation.

There were 17 males and 11 females whose ages ranged between 17 and 50 years.

The type of ureteric anastomosis is shown in *Table I*. Patients receiving grafts several years ago often had either an end-to-end or an end-to-side uretero-ureteric anastomosis. In later grafts ureterovesical anastomosis was usually performed. The ureterovesical anastomosis was performed by a direct anastomosis from outside the bladder into the lateral aspect of the bladder dome, with or without a short intramural tunnel.

Table I.—TYPE OF URETERIC ANASTOMOSIS

Type of Anastomosis	*No. of Patients*
Ureterovesical	17
Uretero-ureteric	
End to end	4
End to side	7
Total	28

Assessment of Reflux.—Voiding cysto-urethrography was carried out, with extreme care being taken to avoid introducing infection. A urethral catheter was passed into the bladder and the urine obtained was cultured. Sodium iodide solution, 12·5 per cent, in neomycin, 2 per cent, was used as contrast material. A preliminary film was taken, the patient was screened, and exposures were made after the bladder had been filled with contrast, and during and after voiding.

Reflux was considered marked if it occurred freely into the ureter and pelvicaliceal system, but mild if it was transient, only occurring during voiding and not reaching the pelvicaliceal system.

Midstream specimens of urine were obtained 1 week after the cysto-urethrogram. Only 1 patient had a colony count of more than 10,000 organisms per ml. which was a result of catheterization. Following a 2-week course of chemotherapy the urine culture was sterile and has remained so.

Assessment of Infection.—Cultures of midstream urine (or of specimens from retention catheters in the postoperative period) were obtained daily immediately after transplantation and then subsequently at each follow-up visit. Counts of more than 100,000 colonies per ml. were regarded as indicating infection. In a small number of cultures, counts between 10,000 and 100,000 were reported, and in deciding their significance the cultures obtained immediately before and after were taken into account.

At least two episodes of infection had occurred in the preceding 8 months in all patients who were classed as being infected. Infections occurring in the immediate post-operative period have been excluded.

Assessment of Renal Function.—Serum creatinine has been the most reliable test of renal function

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[*] Presented at the joint Annual Meeting of the Royal Australasian College of Surgeons and the Surgical Research Society of Australasia at Brisbane, Australia, on 18 May, 1970.

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in our experience. A serum creatinine of less than 1·8 mg. per cent has been regarded as indicating good function and a value of more than 1·8 mg. per cent as indicating poor function.

RESULTS

Vesico-ureteric reflux was demonstrated in 13 of the 28 patients (*Table II*). Three had reflux into a non-functioning ureteric stump (*Fig.* 1). Nine refluxed up the ureter to the transplanted kidney (*Fig.* 2). One patient refluxed into both ureteric stumps as well as up the ureter to the transplanted kidney (*Fig.* 3).

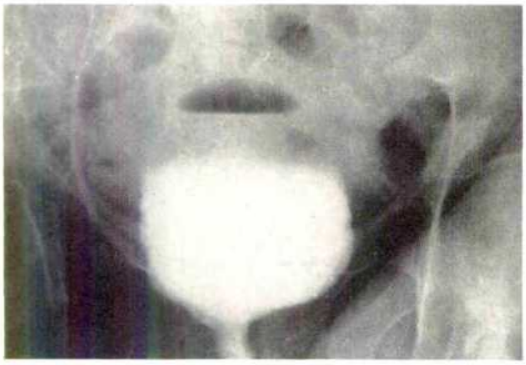

FIG. 1.—Reflux into a non-functioning ureteric stump.

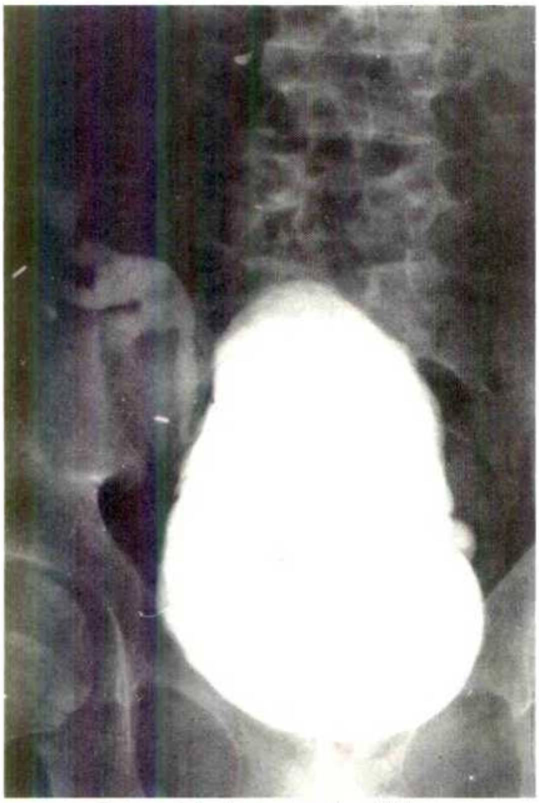

FIG. 2.—Reflux into a transplanted kidney.

As shown in *Table III* the incidence of reflux into the transplanted kidney was much higher after ureterovesical implantation than following uretero-ureteric anastomosis.

Thirteen of the 28 patients had had at least two urinary-tract infections in the 8 months before investigation. Reflux was more frequent in these patients than in those without infection (*Table IV*).

Table II.—INCIDENCE AND TYPE OF URETEROVESICAL REFLUX

Type of Reflux	*No. of Patients*
To transplant	9
Into a ureteric stump	3
To transplant and into ureteric stumps	1
Total	13

Table III.—REFLUX AND THE TYPE OF URETERIC ANASTOMOSIS

TYPE OF ANASTOMOSIS	TOTAL NO. OF PATIENTS	NO. OF PATIENTS WITH REFLUX
Ureterovesical	17	9
Uretero-uretic	11	1
Total	28	10

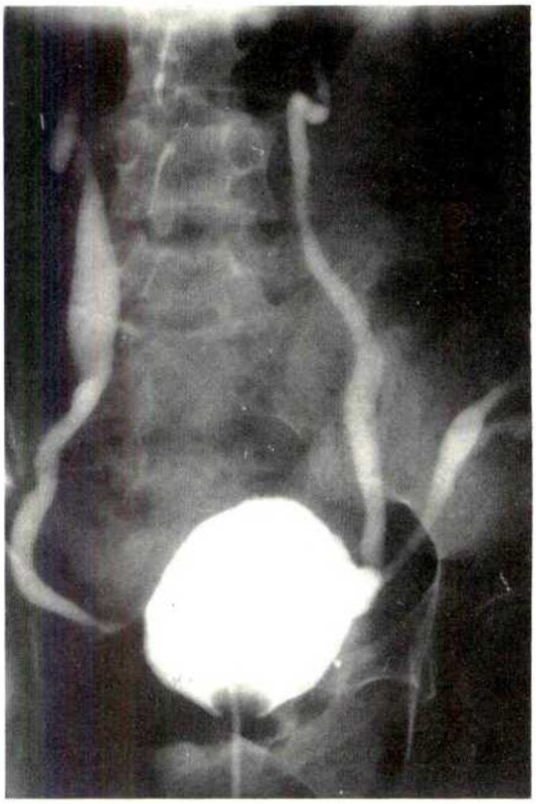

FIG. 3.—Reflux into both non-functioning ureteric stumps and to the transplanted kidney.

In considering the effect of reflux on the transplanted kidney the patients have been grouped according to the degree of reflux and the presence of infection (*Table V*). It can be seen that marked reflux of sterile urine occurred in 3 patients with normal renal function. Mild reflux associated with infection occurred in 2 patients who have normal renal function. In all 4 patients with the combination of marked reflux and urinary infection a depression of renal function has occurred. In 2 of the 4 the deterioration has been gradual. In the other 2 the depression of renal function varies with episodes of infection; in 1 the renal function between attacks remains normal but the other patient has suffered a gradual deterioration in function.

Table IV.—ASSOCIATION OF URINARY-TRACT INFECTION AND REFLUX

OCCURRENCE OF REFLUX	NO. OF PATIENTS WITH INFECTION	NO. OF PATIENTS WITH NO INFECTION
With reflux	10	3
No reflux	3	12
Total	13	15

$\chi^2 = 6{\cdot}92$ with Yates correction factor; $P < 0{\cdot}01$.

Table V.—RELATIONSHIP BETWEEN REFLUX TO THE TRANSPLANTED KIDNEY, INFECTION, AND RENAL FUNCTION

RENAL FUNCTION	MILD REFLUX		MARKED REFLUX	
	With Infection	No Infection	With Infection	No Infection
Normal	2	1	—	3
Poor*	—	—	4	—

* Poor renal function = serum creatinine of more than 1·8 mg. per cent.

Table VI.—URINARY INFECTIONS IN RELATION TO SEX

SEX	TOTAL NO. OF PATIENTS	NO. OF PATIENTS WITH INFECTION
Female	11	7
Male	17	6
Total	28	13

Two of the 3 patients, who have reflux into a ureteric stump only, have normal renal function. The remaining patient has had severe pulmonary and gastro-intestinal complications with gradual deterioration of renal function, which appears to be more related to periods of hypertension and the use of several potentially nephrotoxic drugs than to urinary infection alone.

DISCUSSION

The high incidence of reflux in patients with renal transplants is not surprising since the most common form of ureteric anastomosis, ureterovesical implantation, was carried out without any special anti-reflux technique. Of the 17 patients implanted in this fashion, 9 showed reflux.

One out of the 11 patients who were anastomosed by the uretero-ureteric technique had reflux into a ureter. It seems likely that this orifice was abnormal prior to transplantation.

Any reflux occurring in a patient after transplantation must be considered undesirable, but it is not easy to decide exactly how undesirable. Reflux may be compatible with normal renal function, even if marked, provided that the urine is sterile, as was seen in 3 patients. Even in the presence of recurring infection, mild reflux has not caused a detectable change in renal function. However, the 4 patients who had a combination of recurring infection with marked reflux all have evidence of renal damage. It was not possible from these studies to determine whether reflux was causative in producing recurrent infection, but it is clear that persisting urinary infection and reflux are often associated, and if both are marked, deterioration of renal function may occur.

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LYMPHANGIOGRAPHY AND SURGERY IN LYMPHANGIOMA OF THE SKIN

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SUMMARY

The results of surgery in a group of 7 patients with lymphangioma circumscriptum are presented. Lymphangiography was carried out in 5 of these patients and in 1 further patient who was not submitted to surgery.

Lymphangiography of the affected limb revealed normal subcutaneous lymphatic vessels and normal filling of nodes in the regional node areas. No direct connexion between the lymphangioma and the subcutaneous lymphatics or regional lymph-nodes was demonstrated.

Lymphography helps to show the extent of the underlying pathology before operation. It is also helpful in showing the relation of the lesion to the main lymph pathways of the area so that they may be preserved during operation.

Surgical treatment for patients with lymphangioma should only be undertaken if a definite cosmetic improvement can be assured. Even with discrete lesions regional excision has to be wide in extent owing to the marked tendency to subcutaneous extension of the abnormality. With these conditions satisfied the results of surgery should be good. With more extensive lesions partial excision of the most troublesome areas in one or more stages may give considerable benefit.

LYMPHANGIOMA circumscriptum is a variety of lymphangioma in which a local eruption of persistent thin-walled translucent vesicles appears in groups or patches on the skin. The first report in the literature was probably that of Fox and Fox (1879), and by 1893 Francis was able to review 28 cases, setting out the main clinical and pathological features of the condition. Since that time there have been numerous isolated case reports, some of which have recorded the recurrence of lymphangioma circumscriptum following surgery. We have, however, been unable to find any report of a series of patients who were treated surgically and were submitted to follow-up examination.

The present paper reports the results of surgery in 7 patients with lymphangioma circumscriptum, 5 of whom were investigated by lymphangiography prior to surgery. One further case was investigated by lymphangiography but was not submitted to operation.

MATERIALS AND METHODS

The main indications for investigation and consequent surgery in our patients were as follows:—

1. *Cosmetic Reasons.*—All the patients were troubled by the appearance of the lesion. On occasion, in the case of a child, it was the mother who was worried and who sought advice. This factor alone was not an absolute indication for surgery, which depended in each individual case on surgical judgement as to whether the scar would be more acceptable than the lesion.
2. *Troublesome and Recurrent Leakage of Lymph and Blood.*—This was occasionally a major symptom and often developed from a relatively localized area of the lymphangioma.
3. *Recurrent Infection of the Lymphangioma.*—Should infection occur in a lymphangioma, recurrent attacks of inflammation often develop, necessitating excision of the lesion.

Lymphography Technique.—The technique of lymphography was essentially the same as that described by Kinmonth (1954) with regard to direct intralymphatic injection of subcutaneous lymphatic trunks. Patent blue violet (10 per cent aqueous solution) was injected into the distal area of the limb under investigation. After massage of the limb a proximal incision, usually on the dorsum of the hand or foot, revealed a blue-coloured lymphatic trunk. This was then cleaned of surrounding fat and cannulated with a No. 30 needle swaged to polythene tubing. Ultra-fluid lipiodol, in quantities that have previously been recommended (Guiney, Gough, and Kinmonth, 1964), was then injected and radiographs were taken during the procedure. Further films of the limb and lymph-node areas were taken 24 and 48 hours later. In 3 patients, slow infusion of ultra-fluid lipiodol was made directly into one of the vesicles of the lymphangioma. Progress of the contrast material was followed with radiographs at intervals up to 5 days following the procedure.

Surgical Techniques for Excision of the Lymphangioma.—Occasionally the skin lesion appeared well defined and was easily encompassed by a one-stage surgical excision. Because of the known tendency for abnormal and dilated lymphatic spaces to be more extensive in the dermis and subcutaneous tissue than the visible skin lesion might suggest, the area of the excision was always generous. The lines of the excision were arranged so that they

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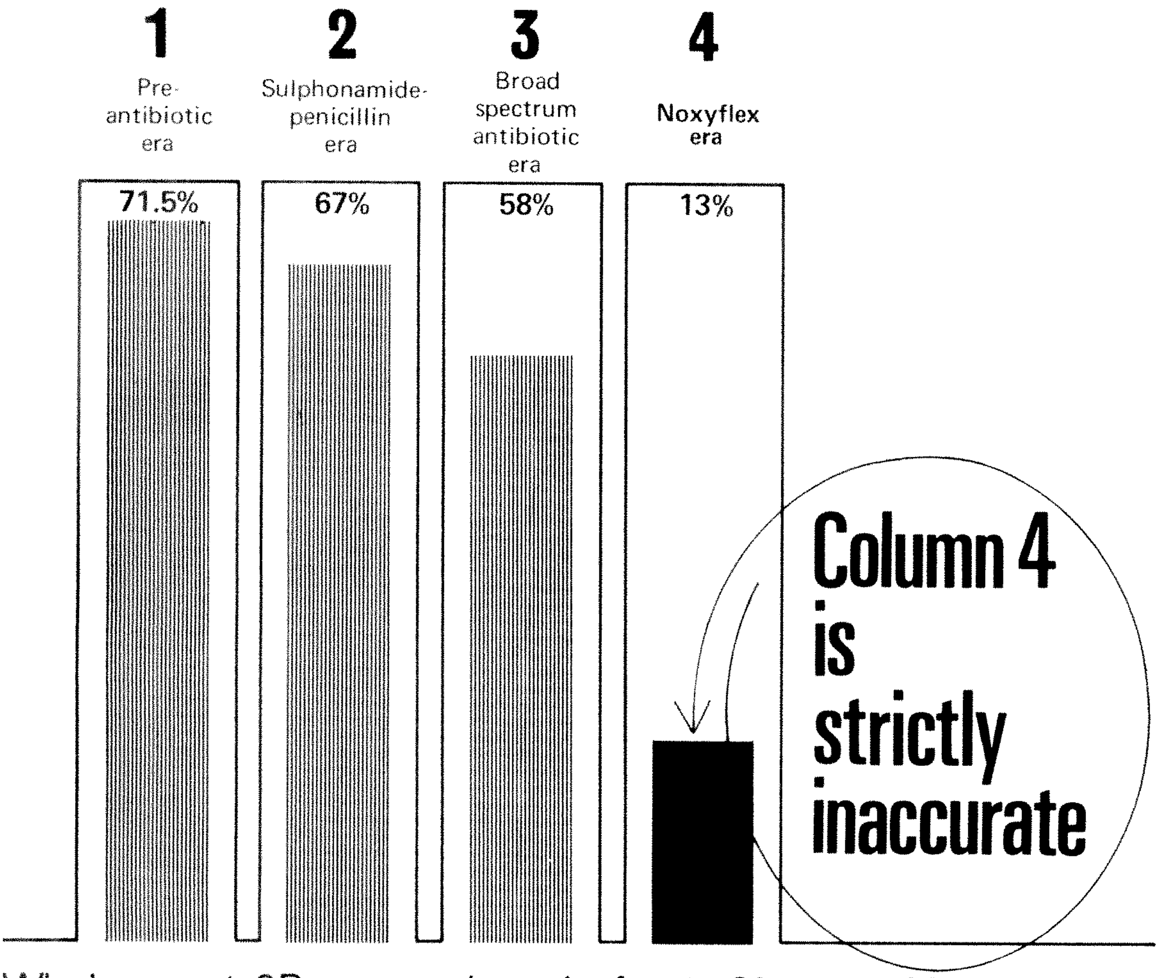

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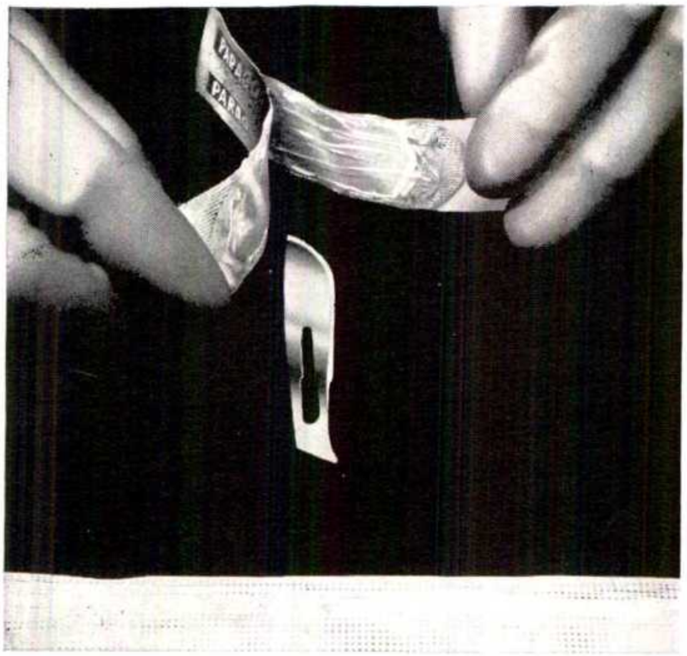

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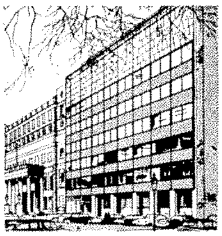

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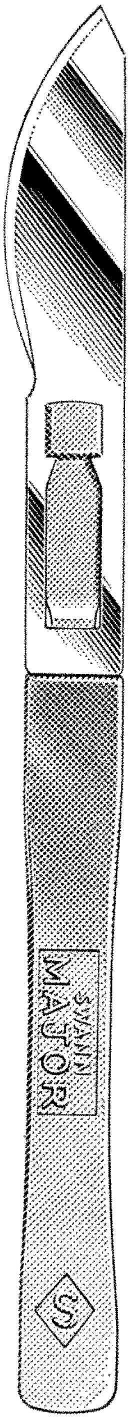

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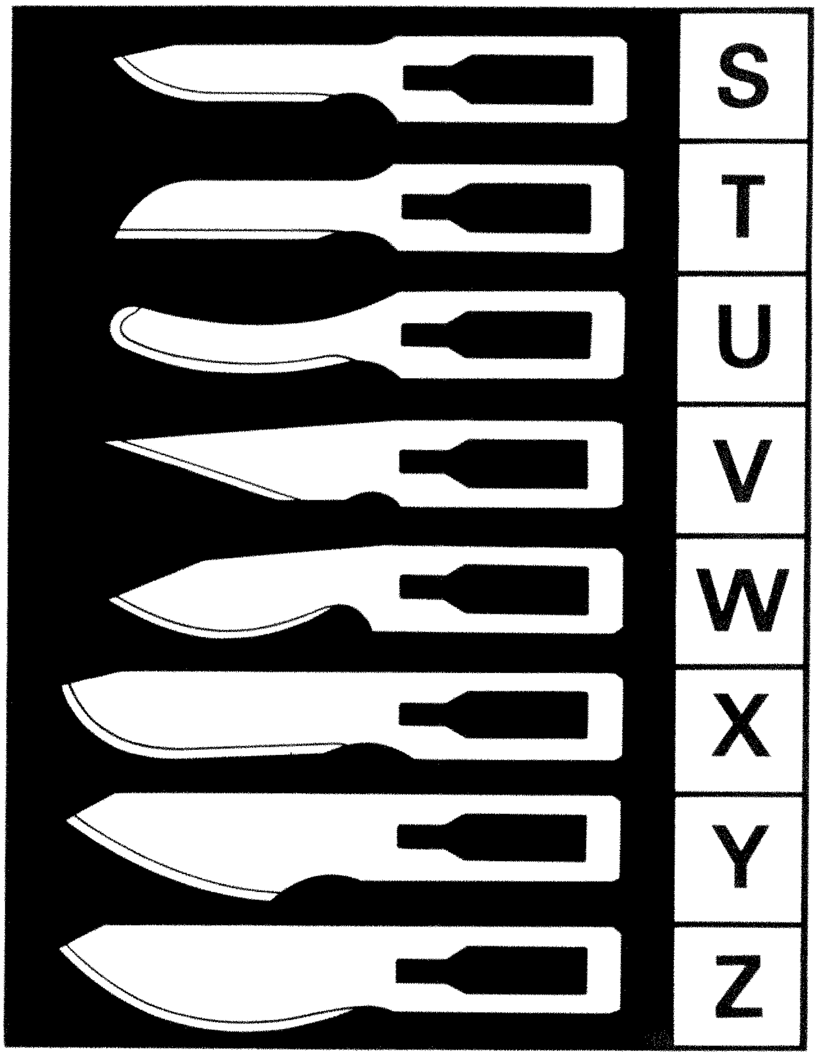

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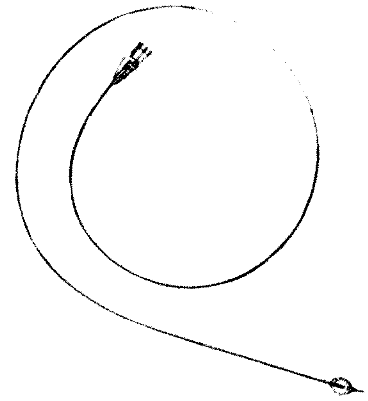

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followed the accepted skin crease lines or Langer's lines, and all subcutaneous tissue down to the deep fascia was excised.

More often patients presented with an extensive lesion and it was obvious that any operation to remove the lesion in its entirety would have to be performed in stages. The full implications of treatment were carefully explained to the patient before any surgery was carried out. In a number of cases no attempt was made to excise the lesion completely but the most troublesome area was excised in one or more stages.

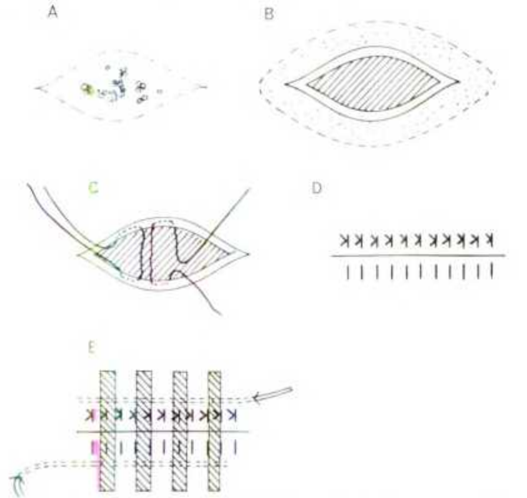

FIG. 1.—A, Elliptical excision of lymphangioma circumscriptum. B, The skin and subcutaneous tissue are excised. The surrounding skin and subcutaneous tissue are undercut equivalent to the transverse diameter of the wound. C, The wound edges are approximated with buried dermal horizontal mattress sutures of 00 catgut. D, The wound margins are further approximated with interrupted vertical mattress sutures of 000 nylon. E, Redivac drains are inserted. The wound is further strengthened with Steristrip dressings.

The details of the surgical technique used are shown in *Fig.* 1. Complete healing of the wound was required before a further stage could be considered, and if it was found necessary 3–6 months were allowed to elapse before the next stage was done.

Assessment of Results.—The assessment of results was based on our own observations at follow-up, together with close questioning of the patient or relative for their impression of the cosmetic appearance. In each case the original indications for operation were reviewed and the results of surgery were assessed in relation to these. Results were classified as 'good' if there was marked improvement, 'satisfactory' if there was only moderate improvement, and 'bad' if there was no improvement or the condition was worse than before surgery.

In addition to being seen in the follow-up clinic, the 6 patients who were treated surgically were sent a questionnaire in May, 1970, requesting answers to the following questions:—

Have any new vesicles appeared since your operation?

How do the scar(s) appear now?

Are they reasonably good, or thickened and unsightly?

Do you feel the operation was worth while in terms of the results produced by it?

Do you think the appearance is better now than it was before the operation was carried out?

Knowing what you do now about the results of surgery, would you have agreed to undergo the operation or would you have preferred the condition left as it was?

All the patients answered and returned the questionnaire. On the basis of these replies the patients' overall views of the results of treatment were also classified as 'good', 'satisfactory', or 'bad'.

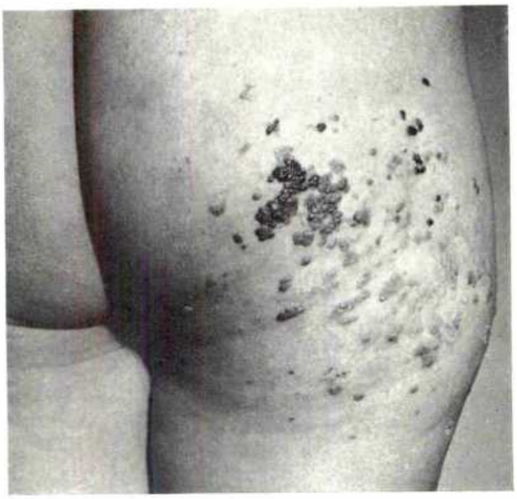

FIG. 2.—Lymphangioma circumscriptum on the buttock before surgery.

CASE REPORTS

Case 1.—Female, aged 25 years. This patient was referred to St. Thomas's Hospital in 1968 with a widespread area of lymphangioma circumscriptum on the right buttock and upper thigh which had first appeared at the age of 14 years (*Fig.* 2). Some slight thickening within the subcutaneous tissue of the buttock could be felt. Occasional bleeding and lymph leakage from the vesicles had occurred in the previous 2 or 3 years and on various occasions they had been treated with diathermy at another hospital. Bilateral pedal lymphangiograms were carried out in 1968 and showed normal subcutaneous lymphatics draining to the inguinal and pelvic lymph-nodes, which also appeared normal (*Fig.* 3). Contrast medium was injected into two vesicles on the right buttock. Some filling of lymphatic spaces deep to the injection site was shown but the contrast medium did not spread from this site (*Fig.* 4). No communication with the lymphatics of the limb or with the regional lymph-nodes was shown. Films taken 2 and 5 days after the original injection of the vesicles showed the contrast medium still present in the subcutaneous lymphatic spaces in the buttock with no evidence of any proximal drainage. The only possibility of removing the lesion was by staged surgery and this was embarked upon. An elliptical area of skin was removed from the buttock in 1968 which included underlying fatty tissue to a depth of 4 cm. This produced a good result and the scar healed well. In February, 1969, a further ellipse of skin (20 × 8 cm.) with most of the remaining vesicles was removed from the buttock (*Fig.* 5). When last seen in March, 1970, there were a few scattered vesicles over the right buttock, but the scars were neat and the patient was pleased with the cosmetic results of surgery and did not wish a third-stage operation.

Case 2.—Female, aged 10 years. At the age of 4 years this girl had developed an area of lymphangioma circumscriptum, 5 × 5 cm., on the upper and inner part of the right thigh. In 1968 she was referred to St. Thomas's Hospital, and bipedal lymphangiography was carried out which showed normal subcutaneous lymphatics in both lower limbs and filling of the inguinal and iliac lymph-nodes. A cannula was passed into a lymphangiomatous vesicle in the area of lymphangioma circumscriptum and 0·75 ml. of ultra-fluid lipiodol was injected. No connexion could be demonstrated between the lymphangioma and subcutaneous lymphatics, and the contrast medium injected into the lymphangiomatous site had not changed its position 4 days later. In June, 1968, an ellipse of skin was removed which included most of the lymphangioma. A few peripheral vesicles were left surrounding the scar. In October, 1969, it was noted that the scar was rather hypertrophic, but this has since flattened. At the present time there is some diffuse swelling in the area beneath the scar and there are five or six vesicles on the skin surface.

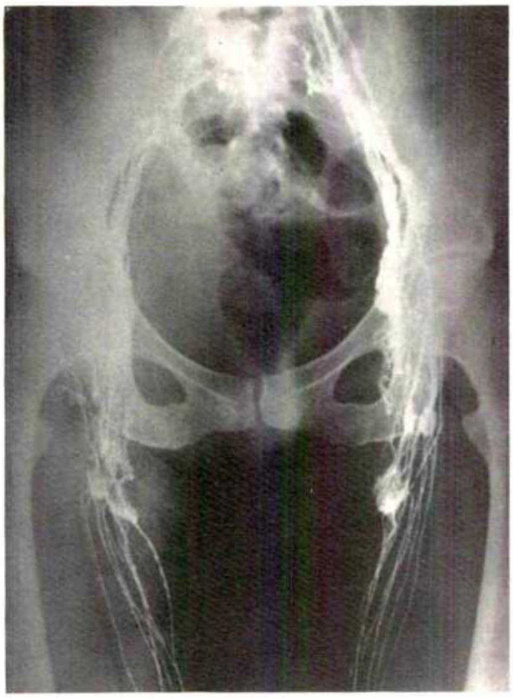

FIG. 3.—Lymphangiogram showing normal subcutaneous lymphatics and pelvic lymph-nodes.

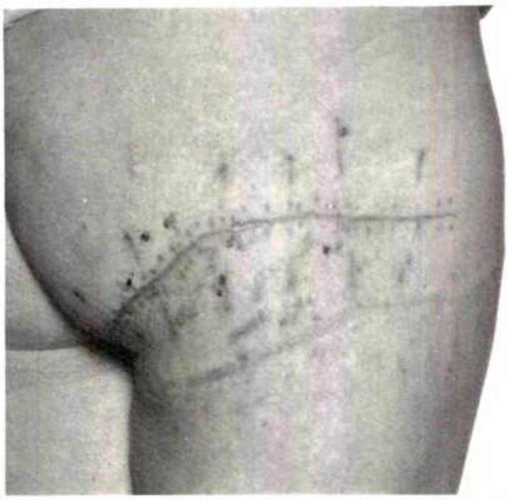

FIG. 5.—The appearance of the buttock after two-stage removal of lymphangioma circumscriptum. A third stage would have removed the area between the scars and left the patient with one scar.

Case 3.—Male, aged 11 years. This patient was first seen at St. Thomas's Hospital in 1968 with an area of lymphangioma circumscriptum on the back of the right shoulder which had appeared 6 years previously. In June, 1968, a right brachial lymphangiogram was carried out. Subcutaneous lymphatics of the area of the lymphangioma circumscriptum were cannulated and 0·5 ml. of ultra-fluid lipiodol was infused. The contrast medium remained in the area of the lymphangioma circumscriptum. No communication between this lesion and the draining lymphatics could be seen. In July, 1968, the whole of the area of lymphangioma circumscriptum was excised together with the underlying subcutaneous fat. The patient made a good postoperative recovery and when last seen there had been no recurrence of the lymphangioma.

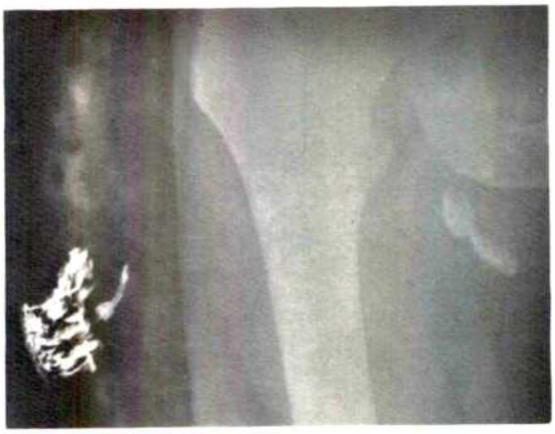

FIG. 4.—Intravesicular lymphangiogram outlining the cystic spaces. There is no communication with the subcutaneous lymphatics.

RESULTS

Lymphography.—In 6 patients the site of the lymphangioma circumscriptum was suitable for lymphangiographic investigation. In all 6 patients the main lymphatic drainage of the affected limb appeared normal and none of the contrast medium injected into the distal subcutaneous lymphatics found its way into the lymphangioma (*Table I*). Injection of contrast medium into the vesicles of the lymphangioma circumscriptum was carried out in 3 patients. Cystic spaces in the subcutaneous tissues deep to the lymphangioma circumscriptum were outlined in these patients but delayed films taken up to 5 days later showed no movement of the contrast medium towards the regional lymph-nodes (*Table I*).

Results of Surgical Treatment.—The results of treatment and the period of follow-up are summarized in *Table II*. In 1 patient (*Case* 3), in whom the entire vesicular area and subcutaneous extension were excised in one stage, there has been no recurrence of the lesion after 2 years. This result was classified as good, although the scar is still rather thickened.

In 5 patients the lesion was too extensive in area to excise completely in one stage and partial excision of the most troublesome area was performed. One of these patients was troubled with recurrent cellulitis, apart from the cosmetic factors, and this, which was the indication for surgery, has not recurred following operation. In 4 patients a few new vesicles have appeared around the scar but there has been no major recurrence. In 1 patient a new subcutaneous swelling has developed beneath the scar. In 1 patient with an extensive lesion on the buttock, partial excision was performed in two stages with a good result.

In only 1 patient was lymphatoma formation a problem in the postoperative period, although slight serous discharge from the incision for a day or two occurred in several others. Hypertrophic thickening of the scar was a marked feature initially in 3 patients, but in each case has subsequently flattened, leaving a scar which is flat but rather broad and unsightly.

Table I.—SITES OF LESION AND RESULTS OF LYMPHANGIOGRAPHIC INVESTIGATION

SUBJECT	AGE AT ONSET	SITE OF LYMPHANGIOMA CIRCUMSCRIPTUM	SUBCUTANEOUS LYMPHANGIOGRAM	INTRAVESICULAR LYMPHANGIOGRAM
Case 1, female, aged 25 yr.	14 yr.	Right buttock and upper thigh. 25 × 15 cm.	Normal bipedal lymphangiogram	No drainage of contrast material up to 5 days
Case 2, female, aged 10 yr.	4 yr.	Upper and inner right thigh. 5 × 5 cm.	Normal bipedal lymphangiogram	No drainage of contrast material up to 4 days
Case 3, male, aged 11 yr.	5 yr.	Back of right shoulder. 7 × 7 cm.	Normal right brachial lymphangiogram	No drainage of contrast material
Case 4, female, aged 18 yr.	6 yr.	Back of left shoulder with underlying swelling. 7 × 5 cm.	Not performed	Not performed
Case 5, female, aged 18 yr.	Birth	Right upper arm with underlying cystic mass. Some extension to axilla and chest wall. 12 × 7 cm.	Not performed	Not performed
Case 6, female, aged 14 yr.	10 wk.	Left breast, axilla, and upper arm. Underlying swelling in the region of the left breast and upper arm. Extensive	Normal left brachial lymphangiogram	Not performed
Case 7, male, aged 27 yr.	8 wk.	Left axilla and upper arm. Underlying swelling. 8 × 9 cm.	Normal left brachial lymphangiogram	Not performed
Case 8, female, aged 16 yr.	Soon after birth	Flexor aspect of the left forearm with underlying swelling. 2 × 1½ cm. Further swelling at left epicondyle	Normal left upper limb lymphangiogram	Not performed

Table II.—ASSESSMENT OF RESULTS OF SURGERY

SUBJECT	INDICATION FOR SURGERY	SURGICAL TREATMENT	ASSESSMENT OF RESULT		COMMENT	LENGTH OF FOLLOW-UP
			Medical Assessment	Patient Assessment		
Case 1, female, aged 25 yr.	(1) Cosmetic (2) Leakage	Excision of most of lesion in two stages	Cosmetic—good Leakage—good	Good	Scars good. A few vesicles still present	1 yr.
Case 2, female, aged 10 yr.	Cosmetic	Most of lesion excised in one stage	Satisfactory	Satisfactory	Scar hypertrophic at first—now flat. Some new swelling under scar	1½ yr.
Case 3, male, aged 11 yr.	Cosmetic	Entire lesion excised	Good	Satisfactory	No recurrence. Scar hypertrophic	2 yr.
Case 4, female, aged 18 yr.	Cosmetic	Excision of most of lesion and subcutaneous swelling. Postoperative radiotherapy to scar	Satisfactory	Good	Scar hypertrophic at first—now flat	1½ yr.
Case 5, female, aged 18 yr.	(1) Leakage (2) Cosmetic	Excision of most troublesome area with underlying cystic mass	Leakage—good Cosmetic—good	Good	Scar thickened. Some new vesicles since operation	6 mth.
Case 6, female, aged 14 yr.	(1) Infection (2) Cosmetic	Partial excision of lesion and underlying mass from left axilla and chest in 1963. Further excision in 1967	Infection—good Cosmetic—satisfactory	Satisfactory	Scars good. Still getting new vesicles	3 yr.
Case 7, male, aged 27 yr.	(1) Leakage (2) Cosmetic	Excision of most of troublesome area	Leakage—good Cosmetic—good	Good	Scars good. No new vesicles	2½ yr.

All the patients felt that surgery had been worth while and were, in general, pleased with the results. We were rather more reserved in our appreciation of the results in view of the occasional unsightly appearance of a hypertrophic scar. However, even when the scar was relatively unsightly, the patient often preferred it to the appearance of the lymphangioma: 'I would rather have the scar than a mass of blisters over my back as people tend to think you have a disease of some kind.'

DISCUSSION

Wegner (1877) originally classified lymphangiomata into simple, cavernous, and cystic forms, and this is commonly accepted. Watson and McCarthy (1940) added two other types, cellular or hypertrophic lymphangioma and diffuse lymphangioma, to this classification. Peachey, Lim, and Whimster (1970) have reviewed 65 cases of lymphangioma involving skin or mucous membrane and have classified these into two main groups.

'Localized' lymphangioma circumscriptum is small, usually less than 1 cm.^{2} in area, and is histologically distinct in that the abnormal lymphatic spaces are confined to the dermis. These lesions often have blood-containing vesicles and can be mistaken for haemangiomata. Excision of these 'localized' lesions is simple and recurrence is unlikely since all the abnormal lymphatic tissue is easily removed.

In the 'classic' type of lymphangioma circumscriptum, with which the present paper is concerned, the appearances are different. Scattered or grouped lymph-containing vesicles occur over an area of skin which may be extensive. Indeed, it may be argued that the adjective 'circumscriptum' is inaccurate as a description of the 'classic' type. One of the authors (J. B. K.) has suggested that the name 'lymphangioma diffusum' would give a truer description of these lesions. Haemorrhage within some of the vesicles is common and variable in degree so that vesicles may have a pink or red coloration. Coagulation of the blood may produce a purple or black appearance. In long-standing cases vesicles may be situated at the top of small papules or there may be a superimposed warty hyperkeratosis.

In many cases several patches of involvement are present within one general area, and although they can occur in any area of the skin they are most frequently found over the proximal parts of the limbs and the adjacent limb girdles. Lesions in the region of the upper arm, axilla, and adjacent chest wall, including the pectoral and scapular regions, are particularly common. Lesions of this type are often present at birth or appear soon afterwards but some occur for the first time in childhood or later. Careful examination often shows some diffuse thickening or swelling in the subcutaneous tissue beneath an area of lymphangioma circumscriptum, denoting a subcutaneous lymphangiomatous element, and in occasional cases the patient gives a history of a diffuse or cystic swelling preceding the appearance of vesicles on the skin surface. In a small group of patients there may be more widespread subcutaneous swelling or generalized enlargement of perhaps an arm or leg.

Histology of the excision specimens in these 'classic' lesions is characteristic. Grouped, cystic lymphatic spaces are present in the papillary layer of the dermis. Dilated lymphatic spaces can be traced deeply into the subcutaneous tissue, where they may involve a larger area than the vesicles on the skin surface would suggest. In cases with obvious subcutaneous swelling, cystic spaces in the subcutis may have a structure similar to that seen in cavernous lymphangioma.

Reports of lymphangiographic investigation in cases of lymphangioma circumscriptum are extremely rare. Russell and Pridie (1967) reported a man aged 18 years who had had an operation for removal of a 'lipoma' of the right hip at 18 months. At the age of 16 years a 'cavernous multilocular haemangioma' had been dissected away from the subcutaneous tissue in the upper thigh, and lesions of lymphangioma circumscriptum had subsequently developed in the region of the right hip. A right pedal lymphangiogram showed contrast medium to flow to the inguinal region where a large collection of contrast material appeared. There was a paucity of lymph-vessels above this, but a large widened vessel was seen coursing more laterally than normal and further collections of contrast material appeared above and medial to the area of non-filling. It was uncertain whether the abnormality shown was due to the lymphangioma or to the previous surgery. Intravesicular lymphangiography was not performed.

In each of 6 patients investigated by lymphangiography in the present series the subcutaneous lymphatics of the affected limb were normal. Contrast medium injected into the vesicles in 3 cases outlined cystic spaces in the subcutaneous tissue deep to the lymphangioma but showed no movement towards the regional lymph-nodes, suggesting that these lymphangiomata have little or no connexion with the normal lymphatic drainage.

In our experience it is often difficult to excise completely the whole of the lymphangioma, which is more extensive in the subcutaneous tissue than the appearance of the vesicular lesions on the skin surface would suggest. If a wide and deep excision of the lesion with removal of all abnormal tissue is possible the chances of permanent cure are good. In some cases simple excision may be carried out in a one-stage operation, while in others complete excision may be possible in two or more stages. Several o our patients with relatively extensive lesions were pleased with the results of a limited surgical excision of the most troublesome area of the lymphangioma Most of the lesions could be excised completely in two or more stages. The tendency to produce hypertrophic and unsightly scars after surgery for lymphangioma has been noted previously by Watson and McCarthy (1940). This has not been a marked feature in our series of patients.

Although all of our patients feel at present that surgery has been worth while we are well aware that the length of follow-up is as yet relatively short. Only observation over a prolonged period of time will show whether the benefits of surgery are maintained

Acknowledgements.—Our thanks are due to Dr H. J. Wallace and those other dermatologists who so kindly referred their patients to us. We are also grateful to Mr. T. W. Brandon of the photographic department of St. Thomas's Hospital for the medical illustrations.

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THE BOERHAAVE SYNDROME

(SPONTANEOUS RUPTURE OF THE OESOPHAGUS)

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Summary

Two cases of spontaneous rupture of the oesophagus are presented. Thoracotomy and surgical closure of the perforations resulted in satisfactory outcome in both instances. It is believed that the second case is the only recorded case in which haematemesis from a bleeding duodenal ulcer was the precipitating factor, and also it is believed that he is the oldest survivor to be reported. The literature, aetiology, and treatment of this interesting disease are discussed.

Late one evening in 1724 a Dutch surgeon named Hermann Boerhaave (Derbes and Mitchell, 1955) was summoned to see Baron Von Wassenaer, Grand Admiral of the Dutch fleet. This gentleman had over-indulged at the dinner table and had taken some olive oil as an emetic. During the subsequent retching and vomiting he suddenly developed severe pain in his chest and declared that he would surely die. At autopsy, Boerhaave discovered the olive oil and a portion of roast duck in the Admiral's pleural cavity which had entered through a tear in the distal oesophagus. Spontaneous rupture of the non-diseased oesophagus is a rare occurrence, but one which is invariably fatal unless promptly recognized and adequately treated.

CASE REPORTS

Case 1.—A 60-year-old white male was admitted to Winneshiek County Memorial Hospital, Decorah, Iowa, in January, 1966, with severe epigastric and low anterior chest pain. Six hours previously he had awakened with a headache for which he had taken two aspirin tablets. He had become nauseated, had retched violently, and had vomited about 100 ml. of gastric contents. Direct and specific questioning revealed that he had then immediately experienced severe lower chest and high epigastric pain. This pain radiated into his left supraclavicular region and it was aggravated by breathing, coughing, and swallowing.

Examination shortly after admission to the hospital and 6 hours subsequent to the onset of his illness revealed a very ill man, propped up in bed, with shallow, rapid respirations, and peripheral cyanosis. His blood-pressure was 126/80, and his pulse was 100 per minute. Clinical examination of the heart and lungs was unrevealing. Abdominal examination showed marked, generalized, board-like rigidity. Abdominal tenderness was conspicuous by its absence—only minimal inconstant tenderness being present high in the epigastrium. The bowel-sounds were hypo-active. The rest of the physical examination was essentially negative.

The history was suggestive of spontaneous rupture of the oesophagus, but the much more common entities of myocardial infarction and perforated peptic ulcer had to be eliminated, if possible. An electrocardiogram was interpreted as being normal. An upright chest radiograph, together with flat and decubitus radiographs of the abdomen, failed to reveal any evidence of free air. Lipiodol oesophagrams were then carried out in the supine and left lateral positions but these did not show any leakage from the oesophagus. In spite of this the original diagnosis of probable spontaneous rupture of the oesophagus was maintained, chiefly on the basis of the classic clinical history and the rapid progressive deterioration of the patient's general condition over a short period of time. The patient was taken to the operating room 2 hours after admission and 8 hours after the onset of his illness.

The mediastinal oesophagus was approached through a left posterolateral thoracotomy incision between the seventh and eighth ribs. There was no free fluid in the pleural cavity, but upon opening the distal mediastinal pleura a foul odour was noted, and the peri-oesophageal tissues were oedematous and inflamed. A 2-cm. longitudinal, full-thickness tear was located on the left posterolateral aspect of the oesophagus, approximately 5 cm. above the diaphragm. A nasogastric tube was passed into the stomach under direct vision. The edges of the laceration were débrided and closed in layers with interrupted 000 chromic catgut sutures. The posterior leaf of the mediastinum pleura was tacked over the repair, but the rest of the inferior mediastinum was left open for drainage purposes. The chest was closed, leaving a large chest tube which was connected to an under-water seal.

Postoperatively, the patient was very ill for several days, with recurrent fever spikes to 39·6° C. and marked toxic psychosis. The nasogastric tube was removed on the fourth postoperative day and oral feeding was started. The chest tube drained significant amounts of purulent fluid until the tenth day when the drainage ceased and the tube was removed. The patient's hospital stay was prolonged by two loculated empyematous pockets which responded to repeated thoracenteses. The patient was discharged 5 weeks after operation, having lost 135 kg. in weight.

Three months after discharge he had returned to full employment. A radiograph of his chest was normal, except for minimal pleural thickening, and he had regained his weight-loss.

Case 2.—This patient was an 80-year-old retired farmer with a reputation in his community for being a prodigious beer drinker. He was admitted to hospital in February, 1968, with haematemesis, severe abdominal pain, and incipient shock. He was quite confused and a very poor historian, but questioning revealed that 4 hours prior to admission he had felt weak and had vomited several hundred ml. of dark blood. He had drunk several bottles of beer and several glasses of whisky, but had still continued to have haematemesis. Direct and specific questioning revealed that during the course of one bout of vomiting he had suddenly developed severe upper abdominal pain.

The patient was examined shortly after admission to hospital, and at that time he was propped up in bed and was quite dyspnoeic. His skin was cool and clammy and he was obviously very ill, with a rapid weak pulse of 110 per minute. His blood-pressure was 96/70. At that time, the patient's severe pain was localized mainly in the epigastric region. Bowel-sounds were hypo-active and there was generalized abdominal rigidity, which was more marked in the upper abdomen. Again, as in *Case* 1, tenderness was conspicuous by its absence. There was no subcutaneous emphysema and the heart sounds were clear and distinct. The lungs were clear to percussion and auscultation. Swallowing of saliva did not aggravate the pain, although coughing and deep breathing did.

During the course of this physical examination he vomited 200 ml. of bright red blood which smelt strongly of alcohol. He was still definite in relating the onset of his abdominal pain to a previous bout of haematemesis. A series of radiographs for free air had been ordered previously by his family physician but they had been negative. An electrocardiogram was done, but this was also normal. Blood was being cross-matched for the patient and vigorous replacement of fluids and electrolytes under central venous pressure monitoring was being done when the patient was taken to the operating room 1½ hours after admission and 6 hours after the onset of his illness. The preoperative diagnosis was probable bleeding peptic ulcer with resultant post-emetic spontaneous rupture of the oesophagus.

The abdomen was opened through an upper-right paramedian incision for the purpose of locating and stopping the source of bleeding and also because an abdominal source for the patient's severe abdominal pain and rigidity was possible. Gastroduodenotomy disclosed a hyperaemic ulcer, 1 cm. wide, on the posterior wall of the duodenum, with a readily discernible vessel in the centre of the ulcer bed which was not bleeding at that time. The vessel was oversewn with a heavy silk figure-of-eight suture. The stomach was emptied of several hundred ml. of old blood and clots, and the gastroduodenotomy was closed by a single-layered silk, Weinberg-style, Heineke-Mikulicz pyloroplasty. Exploration of the entire abdominal cavity for further pathology was negative. Curiosity led to a careful scrutiny of the oesophagogastric junction and the overlying peritoneum. There was absolutely no evidence of inflammation or oedema or other signs of distal mediastinal pathology visible from within the abdomen. A gastrostomy with a No. 18 Foley catheter was performed and the abdomen was closed in the usual fashion—the concomitant vagotomy being done through the chest. The patient was turned into a left midlateral position and the chest was opened through the bed of the seventh rib. About 200 ml. of a turbid coloured fluid were present in the pleural cavity. The distal mediastinal pleura appeared oedematous but was grossly intact. On opening the pleura a large amount of necrotic tissue and several beans presented. A longitudinal laceration, 2 cm. long, through all layers was present in the posterolateral aspect of the distal oesophagus, 4 cm. above the diaphragm. A nasogastric tube was passed into the stomach under direct vision and the edges of the laceration were débrided and closed in layers with 000 chromic catgut. A bilateral truncal vagotomy was done. The anterior leaflet of the mediastinum was left open for drainage purposes. The chest was closed in the usual fashion with under-water seal drainage. The patient had a comparatively smooth postoperative course, apart from a postoperative psychosis which cleared up before his discharge on the eighteenth postoperative day. He has since remained well.

DISCUSSION

This disease is not a common one and has only recently been described in some of the better surgical textbooks. Derbes and Mitchell comprehensively reviewed the subject in 1956 and reported 157 cases collected from the world literature. Three years later Dorsey, Hohf, and Lynn (1959) reported the first spontaneous rupture of the oesophagus in a neonate, and since that time there have been 3 further cases in neonates (Wiseman, Celano, and Hester, 1959; Hochberg and Parlamis, 1961; Le Brigand, Bordes, and David, 1961). Single cases of oesophageal rupture in adults were reported by Mahon and Robision in 1960 and by Ross in 1961. The preoperative diagnosis in both of these cases was perforated peptic ulcer. The case reported by Ross (1961) was found to have a rupture of the middle third of the oesophagus at autopsy. There have been only 3 other reported cases of spontaneous middle-third perforation and 1 case of cervical oesophageal rupture (McKeown, 1965). Briggs, Hamel, and Schulkins reported 8 cases in 1961, 1 of which was diagnosed correctly on admission. Three fatal cases were reported by Bruno, Grier, and Ober in 1963. In reviewing all of their cases of perforation of the oesophagus from all causes (instrumental, anastomotic leak, etc.), Foster, Jolly, and Sawyers (1965) found 5 cases of spontaneous rupture. An excellent collective review on the subject was published by Tesler and Eisenberg in 1963. In 1968 Thal reported 6 cases which were treated by his fundic patch valvuloplasty operation, with 5 cures. In 1969 Wychulis, Fontana, and Payne, from the Mayo Clinic, published their experience with instrumental and non-instrumental perforations of the oesophagus. They presented 4 cases of post-emetic rupture occurring in non-diseased organs, with a survival rate of 50 per cent. In the same study they presented 4 other post-emetic perforations associated with oesophagitis or stricture. There were no survivors in this latter group, all of whom were operated on more than 24 hours after the onset of their illness. In 1969 Berne, Shader, and Doty reported 5 cases with 5 cures. Of interest and much significance is the fact that all of these cases were treated successfully by an abdominal approach, which is discussed later in this paper. Apparently, this disease is being recognized more frequently in recent years, and therefore the results from earlier treatment are improving.

Aetiology.—The common physiological denominator in nearly all cases is an explosive act of vomiting or violent retching, often occurring after a large meal. A few cases have been reported where vomiting did not occur, but these cases were associated with acts which increased intra-abdominal pressure: childbirth (Kennard, 1950), straining at defaecation (Beal, 1959), and a convulsive seizure (Klein and Grossman, 1943). Two cases have been reported which followed forceful swallowing (Conte, 1966). No other known case has been reported where massive upper gastro-intestinal haemorrhage was the precipitating factor, as occurred in the second patient presented here, and incidentally it is also believed that he is the oldest survivor reported. Mackler (1952), on the basis of extensive experimental work on fresh cadaveric oesophagi, believes that rupture is due to a sudden violent increase in intra-abdominal pressure with explosive expulsion of a large amount of gastric contents into a fully relaxed oesophagus, the tear occurring where this massive distension is initially sustained—the distal oesophagus. It may also be significant that the distal oesophagus lacks the buttressing quality afforded the proximal and mid-oesophagus by such comparatively unyielding structures as the trachea, aortic arch, descending aorta, left bronchus, pericardium, and various autonomic nerve plexuses. However, in 95 per cent of cases the tear characteristically occurs in the left postero-lateral aspect of the distal oesophagus. At present there is no suitable explanation for this particular site of predilection. The tear is nearly always longitudinal in nature, measuring 2-4 cm., and located 3-6 cm. above the diaphragm. The longitudinal nature of the tear is explained by Derbes and Mitchell (1956) by mathematical analysis, using the principle of free body diagrams which show that hydrodynamic factors incident to increased internal pressure compel the oesophagus to tear in a vertical plane.

Signs and Symptoms.—The classic symptomatology consists of sudden, severe, low anterior chest or epigastric pain, precipitated by a violent act of vomiting or retching. The pain is unremittingly excruciating and may radiate into the neck, arms, or back. Dyspnoea, cyanosis, and orthopnoea develop rapidly, and peripheral vascular collapse may soon appear. Swallowing often aggravates the pain, and if the swallowing is followed shortly thereafter by a bout of coughing, it may safely be assumed that the mediastinal pleura has ruptured and that the oesophageal tear communicates with the pleural cavity. It should be remembered that any act which increases intra-abdominal pressure, even forceful swallowing, may be the precipitating factor.

Physical examination usually reveals a critically ill patient, most often a male—males outnumber females by 5 to 1. The patient is usually sitting up in bed in a crouched forward position. Varying degrees of dyspnoea and cyanosis are often present. Subcutaneous emphysema is frequently present over the chest wall and classically in the suprasternal notch. Evidence of hydro- or pneumothorax may be present on clinical examination. The abdomen is often rigid with varying degrees of epigastric or generalized abdominal tenderness. Radiographic examination of the chest is helpful if it shows free mediastinal air or hydro- or pneumothorax. Lipiodol or gastrografin swallow is diagnostic if the contrast material is shown to leak into the mediastinum or pleural cavity. Oesophagoscopy has been used successfully on several occasions (Carter and Hinshaw, 1965).

Differential Diagnosis.—Many acute surgical and medical catastrophes may partly mimic and be mistaken for spontaneous rupture of the oesophagus. The most common misdiagnosis is a perforated ulcer. This is followed by myocardial infarction, dissecting aneurysm of the aorta, spontaneous pneumothorax, acute cholecystitis, pancreatitis, pulmonary embolism, incarcerated or strangulated diaphragmatic hernia, etc. Some of the diagnostic aids already alluded to may be of great value, but a suspicious awareness of the condition is of equal or greater importance in reaching a correct diagnosis.

Treatment.—There is universal agreement among writers on the subject that surgical repair should be performed as soon as possible. The first successful surgical repair was performed by Barrett (1947).

A few isolated cases of recovery have been reported following closed-chest drainage. In their review of 157 cases collected from the world literature Derbes and Mitchell (1956) found that 55 cases had been treated surgically, with a mortality rate of 36 per cent. They were also able to document in a most dramatic fashion the fate of 71 of the remaining cases which had been treated by non-surgical methods. Of these 71 medically treated cases, 25 per cent died within 12 hours, 75 per cent were dead within 36 hours, while the remainder were all dead within 7 days.

As has previously been mentioned, the best results are obtained when the diagnosis is made early in the course of the disease and surgical repair is performed promptly. Frequently, however, the perforation may have occurred many hours or days before the correct diagnosis is made, and in the past the mortality in this group has been very high. These critically ill patients, when subjected to thoracotomy, present a very perplexing problem to the surgeon. The distal oesophagus is extremely inflamed and oedematous and is surrounded by a suppurative mediastinitis. After the necessary débridement of the necrotic edges of the laceration, these inflamed and swollen oesophageal tissues do not readily retain sutures placed for closure of the defect, and breakdown of the repair is a frequent unfortunate outcome.

In recent years Thal (1968) has applied his fundic patch valvuloplasty operation to these late post-emetic perforations, ranging from 18 to 36 hours in duration, and has reported excellent results in 5 out of 6 cases. This operation, which is more frequently used for distal oesophageal acid peptic stricture, achalasia, and hiatus hernia, with some modification in these latter cases, consists essentially of the following steps: a thoracic approach, generous division of the diaphragm through the central tendon, and free mobilization of the upper stomach by division of the vasa brevia. The fundus of the stomach is then readily brought up into the chest and the necrotic edges of the old perforation are widely débrided. The fundus of the stomach is then placed over the oesophageal defect and sutured to the edges of the defect which are free of any tension. This fundic patch later becomes lined with squamous epithelium. A functioning, competent oesophagogastric valve is then obtained by a second layer of sutures approximating the remainder of the fundus to the right and left posterolateral aspects of the oesophagus which, in fact, invaginates the distal oesophagus into the fundus. At the end of the procedure the stomach embraces at least two-thirds of the circumference of the oesophagus over a length never less than 5 cm. Woodward (1968) has modified this procedure by wrapping the fundus around the complete circumference of the oesophagus after the insertion of the fundic patch.

Whatever the eventual place accorded fundic patch valvuloplasty in the treatment of oesophageal acid peptic stricture, achalasia, and hiatus hernia, it has unquestionably proved its merit in managing those cases of spontaneous post-emetic perforation of the oesophagus in which the diagnosis and treatment are long delayed. In the past the surgical approach to the oesophagus in these cases was through a thoracotomy incision. However, nearly all of these lacerations occur in the distal oesophagus and since experience with transabdominal vagotomy for peptic ulcer has demonstrated that the distal oesophagus can be very adequately exposed and mobilized through an upper abdominal incision, this seemed a logical surgical approach to Berne and others (1969). In 1969 Berne and others presented 5 cases in which the rupture was proved radiographically to exist in the distal oesophagus. All cases were operated on by an upper abdominal midline incision, and the distal oesophagus was mobilized by performing a bilateral truncal vagotomy. In all cases a circumoesophageal gastric fundoplication was used to buttress the repair. In addition, a gastric drainage procedure and gastrostomy was done. The operative site was drained transabdominally by soft rubber or sump drains, and closed-tube thoracostomy drainage was used as indicated. A satisfactory outcome was obtained in all 5 cases.

In 1965 Sanderson reported an interesting case who recovered from an obscure, almost fatal illness which had been precipitated by nausea and vomiting. Three months later the patient underwent a thoracotomy for decortication of visceral and parietal pleura because of marked pleural thickening. Pathological examination of the submitted specimens showed vegetable fibres within multiple granulomas. In retrospect, this is probably the only patient who recovered from a spontaneous rupture of the oesophagus without surgical aid.

In recent years there have been very encouraging results obtained by the conservative management of upper oesophageal perforation caused by endoscopy. Mengoli and Klassen (1965) reported 18 such cases who were treated conservatively, with only 1 death. Shapiro (1965) has accumulated a series of 24 cases who were treated conservatively, without a single fatality. In 1969 Wychulis and others (1969) presented 24 cases of instrumental cervical oesophageal perforation. All of these recovered with conservative treatment, which included cervical mediastinotomy with drainage in 17 cases. Instrumental perforations occur during the course of an endoscopic examination on an empty stomach, and are sometimes suspected or recognized at the time that they occur. The most common location for endoscopic perforation is the cervical oesophagus, where local tenderness, subcutaneous emphysema, pain, and fever often appear early and attract the attention of the alert endoscopist. Treatment, which usually includes surgical drainage, is started early in most cases, with excellent results. On the other hand, spontaneous rupture of the oesophagus occurs explosively on a full stomach with consequently greater spillage and contamination of the mediastinum; moreover, the diagnosis and treatment of spontaneous rupture are often delayed for many hours. It is very unlikely that the results from conservative treatment, even with the help of modern therapy, would match those obtained by surgical closure of the perforation.

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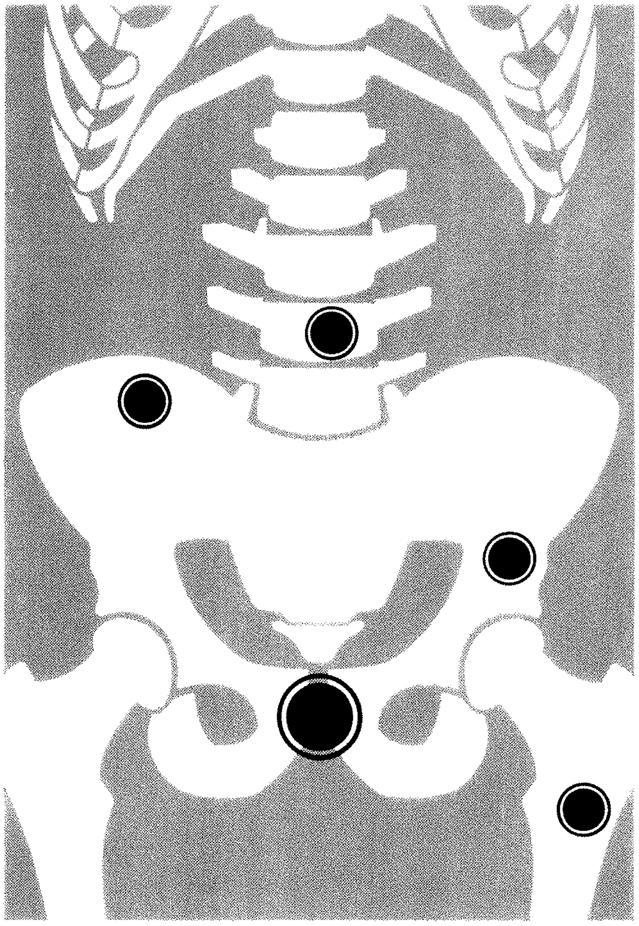

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THE EFFECTS OF CALCULI ON URETERAL FUNCTION

By J. A. ROSS and P. EDMOND

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SUMMARY

The dynamic action of the renal pelvis and ureter has been studied in 50 patients with ureteral colic due to calculi.

Calculi in the renal tract, passing down and obstructing the ureter, profoundly disturb the normal intraluminar pressure and peristaltic activity. Initially, there is a rise in pressure above the obstruction with increased peristaltic activity, which is later followed by a marked depression of this activity.

Fatigue from prolonged stretching of the ureteral muscle and the lack of normal stimulus owing to diminished secretion of urine are considered to be the most likely explanation for this loss of activity.

Urgent relief of the obstruction is the logical treatment, and the policy of forcing fluids in the presence of an obstructed ureter may be questioned. The relief of pressure with retrograde catheterization at an earlier stage than is the current practice should be considered.

MOST patients with colic resulting from calculous disease of the upper urinary tract are treated empirically and they pass the calculus spontaneously. When symptoms or stones persist retrograde catheterization may be performed in order to provide both information and treatment.

Ureteral colic has gross effects on the physiological action of the kidney and its outflow tract (Ross, McNair, Isaac, Thomson, and High, 1962; French and Robb, 1963; Smith, 1966). In 87 patients with renal colic associated with calculi, intravenous pyelography during the attack showed delayed or impaired function with nephrogenic effects in 82 instances (94 per cent). Further confirmation of the rise of intrarenal pressure is the development of renal peripelvic and pyelosinus extravasation which have been reported in acute renal and ureteral colic (Harrow, 1966, 1969; Hale and Whitehouse, 1970) (*Fig.* 1).

Pressure recordings during retrograde pyelography have been used to study the dynamic activity of the ureter in various conditions (Ross, Edmond, Coull, and Simpson, 1965; Ross, Edmond, Coull, and Griffiths, 1967; Edmond, Ross, and Kirkland, 1970). This technique has now been employed in the investigations of patients with calculous disease.

MATERIALS AND METHODS

Fifty patients who had been admitted to hospital with ureteral colic were studied. Urinary infection was not a prominent feature in these patients and a significant culture was obtained in only 7 cases: *Escherichia coli* in 4, *Proteus* in 1, *Staphylococcus albus* in 1, and a mixture of *E. coli*, *Proteus*, and enterococci in 1.

The *site* of recording in relation to the position of the calculus was as shown in *Table I*.

Time Factor.—Patients were treated initially with analgesics, antispasmodics, and fluids. Retrograde ureteral catherization was carried out if the stone had not moved appreciably or if discomfort persisted.

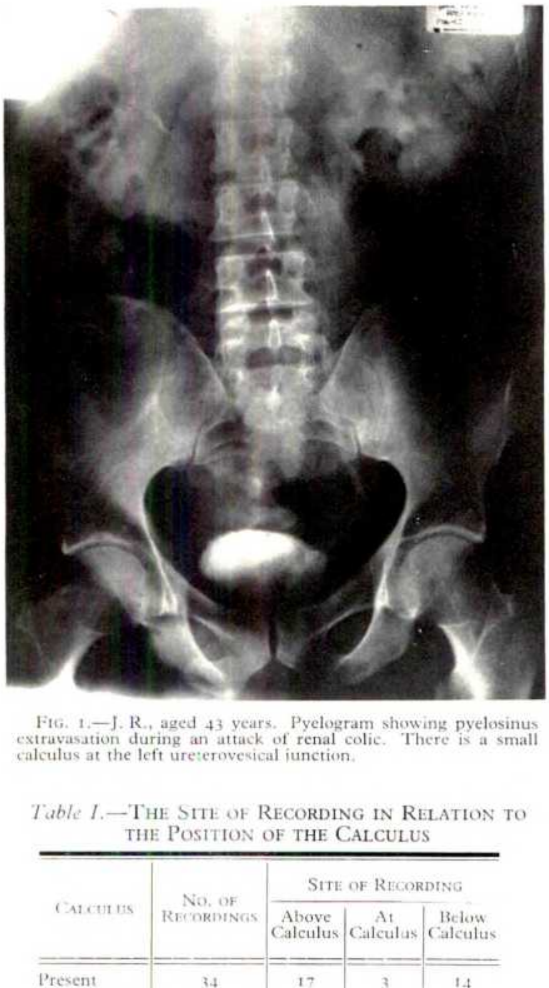

FIG. 1.—J. R., aged 43 years. Pyelogram showing pyelosinus extravasation during an attack of renal colic. There is a small calculus at the left ureterovesical junction.

Table I.—THE SITE OF RECORDING IN RELATION TO THE POSITION OF THE CALCULUS

CALCULUS	NO. OF RECORDINGS	SITE OF RECORDING		
		Above Calculus	At Calculus	Below Calculus
Present	34	17	3	14
Passed or removed	16	—	—	—

In 5 patients colic was present at the time of recording. In the others the recordings were made within 5 days of the patient's admission or within 5 days of the intravenous pyelogram showing nephrogenic effects. In 1 patient a second record was taken from the same level 2 years after the removal of a calculus.

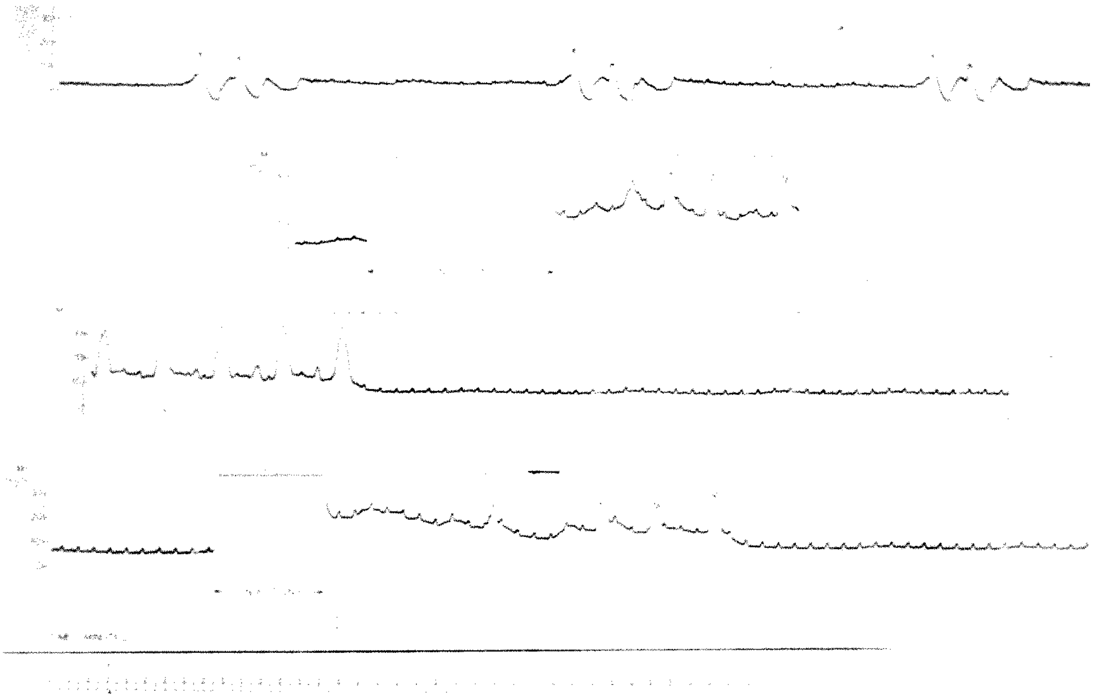

FIG. 2.—E. H., aged 32 years. Consecutive tracings showing slow infrequent contractions above a calculus which is still in situ in the lower third of the ureter. Peristalsis was stimulated by the injection of fluid (twice), which also caused a rise in basal pressure.

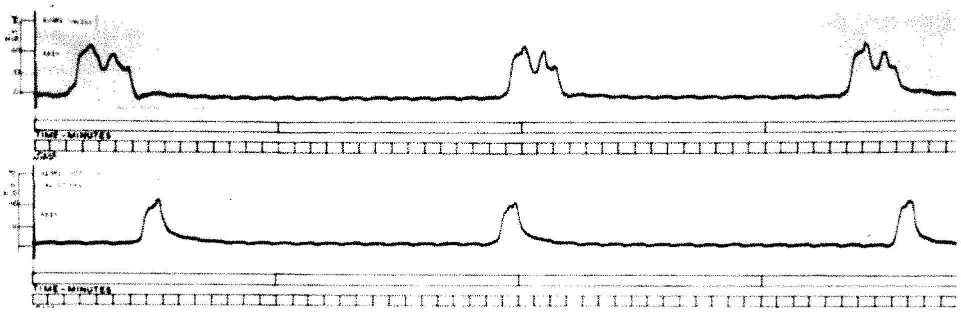

FIG. 3.—M. W., aged 56 years. This patient had had severe right renal colic 4 days before the pressure was recorded. The upper tracing was taken just below the calculus at the pelvi ureteral junction, while the lower tracing was recorded at 15 cm. from the bladder. Note the slow, rather prolonged contractions.

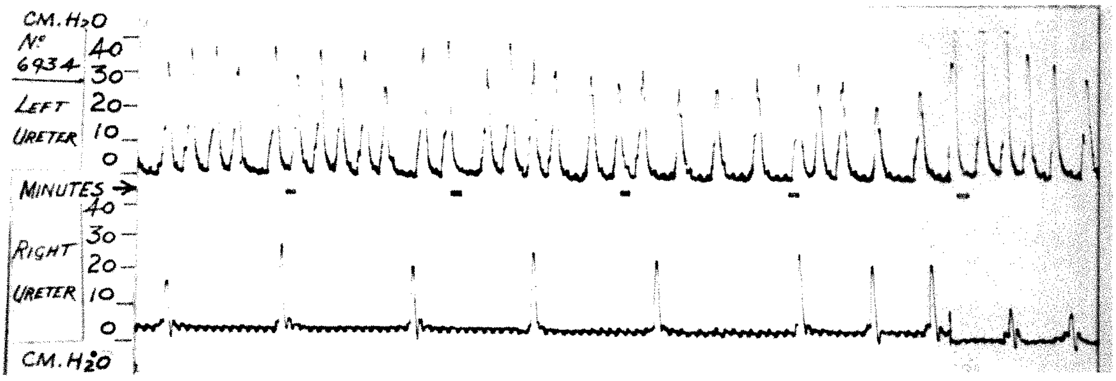

FIG. 4.—J. C., aged 59 years. Tracings made 10 days after an attack of right renal colic. Both ureters were recorded simultaneously. Note the contrast between the normal contractions of the left ureter and the much smaller and slower contractions of the right ureter.

OBSERVATIONS

The rate, amplitude, rhythm, and form of the peristaltic wave were noted and in some patients records were obtained from the unaffected side and were available for comparison.

The normal basal pressure in the ureter is about 14 cm. H_2O (Rattner, Fink, and Murphy, 1957; Ross and others, 1967), but it can readily be raised by extrinsic compression and by injection of fluid. In 5 patients where records were taken above the calculus during an attack of colic, a high basal pressure was demonstrated. Even in the absence of colic the basal pressure was invariably increased to some degree above the calculus.

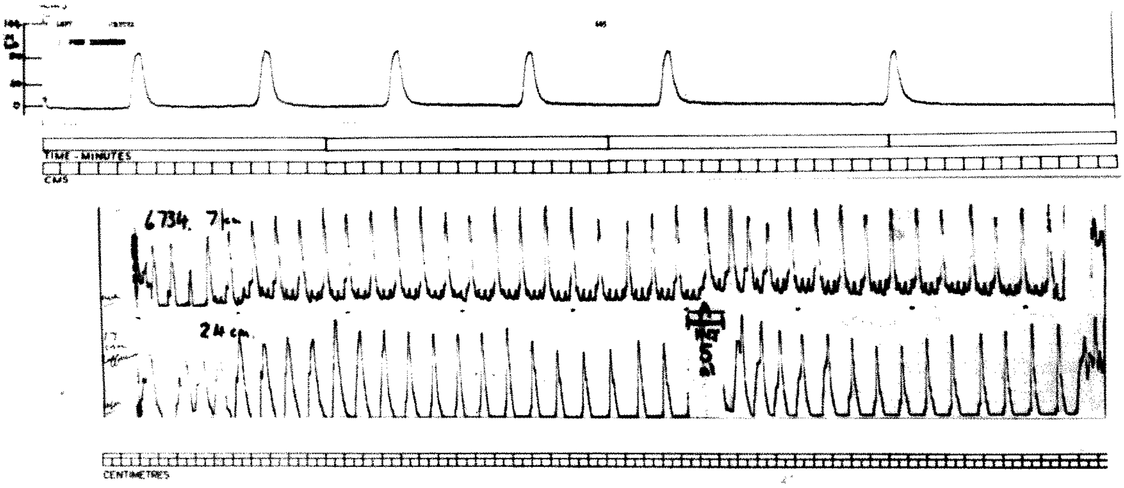

FIG. 5.—E. S., aged 27 years. The top tracing is from the left ureter at 11 cm. from the bladder, just below a calculus. Note the infrequent contractions. The calculus was subsequently removed at operation. The lower tracings are from the same patient 2 years later. Simultaneous tracings from the left ureter at 7 (middle tracing) and 24 cm. (bottom tracing) show normal activity.

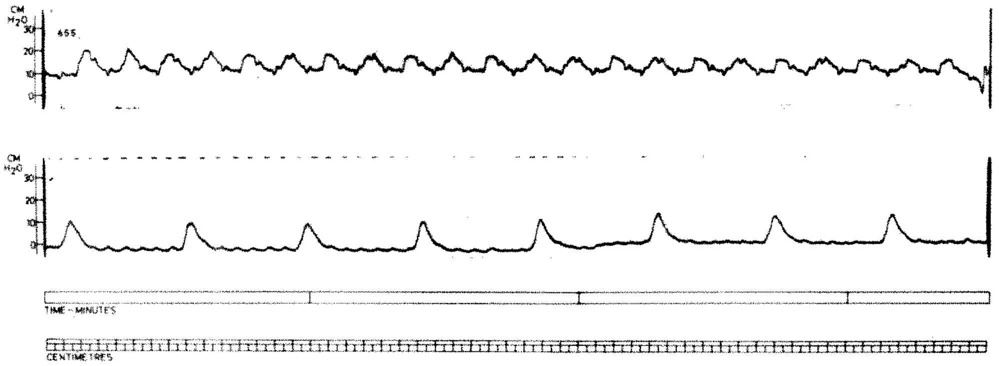

FIG. 6.—T. L., aged 38 years. A calculus was present in the left ureter. The upper tracing shows a rise in basal pressure and an increased rate of contraction but no increase in amplitude during an attack of colic. This contrasts with the normal pressure and the reduced rate of contraction in the lower tracing, for which the patient was conscious and pain-free and had unimpeded drainage down the ureter.

In obstructed ureters, when filled with radio-opaque fluid for pyelography purposes, the basal intraluminar pressure rose considerably and took much longer to return to normal than in unobstructed ureters (*Fig.* 2). Zimskind, Davis, Lewis, De Caestecker, and Berwind (1968) showed experimentally in dogs that after acute ureteral obstruction, pressure in the ureter rises sharply and remains elevated for the following 8 hours.

Reduction in the rate or amplitude, and sometimes both, of the peristaltic contractions was demonstrated in the 45 instances where pain was not a feature at the time of the examination. This finding was irrespective of the level at which the record was obtained (*Figs.* 3, 4). Several factors probably contribute to this:—

1. Infection.—This was not an important factor in the present series since in most records with marked diminution in rate and amplitude of the peristaltic waves the urine was sterile. Under experimental conditions, coliform organisms have been shown to reduce peristaltic activity (Teague and Boyarksy, 1968a, b). In long-standing infected cases it is inevitable that the associated fibrosis of the pelvic and ureteral muscle would be an important factor in diminished activity, as has been shown in other conditions (Ross, Edmond, and Kirkland, 1968).

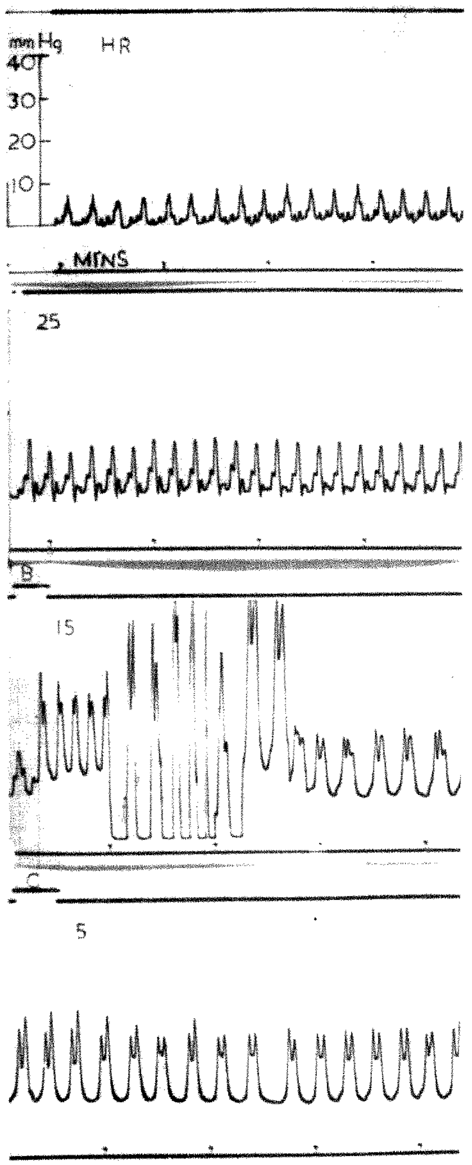

FIG. 7.—H. R., aged 23 years. A small (2-cm.) calculus was arrested at 15 cm. The pressure recordings show hyperactivity at the level of the calculus. Reading from the top to the bottom the tracings correspond to the level of the pelvis, and 25, 15, and 5 cm. from the bladder.

2. Antispasmodic Drugs.—In 6 patients who were being treated with antispasmodic drugs, records were taken from the normal side as well as from the side affected by the calculus. In each instance normal peristalsis was observed on the normal side, suggesting that the drugs did not have any appreciable physiological effect at the time of study.

3. Hypoplasia of the Pelvic and Ureteral Musculature.—Diminished ureteral activity could result from hypoplasia of the muscles. This may be a factor in a small number of patients, but a return to the normal pattern of activity after the passage of a calculus is usually observed (*Fig.* 5).

4. Fatigue of the Musculature.—The muscle of the renal outflow is active at first in the endeavour to pass the calculus. In records during colic this activity was noted (*Figs.* 6, 7), and it is often successful in ridding the ureter of its obstruction. In a personal series (J. A. R.) of 91 patients with ureteral colic (50 right-sided, 41 left-sided) only 9 required operative removal of the calculus. Records were usually taken after the colic had subsided, and the diminished activity observed may be due to temporary fatigue from overstretching of the musculature. When a ureter is distended the intraluminal pressure rises, the contractions practically cease or their effective amplitude becomes small, and they do not regain their normal amplitudes for some minutes (*Fig.* 8).

Murnaghan (1957) has demonstrated that after prolonged stretching, muscle ceases to function normally. If the outlet of the isolated ureter is completely occluded the entire musculature becomes overstretched and eventually inert under these adverse conditions. Forced diuresis, which is so often employed in the treatment of renal colic, will tend, initially, to increase the overdistension, and this in turn may decrease the effective peristaltic activity of the ureter.

5. Absent or Diminished Flow of Urine.—The changing volume of its contents is the main stimulus to ureteral activity (Lapides, 1948). When the outflow from the kidney is obstructed by a calculus the pressure within the pelvis rises, initially producing the 'nephrogenic' effect seen on the intravenous pyelograms and later even disruption of the pelvis. This initial rise in pressure is not maintained when the kidney ceases to form urine, and pressure in the pelvis becomes equal to, or higher than, the glomerular filtration level.

The reduced activity of the ureter after a calculus has passed indicates that normal function may not have returned and that the stimulus of a normal flow of urine may still be lacking. How long the ureter

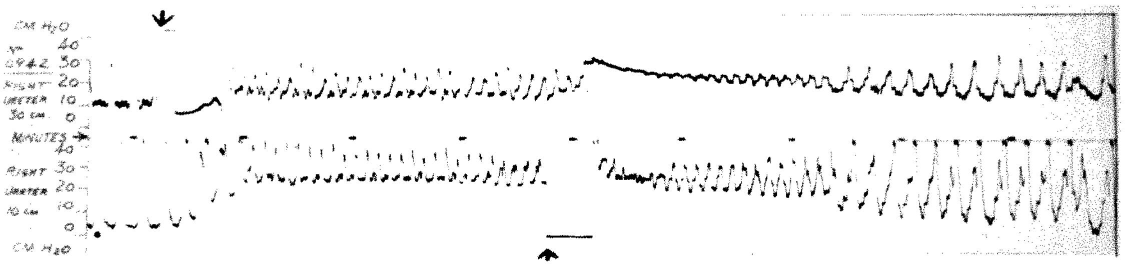

FIG. 8.—A. H., aged 50 years. Simultaneous tracings from the right ureter at 30 cm. (upper tracing) and 10 cm. (lower tracing) from the vesico-ureteral junction, showing the effect of stretching the ureteral wall by filling first at 30 cm. and then at 10 cm. (arrows).

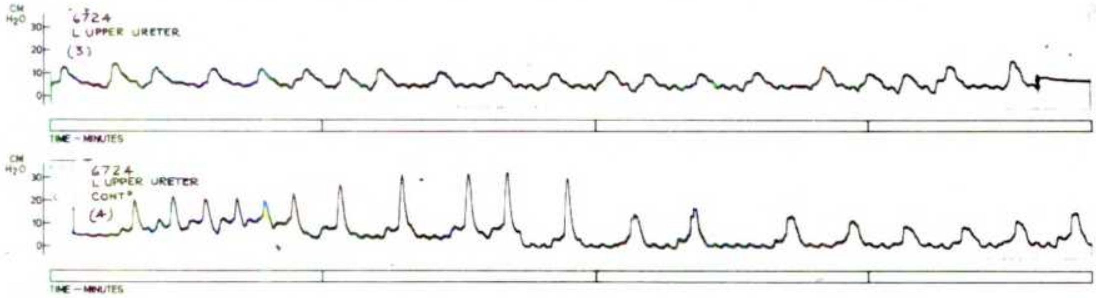

FIG. 9.—M. K., aged 31 years. A calculus was present in the left pelvis. A tracing from the left upper ureter below the calculus shows small contractions, which were stimulated to a bigger amplitude by injecting 5 ml. fluid at the beginning of the lower tracing.

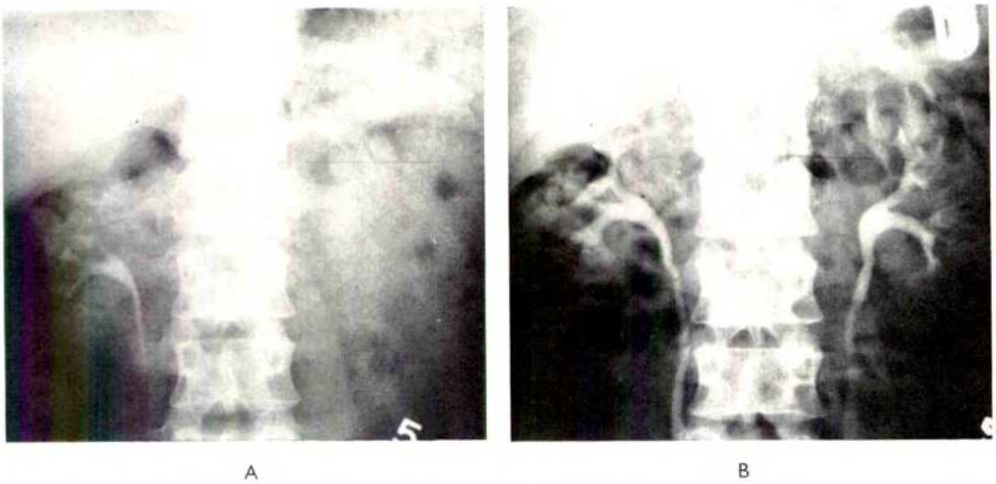

FIG. 10.—T. H., Intravenous pyelograms taken (A) during an attack of left renal colic, and (B) 6 days later, showing recovery of function after the passage of a small calculus.

takes to recover is not known, but peristalsis can be immediately reactivated below a calculus by injecting a quantity of fluid from below (*Fig.* 9). Intravenous pyelograms after the passage of a calculus often show a return to normal excretion (*Fig.* 10). Davies, Jones, Croft, and Shuttleworth (1969), in their assessment of pyeloplasty by radioactive renography, show that the parenchymal function returns to normal earlier than had been suspected, and Caine and Hermann (1970) have shown that, even after anastomosis, transmission of the peristaltic wave occurs between the twenty-third and the twenty-sixth days.

The period of delay in the return of function after the passage of a calculus must vary in individual cases, but in the early postcolic phase the absence of the normal stimulus is probably one of the main factors causing the reduced activity of the ureter which is so constantly observed.

Acknowledgements.—We wish to thank Dr. J. G. Sclater, Dr. J. Munro, and Mr. J. Cook for their co-operation in this study.

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CARCINOMA OF THE DUODENUM

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SUMMARY

Five patients with carcinoma of the second part of the duodenum, presenting with obstructive jaundice, are discussed. The diagnosis was established at operation and radical surgery was not possible in any case. Local excision of the tumour and the adjacent duodenal wall with reanastomosis of the bile-duct and pancreatic duct to the duodenum were performed. Three patients died from the disease within 1 year of operation and 2 patients are still alive 16 and 18 months after operation. The clinical features of this disease are reviewed.

PRIMARY carcinoma of the duodenum is rare. The initial symptoms are vague, and patients with this condition often present a perplexing diagnostic dilemma. The diagnosis is frequently not established until the pathological process has extended beyond the bounds of surgical redemption.

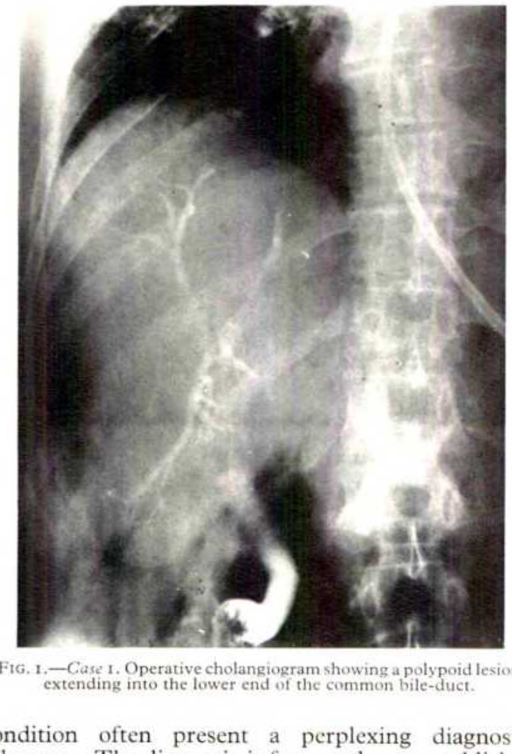

FIG. 1.—*Case* 1. Operative cholangiogram showing a polypoid lesion extending into the lower end of the common bile-duct.

The purpose of this paper is to report 5 cases of carcinoma of the duodenum presenting with obstructive jaundice and to review the disease.

CASE REPORTS

Case 1.—Mrs. E. H., a housewife aged 61 years, had had transient episodes of obstructive jaundice in 1957 and 1964. In December, 1968, she had been admitted elsewhere with a third attack of jaundice. Laparotomy had revealed non-calculous cholecystitis with one minute calculus in the common bile-duct. A dilator had passed easily into the duodenum. Cholecystectomy had been performed. A subsequent T-tube cholangiogram had shown a filling defect of the medial duodenal wall but the contrast medium had flowed freely into the duodenum.

One month later the patient was admitted to the Royal Free Hospital with recurrent obstructive jaundice. Laparotomy revealed a polypoid neoplasm of the medial duodenal wall which was shown by cholangiography to be extending into the lower end of the common bile-duct (*Fig.* 1). There were several enlarged lymph-nodes in the porta hepatis and lesser omentum. Local excision of the tumour (*Fig.* 2) and the adjacent duodenal wall were performed, and the common bile-duct and pancreatic duct were reanastomosed to the duodenum separately.

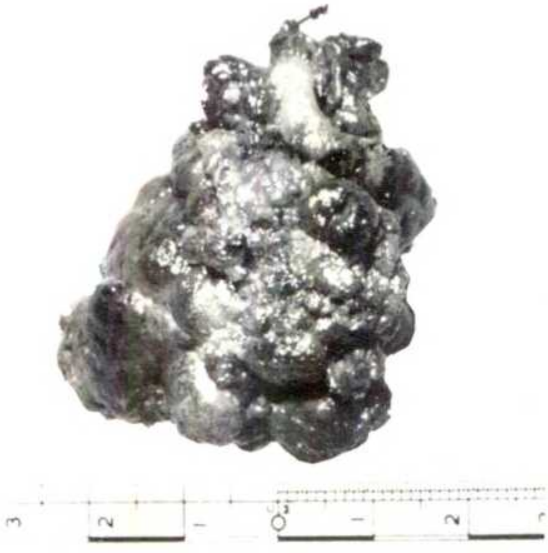

FIG. 2.—*Case* 1. Tumour excised from the duodenal wall.

Histologically, the tumour was a well-differentiated papillary columnar-cell carcinoma of the duodenum (*Fig.* 3).

The patient remains well to date.

Case 2.—Mrs. L. T., a housewife aged 53 years, had developed transient obstructive jaundice in November, 1968, after removal of a benign ovarian cyst. Jaundice had recurred 1 month later. She had complained of pruritus for 1 year and had lost 19 kg. in weight. When admitted to hospital, hepatomegaly was the only abnormal physical sign. The haemoglobin was 10·5 g. per cent, serum bilirubin 0·8 mg. per cent, and alkaline phosphatase 46 K.A. units. A cholecystogram showed no concentration of dye in the gall-bladder after a double dose of contrast. Liver biopsy showed changes suggestive of large-duct obstruction, and a liver scan showed filling defects in both lobes of the liver. Preoperative percutaneous cholangiography demonstrated a dilated biliary tree with obstruction at the lower end of the common bile-duct (*Fig.* 4).

At operation there was a pedunculated neoplasm of the medial wall of the second part of the duodenum adjacent to the ampulla of Vater. There were several secondary deposits in the liver. Local excision of the tumour and adjacent wall was performed and the common bile-duct and pancreatic duct were reanastomosed separately to the duodenum.

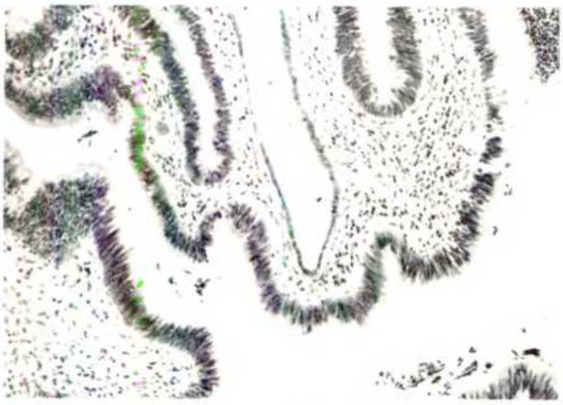

FIG. 3.—*Case* 1. Adenocarcinoma of the duodenal wall. (× 20.)

Histologically, the tumour was a papillary adenocarcinoma arising from the duodenal wall (*Fig.* 5).

When last seen in December, 1969, she felt well but had hepatomegaly.

Case 3.—Mr. H. P., aged 59 years, was known to have familial intestinal polyposis. He had had abdomino-perineal excision of a carcinoma of the rectum in 1953 and a total colectomy for carcinoma of the ascending colon in 1955. He had then remained well until 1968 when he had started to lose weight and had become jaundiced.

When admitted to the Royal Free Hospital in December, 1968, he was jaundiced and the liver was enlarged. The E.S.R. was 122 mm. per hour, serum bilirubin 3·6 mg. per cent, and alkaline phosphatase 100 K.A. units. A percutaneous liver biopsy showed the histological features of large-duct biliary obstruction, and percutaneous cholangiography showed a grossly dilated biliary tree (*Fig.* 6).

At operation there was a papillary neoplasm of the medial wall of the second part of the duodenum, infiltrating the duodenal wall and obstructing the common bile-duct and pancreatic duct. Resection was not possible and cholecystectomy, choledochojejunostomy, and gastrojejunostomy were performed.

Biopsy of the tumour showed an invasive papillary adenocarcinoma of the duodenum (*Fig.* 7).

He developed jaundice and hepatomegaly and died in October, 1969, 9 months after operation.

Case 4.—Mrs. M. H., a housewife aged 82 years, was admitted to the Royal Free Hospital in July, 1967, with a 3-week history of right hypochondrial pain and jaundice. The liver and gall-bladder were palpable. The serum bilirubin was 6·2 mg. per cent and alkaline phosphatase 123 K.A. units. An operative cholangiogram showed a dilated common bile-duct (*Fig.* 8).

Exploration revealed a sessile neoplasm of the medial wall of the second part of the duodenum, obstructing the common bile-duct and pancreatic duct. Local excision of the tumour was performed.

Histological examination showed a well-differentiated adenocarcinoma arising from the duodenal mucosa (*Fig.* 9).

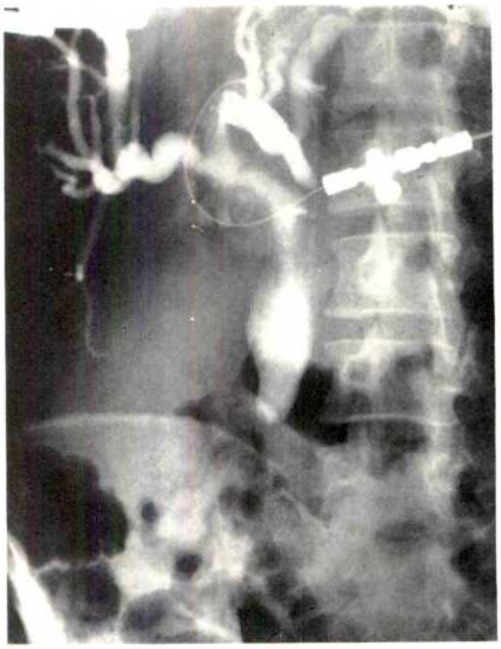

FIG. 4.—*Case* 2. Percutaneous cholangiogram showing obstruction of the lower end of the common bile-duct.

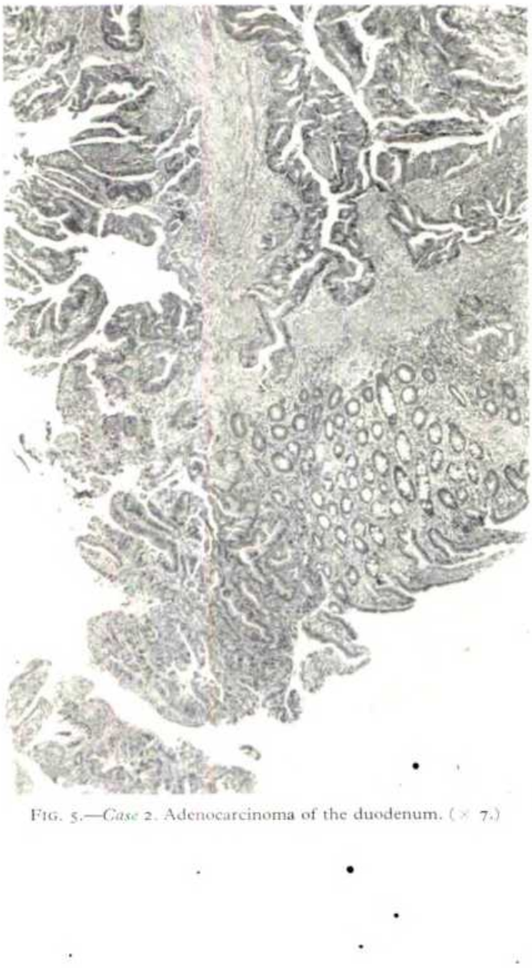

FIG. 5.—*Case* 2. Adenocarcinoma of the duodenum. (× 7.)

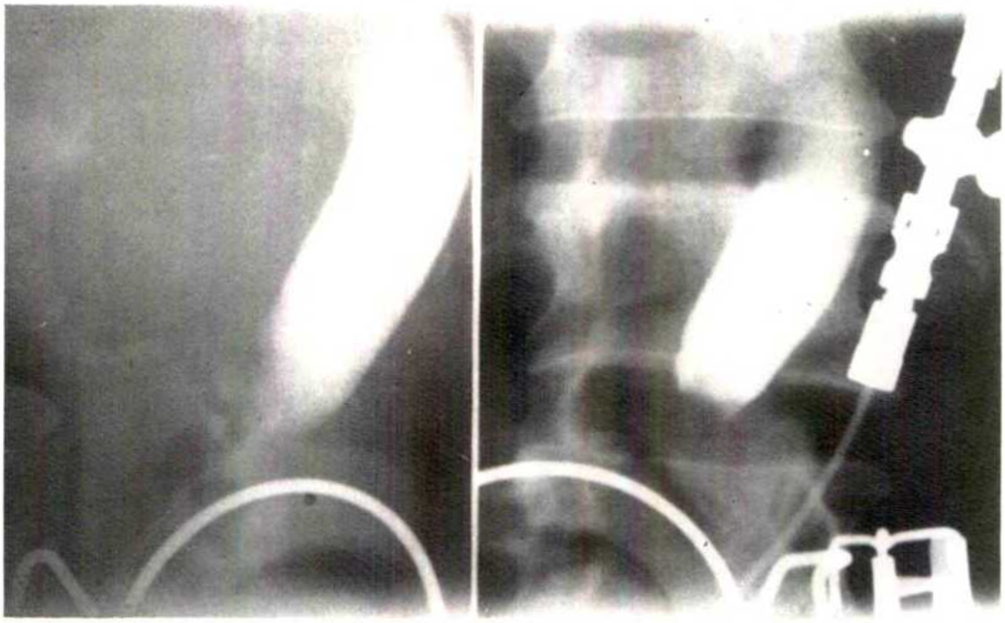

FIG. 6.—*Case* 3. Percutaneous cholangiograms showing obstruction of the lower end of the common bile-duct.

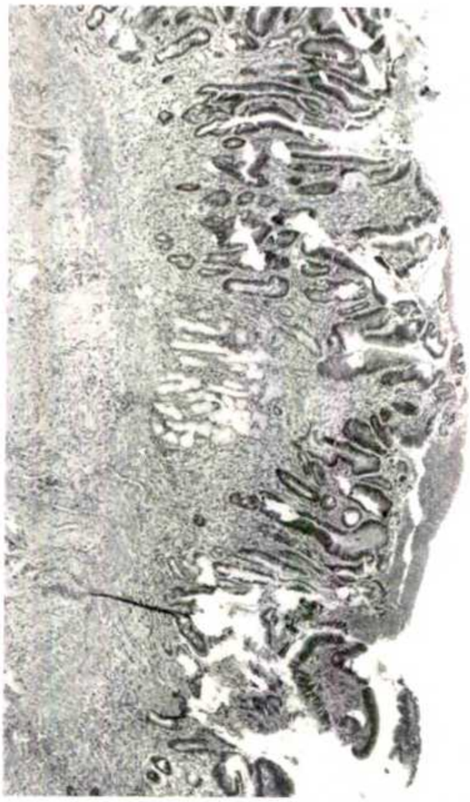

FIG. 7.—*Case* 3. Biopsy of a tumour showing an adenocarcinoma of the duodenum.

The patient remained well until August, 1968, when the jaundice recurred, and she died 12 months after operation.

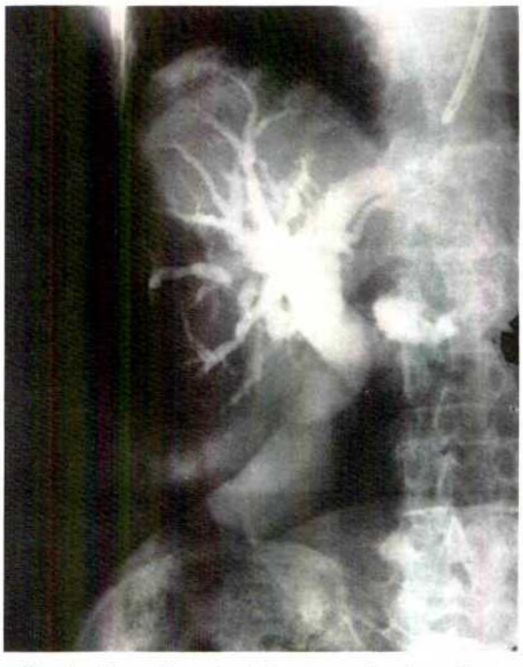

FIG. 8.—*Case* 4. Operative cholangiogram showing a dilated common bile-duct.

Case 5.—Mr. P. C., aged 64 years, was admitted to the Royal Free Hospital in July, 1967, with jaundice, epigastric pain, and weight-loss. He was deeply jaundiced and the liver was enlarged. The E.S.R. was 122 mm. per hour, serum bilirubin 12·5 mg. per cent, and alkaline phosphatase 41 K.A. units.

At operation the common bile-duct was grossly dilated. Cholangiography confirmed an obstruction at the lower end of the duct (*Fig.* 10). Exploration revealed a pedunculated neoplasm of the medial wall of the second part of the duodenum, obstructing the common bile-duct and pancreatic duct. Local excision of the tumour was performed and the common bile-duct and pancreatic duct were anastomosed separately to the duodenum.

Histologically, the tumour was a well-differentiated adenocarcinoma of the duodenal mucosa (*Fig.* 11).

In February, 1968, the patient developed jaundice, ascites, and massive hepatomegaly, and he died in March, 1968, 8 months after operation.

HISTORICAL REVIEW

Primary carcinoma of the duodenum was first described by Hamburger in 1746, but it was not until 1932 that the clinical and pathological features were correlated by Mateer and Hartmann. Resnik and Cooper (1958), in a review of the literature of 1948–56, could only find 7 cases that had survived for more than 5 years after definitive surgical treatment. They attributed the poor results, first, to the inability of the clinicians and radiologists to establish the diagnosis while the lesion was still surgically remediable, and, secondly, to the timidity of surgical treatment once the diagnosis had been established.

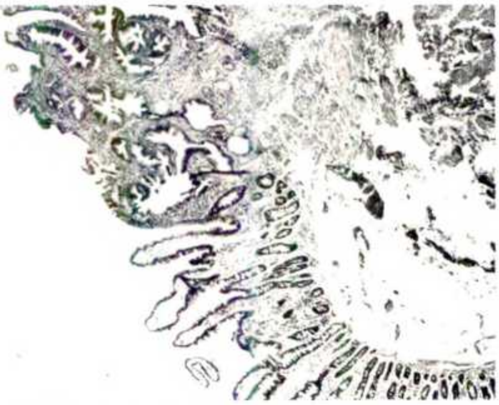

FIG. 9.—*Case* 4. Section showing the transition from normal duodenal mucosa to adenocarcinoma. (× 5.)

INCIDENCE

Primary carcinoma of the duodenum accounts for 0·03–0·05 per cent of all carcinomas (Eger, 1933; Howard, 1943; Burgerman, Baggenstross, and Cain, 1956). Three per cent of gastro-intestinal carcinomas occur in the small intestine and, of these, 45 per cent arise in the duodenum (Burgerman and others, 1956). In 1916 Jefferson stated: ‘considering the shortness of the duodenum, it is evident that inch for inch it is more liable to cancer than the rest of the small intestine’. Primary carcinoma of the duodenum is most common in the fifth and sixth decades but can occur as early as the second decade. Most series report an equal incidence in both sexes.

PATHOLOGY

In a review of 25,032 necropsies Burgerman and others (1956) found 31 cases of malignant duodenal tumours, excluding ampullary lesions. Of these, 87 per cent were adenocarcinomas and the remainder were leiomyosarcomas, lymphosarcomas, and reticulum-cell sarcomas. Thirty-five per cent were situated in the first part of the duodenum, 45 per cent in the second part, and 10 per cent in the third and fourth parts. The macroscopic appearance of duodenal carcinoma takes one of four forms: ulcerative,

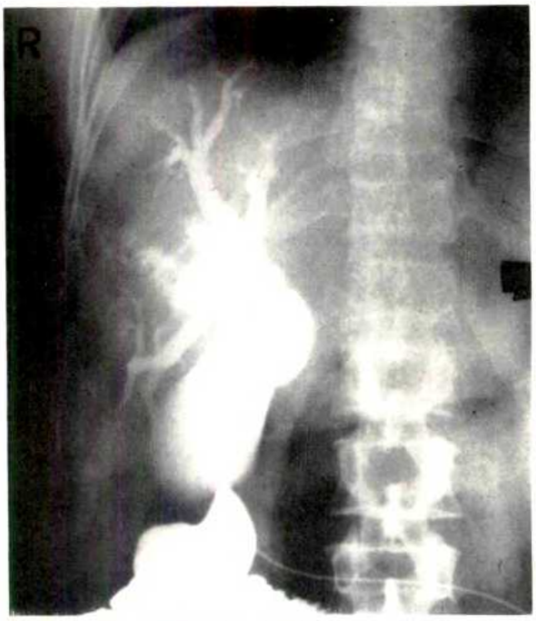

FIG. 10.—*Case* 5. Operative cholangiogram showing a grossly dilated common bile-duct.

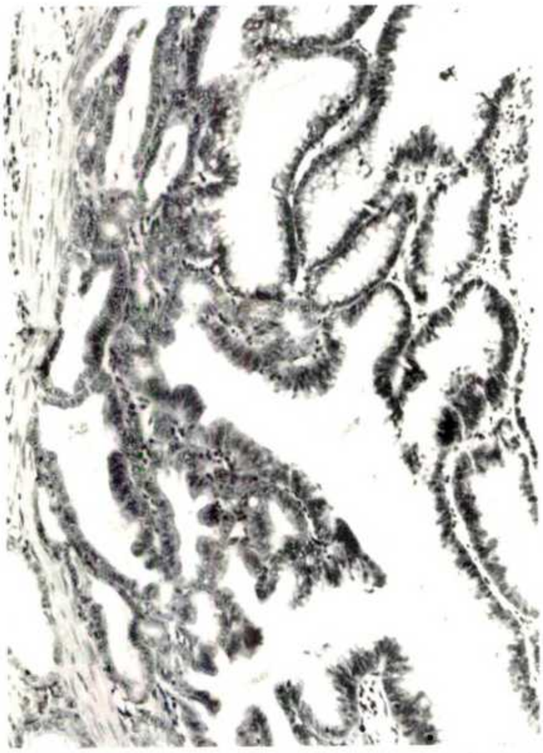

FIG. 11.—*Case* 5. Well-differentiated carcinoma of the duodenal mucosa. (× 27.)

polypoid, annular, and infiltrative, and the average diameter is 4·6 cm. Duodenal carcinomas metastasize to the regional lymph-nodes and the liver, but they may produce widespread metastases later in the course of the disease. Metastases were present in 20 of the 31 cases reported by Burgerman and others (1956). Brenner and Brown (1955), Burgerman and others (1956), and Dixon, Lichtman, Weber, and McDonald (1966) believe that periampullary lesions should be excluded unless there is conclusive proof of their origin from the duodenal mucosa, and this may be extremely difficult to establish. Lieber, Stewart, and Lund (1939) reviewed 229 periampullary lesions and accepted only 3 cases of duodenal origin. All 5 cases reported in the present series were papillary adenocarcinomas and were seen to arise from the duodenal mucosa. They assumed a polypoid form and extended into the duodenal lumen. The transition from normal to neoplastic mucosa is well seen in *Fig.* 9. All cases of periampullary carcinoma when the tissue of origin was in doubt were excluded from this series.

CLINICAL FEATURES

The average duration of symptoms before diagnosis is 10 months. Iovine and Tsangaris (1961) classified the clinical complex into four groups: (1) duodenal obstruction, (2) biliary obstruction, (3) ulceration with haemorrhage, and (4) penetration. Burgerman and others (1956), reviewing 31 cases of duodenal carcinoma, found the incidence of symptoms to be as follows: abdominal pain, 74 per cent; weight-loss, 74 per cent; vomiting, 55 per cent; haematemesis, 23 per cent; melaena, 29 per cent; jaundice, 23 per cent; abdominal mass, 19 per cent; anaemia, 55 per cent.

Abdominal pain is usually localized in the right hypochondrium and has a dull continuous aching quality. Colicky pain occurs with duodenal obstruction. Weight-loss is a constant feature, averaging 10·9 kg. over a period of 3–12 months. Hypochromic anaemia is usually associated with haematemesis and melaena, and occult blood is found in the stools in 48 per cent of cases. The incidence of jaundice in carcinoma of the duodenum—23 per cent of all cases (Burgerman and others, 1956)—is low compared with the figure of 89–100 per cent for other forms of malignancy in this area (Warren, Cattell, Blackburn, and Nora, 1962). However, jaundice is usually the presenting symptom with duodenal carcinoma situated near the ampulla of Vater, as in the 5 cases reported here.

Diagnosis is established by radiological study of the upper gastro-intestinal tract, and the important radiological features are alteration of the mucosal pattern, intraluminal filling defects (tumours larger than 1 cm. should be demonstrable), altered contour and flexibility of the duodenum, and the effects of duodenal obstruction. Radiological study of the duodenum has been enhanced by the introduction of hypotonic duodenography (Kreel and Mackintosh, 1968), and greater use of this technique should enable more frequent preoperative diagnosis.

TREATMENT

Approximately 50 per cent of cases come to surgery, and of these, 54 per cent have palliative surgery and 38 per cent have radical surgery (Berger and Koppelman, 1942). The main operative procedures employed are pancreaticoduodenectomy, segmental resection of the duodenum with or without a portion of the adjacent pancreas, and local resection of the tumour.

Local resection of the tumour is the operation of choice in lesions that are locally malignant and that have not invaded the pedicle or adjacent duodenal wall. This is particularly suitable in elderly patients in whom more extensive procedures might be undesirable. Local excision of the tumour and the adjacent duodenal wall with reconstruction of the biliary and pancreatic ducts is suitable as a palliative procedure in patients unfit for more extensive surgery or when pancreaticoduodenectomy would not be curative. In the 5 cases reported in this series, all symptoms were relieved. Two patients are still alive and 3 have died 8, 9, and 12 months after operation respectively.

Since duodenal carcinoma spreads primarily by lymphatic extension, the ideal treatment is removal of the primary lesion and its lymphatic drainage pathways, as in pancreaticoduodenectomy. The operative morbidity of this procedure is 18·5 per cent and the 5-year survival is 40 per cent (Warren and others, 1962).

DISCUSSION

The 5 patients reported in this series were over the age of 50 years, and 4 had obstructive jaundice at the time of admission. There were no specific clinical features to indicate the nature of the pathology, and the diagnosis in each case was established at operation, although previous barium studies in 1 case suggested the diagnosis.

There were no specific biochemical changes in this series. Very high levels of alkaline phosphatase usually indicate hepatic metastases.

The importance of barium studies of the upper gastro-intestinal tract in patients with obstructive jaundice and occult blood in the stools cannot be overstressed. Tumours of the duodenum of more than 1 cm. are usually demonstrable. Hypotonic duodenography (Kreel and Mackintosh, 1968) is advisable when barium studies alone are unsatisfactory. Cholangiography is advisable in patients submitted to surgery for obstructive jaundice, and particularly when the diagnosis is in doubt. In this series the site of obstruction was demonstrated in each case. Percutaneous transhepatic cholangiography (George, Young, Walker, and Sherlock, 1965) is best performed in the immediate preoperative period and the subsequent surgical relief of the obstruction removes the danger of bile leakage from the puncture site.

Careful palpation of the second part of the duodenum should reveal intraluminal neoplasms, but it may be extremely difficult to locate small tumours and duodenotomy should be performed without hesitation when necessary.

The choice of treatment depends on the extent of the lesion and the general condition and age of the patient. Pancreaticoduodenectomy should be performed when feasible as this gives the best results. The operative morbidity is 18·5 per cent and the 5-year survival is 40 per cent (Warren and others, 1962). In the present series radical surgery was not possible in any case and local excision of the tumour and adjacent duodenal wall was performed. This procedure resulted in the relief of symptoms in each case but was not curative. Three patients survived for 8, 9, and 12 months, respectively, but then died with metastases. Two patients are still alive 16 and 18 months, respectively, after operation, but 1 of these had hepatic metastases at the time of operation.

Carcinoma of the duodenum should be considered in the differential diagnosis of all cases of obstructive jaundice. Careful radiological investigation is the most important diagnostic approach and radical surgery holds the best prognosis.

Acknowledgements.—I wish to thank Miss P. George, F.R.C.S., Consultant Surgeon, Royal Free Hospital, for permission to publish these cases and for assistance in preparation of the manuscript. I would also like to thank the Departments of Pathology and Photography, Royal Free Hospital, for the illustrations.

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BILATERAL DOUBLE NIPPLES

BY TERENCE BRIGHTMORE
WESTMINSTER HOSPITAL, LONDON

SUMMARY

Two cases are reported of bilateral double nipples occurring within the areolae of the normal breasts. The association of congenital lesions of the nipple and certain diseases is discussed.

ALTHOUGH the incidence of supernumerary nipples is fairly common their occurrence within the areola of a normal breast is rare, and the presence of such bilateral double nipples is extremely rare (de Cholnoky, 1939). The following 2 cases exhibiting this condition are therefore of interest.

CASE REPORTS

Case 1.—A 37-year-old white female presented at the Breast Clinic of the Royal Marsden Hospital with a 6-month history of bilateral breast tenderness which was unassociated with menstruation. She was nulliparous from choice. There was no other personal or family history of relevance. The upper outer quadrant of her right breast was granular and slightly tender. Within the areola of each breast was a double nipple. On the right side the nipples were distinctly separate, but on the left the nipples were less well demarcated (*Fig.* 1). The patient had been unaware of this condition.

Case 2.—A 28-year-old white female was noted to have bilateral double nipples at a Westminster Hospital antenatal clinic (*Figs.* 2, 3). She had never been aware of this abnormality, although she had noticed a small mole beneath her left breast. As a child she had been told that she had a 'leaky heart valve' and at various times the presence of a cardiac murmur had been noted. There was no cardiac murmur present at any time during obstetrical surveillance or at a further examination 7 years later. Her husband possessed a supernumerary nipple below his left breast. There was no other personal or family history of relevance. No breast abnormalities were noted in her son who was delivered at full term. She did not breast feed him because she did not produce enough milk.

DISCUSSION

The nipple and epithelial lining of the ducts and alveoli of the human breasts are derived from the milk-lines, which are specialized areas of ectodermal thickening on the ventral surface of the embryo extending obliquely on each side from the axilla to the inguinal region. Normally, the milk-lines disappear during embryonal development, and the final disposition of one breast on each side of the median plane in the pectoral region is dependent on the persistence of ectodermal and mesodermal differentiation and growth in this area. In the region of the fourth intercostal space the future lactiferous tubules develop from an ectodermal ingrowth around which mesenchyme proliferates to form the supportive tissue of the breast. In the centre of this ingrowth a shallow pit is formed from which the nipple arises by a process of ectodermal differentiation. At term the foetus possesses fully developed ducts which open into the nipple.

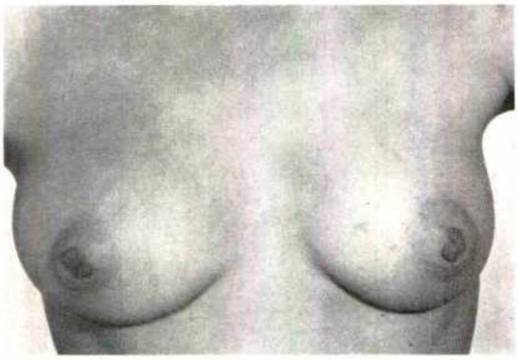
FIG. 1.—*Case* 1. The double nipples are best demarcated on the right side.

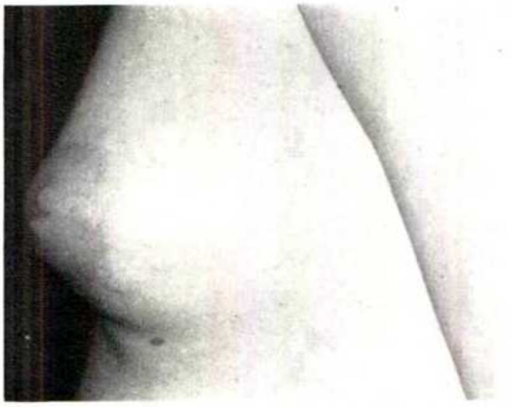
FIG. 3.—*Case* 2. Double nipples on the left side and a submammary mole.

Kajava (1915) classified supernumerary breast tissue into eight categories:—

1. Complete breast: mammary gland tissue, nipple, and areola.
2. Glandular tissue and nipple.
3. Glandular tissue and areola.
4. Glandular tissue only.
5. Nipple and areola with an area of fat replacing mammary glandular tissue—pseudomamma.
6. Nipple only—polythelia.
7. Areola only—polythelia areolaris.
8. Patch of hair only—polythelia pilosa.

The most common forms noted were polythelia and pseudomamma. Kajava (1915) restricted the term 'nipple' to the protuberance in the centre of the areola. Most authors writing on polythelia use the term 'nipple' in a non-restrictive sense as consisting of a papilla (or protuberance), aerola, follicles, and hair (Bruce, 1879). It is rare for supernumerary nipples to contain all of these structures.

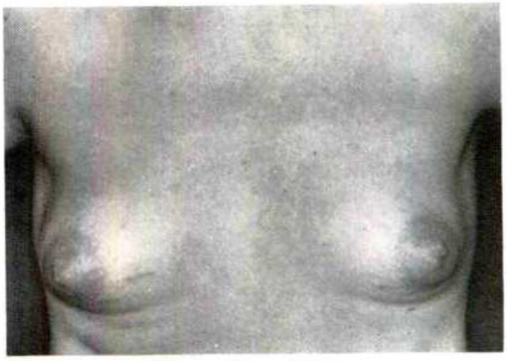
FIG. 2.—*Case* 2. The double nipples are best demarcated on the left side.

Guest (1923) found an incidence of accessory nipples of 0·4 per cent in 20,000 school-children, with a female to male ratio of 2 : 1. In adults the incidence has been recorded as 1 per cent (Hamblen, 1945) and 1–2 per cent (de Cholnoky, 1939), while Evans (1959) found that 5 per cent of healthy adults possessed supernumerary nipples. The laterality and sex incidence are approximately equal in adults, and the presence of more than one accessory nipple is uncommon. In a number of cases a hereditary predisposition has been noted, and Klinkerfuss (1924) recorded a family in which polythelia was present in four generations.

Supernumerary breast tissue may be found anywhere between the axilla and the groin along the site of the milk-line. Accessory nipples are usually found between the breast and the umbilicus and are most common immediately beneath the breast. They are infrequently observed below the umbilicus or above the normal breast. Intra-areolar polythelia is rare and probably originates in utero as a dichotomy of the developing nipple. The rarity of bilateral intra-areolar double nipples is confirmed by the presence of only one report in the literature. Butts (1954) reported a Bush negress of Suriname in her middle twenties with bilateral symmetrical intra-areolar double nipples who was suckling her second child. Each nipple functioned independently. Most authors regard supernumerary breast tissue occurring along the site of the milk-line as an atavistic phenomenon (Lichtenstern, 1878; Darwin, 1888). Brouha (1905) thought that the milk-line had no phylogenetic significance. Hughes (1950) regarded the atavistic explanation of polythelia occurring along the site of the milk-line as an exploitation of this line, and he believed that supernumerary nipples should be regarded merely as accidents of development.

Polythelia is rare in apes (Hartman, 1927), and Mathews and Baxter (1948) could find only 12 recorded cases.

Wakeley (1951) noted that it was curious that so little attention was paid to malformation and diseases of the nipple. A number of authors, however, have drawn attention to the association of congenital abnormalities of the nipples and neurosis, peptic ulceration, cardiovascular disease, migraine, and renal and gonadal hypoplasia.

Harper (1948, 1951) regarded supernumerary nipples as a skin vestige reflecting the early mammalian history of man. He also regarded vascular naevi as vestiges of the respiratory plexus of amphibians, and pigmented moles as primitive skin structures equivalent to the pigmented reptilian tactile organs such as are found in crocodile jaws. He concluded that these atavistic characteristics of skin are accompanied by an unstable central nervous system, as both skin and the central nervous system are derived from ectoderm. He recorded an increased incidence of neurosis in patients with polythelia, vascular naevi, and pigmented moles.

Zălaru (1965) observed an increased incidence of peptic ulceration in cases of polythelia.

Evans (1959) and Czernicka (1964) recorded an increased incidence of polythelia in patients suffering from cardiovascular disease. Evans (1959) noted polythelia only along the site of the milk-line, and in a series of 1059 healthy subjects the incidence was 5 per cent. He found that the incidence of polythelia was much higher in patients with systemic hypertension who had enlarged left ventricles (35 per cent), pulmonary hypertension with right ventricular hypertrophy (44 per cent), and cardiomyopathy (44 per cent).

Ask-Upmark (1954) suggested an association between inverted nipples and migraine, although he offered no explanation. Pronounced eyebrows (due to hypervascularity) and migraine were also linked, and he thought that the common factor in these cases was the behaviour of the arterial system and that this had a genetic basis.

Fleisher (1966) noted that nipples which were lateral to the midclavicular line ('wide-set') were associated with bilateral renal hypoplasia and gonadal dysplasia. If 'wide-set' nipples are present and there are no signs of gonadal dysplasia, then a high index of suspicion of bilateral renal hypoplasia is warranted.

Barnes (1962) thought that the amount of tethering of the nipple to the underlying tissues was more important than its size. The success of lactation often depends on the presence of firm prominent nipples, which are capable of erection, as depressed nipples predispose to cracking as a result of prolonged and ineffective efforts of the infant's gums to grip an insufficiently erectile structure (Saner, 1950).

Although Aird (1958) regarded supernumerary nipples as of no significance, the possibility of the coexistence of the above-mentioned diseases should be borne in mind when confronted with a patient who possesses a congenital abnormality of the nipple.

Acknowledgements.—I should like to thank Professor H. Ellis for his comments; Mr. W. P. Greening and Mr. R. de Vere for permission to report the cases who were under their care; the Departments of Medical Photography at the Royal Marsden and Westminster Hospitals for the illustrations; and Miss H. Rolls for secretarial assistance.

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SOME CLINICAL ASPECTS OF IDIOPATHIC RETROPERITONEAL FIBROSIS

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SUMMARY

A series of 40 patients with idiopathic retroperitoneal fibrosis is discussed with reference to some of the clinical observations. Among other conclusions it appears that corticosteroids should be used more in the treatment of this disease.

OBSTRUCTION of the ureters by retroperitoneal fibrosis of unknown cause has been described over three hundred times since Ormond drew attention to the condition in 1948. The ailment is now well known; authors of recent reviews include Comings, Skubi, Van Eyes, and Motulsky (1967), Webb and Dawson-Edwards (1967b), and Saxton, Kilpatrick, Kinder, Lessof, McHardy-Young, and Wardle (1969). The aetiology is obscure and has not yet been clarified by the undoubted association of some cases with methysergide administration (Graham, 1967). The author has therefore collected and studied clinical data, necropsy reports, pathological material, and sections from 40 patients suffering from fibrosis in the retroperitoneal tissues of the lower abdomen (Mitchinson, 1969). The only criterion for inclusion in this series was lack of obvious cause. The principal pathological findings and aetiology are discussed elsewhere (Mitchinson, 1970). The following observations are based on the clinical data in these 40 patients.

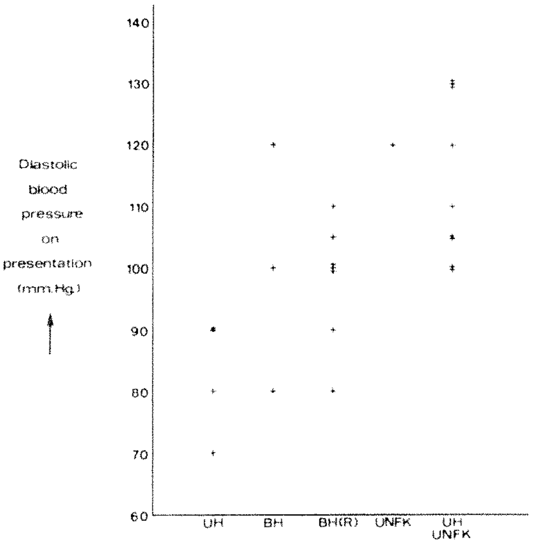

FIG. 1.—The relationship of the degree of renal damage (assessed by pyelography) to hypertension. UH, Unilateral hydronephrosis. BH, Bilateral hydronephrosis. (R), Retrograde pyelography only. UNFK, 'Non-functioning' kidney on intravenous pyelography.

CLINICAL PRESENTATION

Males outnumbered females by 3 to 1, and the usual time of onset of the disease was in middle age, as in previously published accounts (Packham and Yates-Bell, 1968).

Presenting symptoms were similar to those described by other authors and were mainly due to blockage of hollow organs by the progressive inflammation and fibrosis spreading in the retroperitoneal tissue of the lower abdomen. The presentation was due to ureteric blockage in all but 2 patients, who complained of claudication (due to narrowing of the aorta) and abdominal distension (due to narrowing of the colon) respectively. It is important to note that only 4 patients presented with oliguria; the majority had complaints such as loin pain (16 patients), often radiating to the groin (10), vague abdominal or low-back pain (19), vomiting (16), anorexia (7), and considerable weight-loss (11). Only 1 patient had polyuria and polydipsia, which is a recognized but rare complaint in this disease (Tulloch, 1960).

Physical signs were meagre. Eight patients were tender in the loin, and 4 in an iliac fossa. Five had oedema of the legs (due to venous blockage). The only frequent finding on examination was hypertension.

Hypertension.—Although the blood-pressure had not always been recorded at least 17 patients had diastolic measurements of 100 mm. Hg or more on presentation. *Fig.* 1 shows that the observations in this series supported the common assumption that hypertension in this disease is due to renal damage. Two patients who had had one kidney removed showed a gradual increase in blood-pressure during increasingly severe involvement of the remaining kidney. In 3 patients hypertension was relieved by surgical removal of a non-functioning kidney—an important measure which is not always taken.

A few patients presented with what may have been complications of their hypertension (epistaxis in 1, heart failure in 3, headaches in 5). None had evidence of hypertension preceding the disease.

There was no evidence in this series that narrowing of the renal arteries or aorta, or compression of the kidney by fibrosis, contributed to the hypertension.

Measurement of blood-pressure in the legs is not often performed. In future such measurements in suspected cases of retroperitoneal fibrosis might occasionally reveal a degree of aortic narrowing which would be helpful in diagnosis.

CLINICAL INVESTIGATION

Urinary infection was uncommon on presentation (2 males, 3 females), although 10 more patients developed this complication after instruments had been passed into the upper urinary tract, and 1 patient became infected after corticosteroid therapy. These findings conflict with the oft-repeated statement (e.g., Rust and Maas, 1967) that the disease frequently presents as urinary infection.

Pyelography in almost all cases showed the typical ureteric obstruction and medial deviation at the level of vertebra L.3 or L.4. The ureter above the obstruction was often kinked owing to increase in length as well as in diameter, as remarked upon by Hanley (1967).

In 1 patient lymphangiography was performed and was normal. Such exceptions limit the value of the investigation, which has been found useful by some (Bookstein, Schroeder, and Batsakis, 1966; Virtama and Helela, 1967).

The erythrocyte sedimentation rate (E.S.R.) was above 45 mm. in the first hour (Westergren) soon after presentation in all except 3 of the 31 cases tested; 8 had readings exceeding 100 mm. in the first hour. Serial measurements suggested that the raised E.S.R. was due to the activity of the inflammatory process in the retroperitoneum rather than to the degree of renal involvement. This investigation was extremely useful in assessing the progress of the disease, especially in response to treatment.

Plasma protein electrophoresis in 13 patients showed raised α_2-globulins in all cases and raised γ-globulins in 8.

^{131}Iodine hippuran renograms proved useful, especially in assessing changes following therapy (Jose, 1967).

Systemic Idiopathic Fibrosis.—It is now well known that the inflammation and fibrosis which characterize this disease occasionally spread forwards to involve the mesentery or upwards along the aortic axis. In addition, the mediastinum, thyroid, and perhaps the orbit and porta hepatis may be similarly affected. It is not yet clear whether any other disease is related.

In the present series of retroperitoneal fibrosis 4 patients also showed evidence of mediastinal fibrosis, and 1, possibly 2, of thyroid disease resembling Riedel's thyroiditis. Indeed, 1 patient presented initially with a superior vena cava syndrome, and another with a thyroid swelling (described by Turner-Warwick, Nabarro, and Doniach, 1966).

Such widespread involvement has led to suggestions that the disease is a 'connective-tissue disease', and the occasional observation of concomitant arthritis or arteritis has tended to support the idea. In the present series 2 (female) patients had arthritis of a rheumatoid type and 1 (male) had arteritis resembling polyarteritis nodosa. Several others had chronic inflammation of the larger elastic arteries, sometimes including the aorta or a coronary artery.

One patient, out of 10 tested, had 'L.E.' cells reported on one occasion. Other tests and necropsy in this case showed no evidence of lupus erythematosus. The latex slide test for the 'rheumatoid factor' was positive in 1 out of 9 patients tested; this patient's Rose-Waaler test was negative, as in 6 other patients, including 1 with arthritis. A search for thyroid auto-antibodies in 21 patients showed no significant difference from controls who were matched for age and sex.

In summary, the disease is certainly potentially widespread, and involvement of organs distant from the ureters must always be sought. Analogies with 'connective-tissue diseases' are tempting but not yet well supported.

DIFFERENTIAL DIAGNOSIS

When a typical pyelographic appearance, including medial deviation of the ureters, has been demonstrated, any other inflammatory disease is most unlikely, and only retroperitoneal malignant neoplasm remains to be excluded. Such mimicry can be produced by a wide variety of neoplasms, and the hazard is well known (Webb and Dawson-Edwards, 1967a); carcinoma of the prostate is probably the commonest. Unfortunately, the most exhaustive investigations, even including laparotomy and biopsy, have proved eventually to be imperfect in excluding neoplasm in some cases. Such considerations should not be allowed to delay the relief of ureteric blockage by one means or another.

TREATMENT

The conventional treatment of ureteric obstruction has been ureterolysis. The results of 38 well-documented ureterolyses in the series are shown in *Table I*, where 'success' is defined as a functioning kidney (assessed by pyelography) with no more than very slight hydronephrosis at least 6 months post-operatively. The good results are self-explanatory. It is possible that the only short-term failures in this series were when the kidney was already irreparably damaged.

Table I.—ASSESSMENT OF SHORT-TERM RESULTS OF URETEROLYSIS

PREOPERATIVE RADIOLOGICAL ASSESSMENT OF KIDNEY	SUCCESS	FAILURE	REASONS FOR FAILURE	
			No Return of Function	Severe Infection
Hydronephrosis on intravenous pyelogram	18	0	—	—
Hydronephrosis on retrograde pyelography	5	4	0	4
'Non-function' on intravenous pyelogram	3	8	7	1

However, this method of assessment does not show some of the disadvantages of surgical treatment which require attention:—

1. Seven out of 12 patients with unilateral ureteric obstruction developed contralateral ureteric involvement subsequently, usually after a few months but on one occasion 2 years later.
2. Four ureters were found to be obstructed again after successful ureterolysis, usually within 1 year but in 1 case 9 years later, by progression of the disease.
3. The above complications can usually be satisfactorily relieved by further surgery, but this multiplies the operative risk. This is admittedly small. Only 1 patient in this series died in the immediate post-operative period, of pneumonia.
4. When ureterolysis is unsuccessful in restoring function to a non-functioning kidney a second operation (nephrectomy) is required to relieve the hypertension.
5. Ureterolysis treats only one complication of the disease, which may continue to affect other organs

such as the aorta, coronary arteries, mediastinum, or thyroid.

Most observers would conclude that these disadvantages do not detract significantly from the surgical approach to treatment, but there is some evidence that oral corticosteroid therapy deserves wider trial. Corticosteroids are difficult to assess when surgical treatment coincides with their use, but at least 3 patients in this series showed evidence suggesting the rapid efficacy of medical treatment alone. Corticosteroids lack most of the above five disadvantages of surgical treatment but are not without their own disadvantages. When used alone they may also postpone the recognition of a neoplastic mimic of retroperitoneal fibrosis. A discussion of the 3 patients referred to and a suggested compromise between surgical and corticosteroid treatment have been presented elsewhere (Mitchinson, Withycombe, and Arden-Jones, 1971). More observations on the use of corticosteroids in practice are required before there is sufficient evidence on the relative merits of surgical and medical treatment.

In 7 patients, nephrostomy was performed, usually as an interim measure; urinary infection invariably followed and was associated with a poor prognosis. Retrograde pyelography was also occasionally apparently responsible for introducing infection, but less frequently and with less serious sequelae. If uraemia is severe, indwelling ureteric catheters are probably a better interim measure than nephrostomy, if the diagnosis has been made.

CONCLUSIONS

Some aspects of idiopathic retroperitoneal fibrosis merit more attention than they have received; for example, the complication of renal hypertension, the rarity of infection if instruments are not passed into the urinary tract, the widespread nature of the disease, the usefulness of the E.S.R. as a guide to management, and the possibility of the more frequent use of corticosteroids in treatment.

Acknowledgements.—Some of the cases in the series have been reported elsewhere (Jones and Alexander, 1966; Turner-Warwick and others, 1966; Jose, 1967). To these authors and to many other surgeons, physicians, and pathologists my thanks are due for their help and permission to study their patients. I am particularly grateful to Dr. Deborah Doniach who performed and assessed the thyroid auto-antibody tests and to Dr. R. C. B. Pugh for advice.

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PLATELET ADHESIVENESS AND LIPOPROTEIN LIPASE ACTIVITY IN PATIENTS WITH BENIGN AND MALIGNANT DISEASE OF THE PROSTATE*

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SUMMARY

Platelet adhesiveness and lipoprotein lipase (clearing factor lipase) activity have been measured in 22 patients with benign prostatic obstruction and in 20 patients with prostatic carcinoma.

The total platelet counts and the number of adherent platelets were significantly higher and the lipoprotein lipase responses to heparin were significantly lower in the patients with carcinoma.

These results are relevant to the use of oestrogens in the treatment of prostatic carcinoma since these drugs might accentuate the abnormalities found here.

IT has recently been shown that patients with prostatic carcinoma who are treated with oestrogens are more likely to develop thrombo-embolic complications than untreated controls (Veterans Administration Co-operative Urological Research Group, 1967). The reasons for this effect of oestrogens are uncertain. However, the problem may be similar to that found in women taking oral contraceptive agents containing both oestrogens and progestogens in whom significant factors may be alterations in platelet behaviour (Bolton, Hampton, and Mitchell, 1968) and in plasma lipid composition (Wynn, Doar, and Mills, 1966; Brody, Kerstell, Nilsson, and Svanborg, 1968). We have previously demonstrated a reduction in lipoprotein lipase activity in these women (Ham and Rose, 1969). We suggested that this reduction might be one significant factor in the alteration of plasma lipids, since the enzyme has an important role in the transport of lipid across the vascular endothelium.

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* Based on a paper presented to the Surgical Research Society of Australasia in May, 1970.

In 1964 Slack, Seymour, McDonald, and Love demonstrated an inverse relationship between the lipoprotein lipase activity and the platelet adhesiveness in patients with ischaemic heart disease and in controls. Subsequently, it has been shown that after surgical operations platelet adhesiveness is increased (Ham and Slack, 1967) and lipoprotein lipase activity is reduced (Ham and Slack, 1969). A direct relationship between the enzyme activity and platelet adhesiveness has been postulated (Ham, 1969).

This evidence suggested that oestrogen therapy in patients with prostatic carcinoma might produce changes in platelet behaviour and in lipoprotein lipase activity. However, it was necessary to establish first whether these patients were abnormal before commencing oestrogen therapy, and this was the reason for the present study.

MATERIALS AND METHODS

The object of the investigation was to measure platelet adhesiveness and lipoprotein lipase activity in untreated patients with prostatic carcinoma and in a control group of patients with benign prostatic obstruction. There were 20 patients with carcinoma and 22 controls.

Table I.—AGES, BODY-WEIGHTS, AND BLOOD-UREA LEVELS OF THE PATIENTS (MEAN ± STANDARD ERROR)

	Benign Disease	*Malignant Disease*
Age (years)	68 ± 1·8	71 ± 1·8
Body-weight (kg.)	66 ± 2·7	69 ± 2·8
Blood-urea (mg. per 100 ml.)	38 ± 2·8	41 ± 2·5

All the patients admitted to the study were in-patients in a single urological unit. Their mean ages, body-weights, and blood-urea levels are shown in *Table I*. Seven controls and 8 patients with carcinoma were admitted with acute retention. The remaining patients had symptoms of chronic urinary obstruction, and 6 patients with carcinoma had bone pain as well. All patients had operations subsequent to taking blood samples (cystoscopy and biopsy, prostatectomy, or transurethral resection) and the clinical diagnosis was confirmed histologically. All patients with carcinoma had clinical and pathological evidence of invasive carcinoma, the extent of the disease (Bennett, Dowd, and Harrison, 1970) being Stage II in 7 patients, Stage III in 5 patients, and Stage IV in 8 patients.

Blood samples were taken at approximately 8.30 a.m. after a 10-hour fast, using the methods of collection and processing which have been described previously (Ham and Slack, 1967, 1969). The samples were collected immediately before and 10 minutes after an intravenous injection of 10 I.U. heparin per kg. body-weight. The same brand of heparin (Evans Medical Ltd., 1000 I.U. per ml.) was used throughout. The pre-heparin sample was used to measure the haematocrit, total platelet counts, platelet adhesiveness, pre-heparin enzyme activity, and plasma inhibition of lipoprotein lipase. The enzyme response to heparin was measured in the post-heparin sample.

The haematocrit was measured in duplicate using a microhaematocrit method. Platelet counts and platelet adhesiveness were measured using the Wright rotating bulb (Ham and Slack, 1967); the platelet adhesiveness was expressed as the percentage of adherent platelets. Enzyme activity and plasma inhibition were measured by the methods of Slack and others (1964) and Ham and Slack (1969) respectively.

The significance of the differences was tested by Student's t-test. When the results were not normally distributed, as in the case of the platelet counts, the test was performed after logarithmic transformation. Values for P of less than 0·05 were accepted as significant.

RESULTS

The results are shown in *Table II*. The mean haematocrit was significantly lower in the patients with carcinoma and the mean total platelet count and the number of adherent platelets were significantly higher than in the control group. There was no significant difference in the platelet adhesiveness measurements, in the pre-heparin enzyme activity, or in the plasma inhibition of lipoprotein lipase. However, the mean post-heparin lipoprotein lipase activity was significantly lower in the carcinoma patients.

Table II.—ANALYSIS OF RESULTS (MEAN ± STANDARD ERROR)

FACTOR	BENIGN DISEASE	MALIGNANT DISEASE	SIGNIFICANCE OF DIFFERENCE
Haematocrit (per cent)	45 ± 0·8	40 ± 1·3	$P < 0·01$
Total platelet count ($\times 10^3$ per c.mm.)	223 ± 20	294 ± 31	$P < 0·05$
Number of adherent platelets ($\times 10^3$ per c.mm.)	75 ± 9	105 ± 15	$P < 0·05$
Platelet adhesiveness (per cent)	34 ± 1·7	34 ± 2·2	N.S.
Pre-heparin enzyme activity (µEq. per ml. per min.)	0·020 ± 0·006	0·017 ± 0·006	N.S.
Post-heparin enzyme activity (µEq. per ml. per min.)	0·25 ± 0·02	0·19 ± 0·02	$P < 0·05$
Plasma inhibition (per cent)	−19 ± 3	−19 ± 5	N.S.

N.S. = Not significant.

DISCUSSION

The basic reason for this investigation was to determine whether untreated patients with prostatic carcinoma had abnormalities in platelet behaviour or in lipoprotein lipase activity. However, the design of the investigation also provided an opportunity for a comparison between patients with a benign disease and those with a malignant disease producing similar clinical features. There have, of course, been previous studies of coagulation factors in patients with malignant disease (Eastham, 1964; Miller, Sanchez-Avalos, Stefanski, and Zuckerman, 1967; Davis, Theologides, and Kennedy, 1969), and it has been shown that such patients may have an increase in the total platelet count and in the number of adherent platelets. In these earlier studies the controls were normal subjects and it is therefore difficult to determine whether the findings were related to a direct effect of the tumours or to secondary non-specific effects (e.g., weight-loss). In the present study the two groups of patients had similar clinical features and presumably the tumours were responsible for the differences found. It is, of course, uncertain whether the findings are specific to prostatic carcinoma or whether they apply to other forms of malignant disease.

This investigation has demonstrated a significant increase in the total platelet count in the patients with carcinoma, together with a similar increase in the number of adherent platelets. The platelet adhesiveness (percentage of adherent platelets) was similar in the two groups. It is important to note that the haematocrit was significantly reduced in those with carcinoma, and Hirsh, McBride, and Wright (1966) have shown that a decrease in the haematocrit is accompanied by a decrease in the platelet adhesiveness measurement. Thus, differences in platelet adhesiveness might have been shown if the measurements had been performed after correction for the differences in haematocrit.

The mean lipoprotein lipase response to heparin was significantly decreased in the patients with prostatic carcinoma. This reduction was not related to a difference in plasma enzyme activity before the heparin injection, nor was it due to increased plasma inhibition of lipoprotein lipase. Presumably, the tissue enzyme activity was reduced, and since triglyceride uptake in adipose tissue is directly proportional to its lipoprotein lipase content (Garfinkel, Baker, and Schotz, 1967) this reduction might contribute to an alteration in plasma lipid composition.

Finally, patients with prostatic carcinoma are frequently treated with oestrogens in large doses. In other studies (Wynn and others, 1966; Bolton and others, 1968; Brody and others, 1968; Ham and Rose, 1969) oestrogens have been shown to produce abnormalities in platelet behaviour, increases in plasma lipids, and a reduction in lipoprotein lipase activity. Thus, such therapy in patients with prostatic carcinoma might accentuate the abnormalities found here—abnormalities which may be important factors contributing to the increased risk of thrombo-embolism in these patients.

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RETICULO-ENDOTHELIAL SYSTEM ACTIVITY DURING HOMOGRAFT REJECTION AND IMMUNOSUPPRESSION

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SUMMARY

Reticulo-endothelial system activity was measured in the rat by the rate of colloid clearance. Activity was increased following homograft rejection, and in the presence of tumour-specific antigen. Increased activity was also found during immunosuppression with cyclophosphamide, and with methotrexate, despite marked lowering of the white blood-counts.

It is concluded that reticulo-endothelial system activity does not parallel the activity of the lymphoid system in transplantation immunity.

RETICULO-ENDOTHELIAL system activity may be measured by the rate of colloid clearance from the blood-stream (Biozzi, Benacerraf, and Halpern, 1953). Increased activity has been demonstrated in this way after injection with BCG vaccine (Old, Clarke, Benacerraf, and Goldsmith, 1960), and in response to the administration of sheep red blood-cells in sensitized animals (Gabrieli, 1955).

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An increased rate of clearance has been found to accompany skin homograft rejection (Fisher and Fisher, 1964). A study was planned to investigate the relation of reticulo-endothelial activity to the degree of immunological activity in transplantation immunity.

MATERIALS AND METHODS

Wistar rats were used for the experiment; these were of a uniform strain, but were not inbred, and each weighed between 210 and 260 g. Each rat was paired with a control of equal weight.

Table I.—Carbon Clearances in Groups of Animals receiving Homografts and in Control Groups

Time after Operation (days)	Group*	No. of Animals	Carbon Clearance ($T_{\frac{1}{2}}$ in minutes)	Mean Difference (± S.E.)	Significance (P)
4	Operation Homograft	10 9	15·36 16·16	0·80 ± 2·35	> 0·4
7	Operation Homograft	10 10	9·39 9·60	0·21 ± 0·84	> 0·4
14	Operation Homograft	10 9	18·90 4·96	13·94 ± 1·57	< 0·0005
21	Operation Homograft	10 11	16·73 13·50	3·23 ± 1·77	< 0·05
21	Autograft Homograft	10 10	16·92 12·58	3·34 ± 1·23	< 0·01

* Control animals which simply had skin removed are listed as 'operation'.

The uptake of colloidal carbon was studied by the method of Biozzi and others (1953), by injecting 30 mg. of a carbon suspension per 100 g. body-weight into the femoral vein of the anaesthetized animal. Blood samples, 0·1 ml., were then taken under general anaesthesia at 1-minute intervals for 15 minutes from the retro-orbital plexus. The animal was then killed, the spleen was removed and weighed, and tissues were taken for histological examination. The carbon content of the blood samples was estimated in a Unicam SP500 spectrophotometer, at 675 mm. after haemolysis in 4 ml. 0·1 per cent sodium carbonate. Each sample was compared with the sample taken before the injection of carbon.

The colloidal carbon preparation is cleared from the blood-stream exponentially. Graphs of clearance were plotted, and the $T_{\frac{1}{2}}$ of the carbon in the blood-stream of each animal thus obtained (the clearance results are expressed as the time taken for half of the carbon to be cleared from the blood-stream, $T_{\frac{1}{2}}$). Clearance was constant in normal animals as long as the same preparation of colloidal carbon was used, but varied somewhat with different preparations. For this reason animals in an experimental group were tested with the same preparation of carbon as their controls.

Skin-grafts.—Full-thickness skin-grafting between female Wistar rats was carried out by removing a 1-cm.^{2} patch from the back of the donor and placing it in a similar site on the recipient. The panniculus carnosus was scraped off before applying the graft, which was secured with interrupted silk sutures and left without a dressing. If an animal removed the stitches down one side of the graft it was excluded. Grafts were observed daily, and rejection was judged to have occurred when the graft became hard and impliable. Control animals had a piece of skin, approximately 1 cm.^{2}, removed from the back, and the raw area was allowed to granulate. One control grouped was autografted.

Carbon clearances were determined 4, 7, 14, or 21 days after grafting, or after skin removal in the controls.

Immunosuppression.—The maximum doses of cyclophosphamide* and of methotrexate† which could be tolerated by male rats were determined. Groups of rats were then given intramuscular injections of these drugs, or of cortisone, according to the following schedules:—

Group 1. Cyclophosphamide, 5 mg. per 100 g. body-weight, on alternate days for 7 days.

Group 2. Cyclophosphamide, 5 mg. per 100 g. body-weight, on alternate days for 21 days.

Group 3. Cyclophosphamide, 5 mg. per 100 g. body-weight, on alternate days, followed by no treatment for 7 days.

Group 4. Methotrexate, 0·6 mg. per 100 g. body-weight, on alternate days for 7 days.

Group 5. Methotrexate, 0·4 mg. per 100 g. body-weight, on alternate days for 21 days.

Group 6. Methotrexate, 0·6 mg. per 100 g. body-weight, on alternate days for 7 days, followed by no treatment for 7 days.

Group 7. Cortisone acetate, 5 mg. per 100 g. body-weight, on alternate days for 7 days.

Group 8. Cortisone acetate, 5 mg. per 100 g. body-weight, on alternate days for 21 days.

At the end of the period of treatment, peripheral white blood-counts were made and carbon clearances determined in the animals. The control groups received no treatment.

Clearance after Homografting.—The mean rejection time of the skin homografts was 9 days. All the grafts were soft at 7 days and had become hard and black by 14 days.

The clearance of carbon was accelerated 14 days after homografting compared with animals that had simply had a piece of skin removed (*Table I*). This rate of clearance was maintained at 21 days, in comparison with an autografted group and a control group. There was, however, no difference in clearance between grafted and control animals at 4 and 7 days after grafting.

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* Ward, Blenkinsop & Co. Ltd., Wembley, England.

† American Cyanamid Co., New York, U.S.A.

Immunosuppression.—The clearance of carbon in animals on all the cyclophosphamide régimes (*Table II*) was increased despite a marked reduction in the white blood-counts. The animals did not lose weight. Spleen weights were increased in the groups of animals studied at 2 and 3 weeks after treatment had started. Spleens from all the animals on cyclophosphamide showed depletion of lymphoid elements.

Methotrexate treatment (*Table II*) gave similar results to cyclophosphamide with the exception that clearance was not increased after only 1 week's treatment. The effects on body-weight, spleen weight, and white blood-count were similar to those with cyclophosphamide.

Table II.—CARBON CLEARANCES IN GROUPS OF ANIMALS RECEIVING IMMUNOSUPPRESSIVE DRUGS AND IN CONTROL GROUPS

GROUP	NO. OF ANIMALS	MEAN WHITE BLOOD-COUNT	CARBON CLEARANCE ($T_{\frac{1}{2}}$ in minutes)	MEAN DIFFERENCE (±S.E.)	SIGNIFICANCE (P)
Cyclophosphamide					
1 Week	15	4600	12·39	6·02 ± 2·26	<0·05
Control	15	13,400	18·41		
1 Week with recovery	13	7000	10·65	5·51 ± 2·34	<0·02
Control	14	13,600	16·16		
3 Weeks	9	1800	6·87	9·09 ± 2·49	<0·002
Control	9	13,600	15·96		
Methotrexate					
1 Week	9	7200	16·97	0·52 ± 5·20	<0·5
Control	9	13,000	16·45		
1 Week with recovery	11	20,000	10·23	10·46 ± 2·68	<0·0005
Control	11	14,600	20·69		
3 Weeks	11	8000	11·91	6·62 ± 1·41	<0·005
Control	11	15,000	18·53		
Cortisone					
1 Week	15	13,200	21·79	8·18 ± 2·21	<0·002
Control	15	15,000	13·61		
3 Weeks	11	14,000	18·36	0·98 ± 2·56	<0·4
Control	11	14,000	19·34		

Animals treated with cortisone (*Table II*) showed a slowing in clearance after 1 week's treatment, but at 3 weeks the clearance was the same as in normal animals. Body-weight was constant and spleen weight did not alter; there was no fall in the white blood-count.

DISCUSSION

The hypothesis has been advanced by Marshall and Knight (1969) that reticulo-endothelial activity, as measured by particulate clearance from the blood-stream, bears a constant relationship to immunological response in transplantation immunity. This suggestion arose from the observation of an increased rate of carbon clearance in rats following application of a skin homograft (Fisher and Fisher, 1964). Clearance of ^{32}P-labelled *Salmonella typhimurium* was used by Marshall and Knight who showed a similar increase in activity in mice bearing large skin homografts; the magnitude of the response was related to the size of the graft employed. Increased reticulo-endothelial system activity in rats during the growth of methylcholanthrene-induced sarcomas has been reported by Blamey, Crosby, and Baker (1969). These tumours bear tumour-specific antigens. There was again a direct relationship between the size of the tumour and the observed increase in carbon clearance. It was suggested that the increased clearance might reflect a reaction to tumour-specific antigen.

If reticulo-endothelial system activity reflects accurately host–graft reaction, then immunosuppression should decrease reticulo-endothelial system activity.

The present studies confirm the finding of Fisher and Fisher (1964) that an increased carbon clearance follows homograft rejection. However, in the present experiments the increase was found at 14 and 21 days after grafting, and not at 7 days when immunological activity must be present. This conflicts with the report of both Fisher and Fisher (1964) and Marshall and Knight (1969), who detected a change in reticulo-endothelial system activity before rejection had taken place. The demonstration here of a clear increase in carbon clearance only after rejection had occurred casts doubt on the proposal that reticulo-endothelial system activity reflects immunological activity as regards transplant rejection, and suggests that it may reflect other factors, such as phagocytic activity at the graft site.

The demonstration of increased carbon clearance during immunosuppression clearly does not support the hypothesis of Marshall and Knight (1969). The increase was seen in animals on doses of drugs sufficient for considerable immunosuppression, as demonstrated by the associated leucopenia.

Chare and Boak (1969) have shown a similar increase in reticulo-endothelial system activity in mice treated with antilymphocytic serum. They also produced an increased rate of carbon clearance by the injection of dead cells. It may be that the production of dead cells for phagocytosis is a common factor in homograft rejection, tumour growth, immunosuppression, and the graft–host syndrome (Howard, 1964), which stimulated the reticulo-endothelial system. This accords with the observed response to cortisone, where the immunosuppressive effect of the drug is not accompanied by a cytotoxic effect.

Whatever the explanation of the effect of these agents on the reticulo-endothelial system it is clear that the action is very different to that on the lymphoid cells, which are suppressed. This raises the question of whether the lymphoid and the reticulo-endothelial systems ought to be considered as two separate entities rather than as a single functional unit. There have been recent reports of the appearance of reticulum-cell sarcomas in patients undergoing immunosuppression (Doak, Montgomerie, North, and Smith, 1968). The stimulatory effect of immunosuppressive drugs on the reticulo-endothelial system may be of relevance to this.

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Requests for reprints should be addressed to the Tenovus Institute for Cancer Research, Welsh National School of Medicine, Cardiff.

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THE EFFECT OF ELECTRICAL STIMULATION OF THE LEGS ON POSTOPERATIVE THROMBOSIS

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SUMMARY

Stimulation of the muscles of the lower limbs during surgery was evaluated as a means of preventing postoperative leg-vein thrombosis and pulmonary embolism. Of 285 patients submitted to a major operation, 113 were stimulated and 172 were not. The two groups were closely similar in age, operations, anaesthesia, diseases, and severity of disease, but there was a negligible difference in the rates of postoperative thrombosis.

A RATIONALE and method for prophylactic per-operative muscle stimulation were described by Doran and White (1967), but their method has the disadvantages of producing frequent, vigorous movements of the legs during surgery and of not exercising the thighs and buttocks. However, two independent within-patient trials of that method using ^{125}I fibrinogen to assess the venous thrombosis rate showed conflicting results (Browse and Negus, 1970; de Jode, Khurshid, and Walther, 1970). Moloney and Fell (1968) described a method of producing less frequent, undulating movements of the whole of both lower limbs during operation, and the result of a trial of that method is presented here.

The trial was not controlled in the sense that alternative matched patients were stimulated, for it s difficult in a series of patients, including many emergencies (40 per cent of admissions), coming to urgery to achieve continuity of comparison. During he period of the trial the choice of treatment was mostly random, with one surgeon tending to use stimulation and another not. The observer did not know the design of the trial and saw every patient admitted. In the event the two groups of patients were closely similar in respect of age, nature of diseases and operations, surgeons (G. E. M. and two senior registrars) and anaesthetists, and the post-operative management was the same for both groups. Operating time was similar for each surgeon.

MATERIALS AND METHODS

The patients were those admitted to one surgical firm between June, 1968, and July, 1969, undergoing a major operation. Patients with appendicitis were excluded because of considerable variation in the severity of the disease. Seven patients in whom the onset of venous thrombosis preceded operation were also excluded. Many other patients having intermediate and minor procedures were stimulated but were not included in the survey. Although over 300 patients were stimulated, none showed adverse reactions other than transient flushing of the skin at the site of the electrodes.

Each patient was seen daily from the time of admission until the time of discharge by one observer (M. T. M.), who recorded relevant facts and looked for signs and symptoms of leg-vein thrombosis and pulmonary embolism. Signs and symptoms noted were leg pain, particularly muscle pain on walking, swelling, tenderness, pitting oedema, tense swelling of the calf, dilatation of superficial veins, and alteration in skin temperature. Diseases other than thrombosis may cause such signs but nearly always bilaterally and symmetrically, e.g., tenderness in rheumatoid arthritis and in diabetes mellitus, oedema in heart failure and in hypoproteinaemia; an arterial leg lesion is easily distinguished. Because in the diagnosis of thrombosis particular significance was attached to signs and symptoms occurring in one leg only or asymmetrically in time in both legs, some cases of bilateral thrombosis may not have been diagnosed. Pulmonary embolism was diagnosed only when chest signs and symptoms were almost certainly related to that condition.

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Table II.—INCIDENCE OF LEG-VEIN THROMBOSIS AND PULMONARY EMBOLISM RELATED TO AGE IN A PRE-SURVEY GROUP OF PATIENTS

AGE (years)	TOTAL NO. OF PATIENTS	LEG-VEIN THROMBOSIS	PULMONARY EMBOLISM
10–	1	—	—
20–	4	1	1
30–	4	—	—
40–	10	1	—
50–	8	1	—
60–	12	3	—
70–	7	3	—
80–	2	1	1
Total	48	10 (20·8 per cent)	2

Stimulation was carried out by a purpose-built machine (Rank Precision Industries Ltd.) which delivered a surged alternating current, lasting 3 seconds, every 7·5 seconds. The machine was connected to the appropriately covered stimulating electrodes, which had been placed in the positions described by Moloney and Fell (1968), as soon as the patient was anaesthetized. Stimulation was continued from that time until the operation ended. The peak output voltage (between 100 and 200 V.) was adjusted by the anaesthetist to give firm, easily palpable contractions of the calves, thighs, and buttocks, and visible movements of both feet throughout the operation. The operating-theatre personnel were isolated from the apparatus by a rubber macintosh covering the patient's legs. Patients were stimulated whenever possible, but as a result of two operations being carried out simultaneously, faults in the apparatus, holidays, etc., less than half of the patients were treated. Overhydration and low-molecular-weight dextrans were not employed.

Most patients were operated on in the supine position, with the legs elevated to 15° on Sorbo-rubber pads. Eight patients were operated on in the lithotomy position and 7 in the lateral renal position.

Limb blood-flow measurements were made, but the methods and results are outside the scope of this paper.

RESULTS

The number of patients stimulated was 113 and not stimulated 172. The incidence of leg-vein thrombosis was 22 (20 per cent) in the stimulated group and 43 (25 per cent) in the unstimulated group (*Table I*). The difference is not statistically significant: $\chi^2=0{\cdot}9$, $P>0{\cdot}05$. Another similar group of (unstimulated) patients was studied in the same way before the trial was begun and is available for comparison (*Table II*); 10 out of 48 (21 per cent) had venous thrombosis.

Table I.—INCIDENCE OF LEG-VEIN THROMBOSIS AND PULMONARY EMBOLISM

AGE (years)	UNSTIMULATED PATIENTS			STIMULATED PATIENTS		
	Total No.	Leg-vein Thrombosis	Pulmonary Embolism	Total No.	Leg-vein Thrombosis	Pulmonary Embolism
10–	5	—	—	—	—	—
20–	5	1	1	4	1	—
30–	17	2	—	9	—	—
40–	21	3	1	18	2	—
50–	23	8	—	18	4	—
60–	48	12	1	30	3	1
70–	34	9	—	28	10	—
80–	19	8	4	6	2	1
Total	172	43 (25·0 per cent)	7	113	22 (19·5 per cent)	2

The number of pulmonary emboli in each group is too small for conclusions to be drawn.

There were 13 deaths in the unstimulated group and 3 in the stimulated group. One death in the unstimulated group was caused by a pulmonary embolus in a patient who was expected to live. The other deaths resulted from progression of the illnesses causing admission, several patients being emergencies. For the purpose of the survey, thromboses and embolism diagnosed clinically were recorded, any found at autopsy being ignored. Subtraction of the number of deaths from the total in each group does not significantly alter the results.

The two groups have a comparable age distribution (*Table I*). Age and operation are the only two factors known definitely to affect the incidence of thrombosis and embolism.

Specific operations are done for specific diseases and the two cannot be dissociated in groups of patients such as those studied in the present survey. Further, most postoperative complications have an association with, and are really part of, the disease–operation complex, making separate assessment difficult and somewhat artificial. It must also be remembered that patients with the same disease tend to be of similar ages, thus making a clear distinction between age and disease impossible. When every patient has had a major operation it seems most logical to divide the patients according to disease but taking cognizance of the type of operation. This was done for each age-group (*Table III*). The numbers in each category are small but the pattern of distribution is similar for both the stimulated and unstimulated groups except in the category 'other diseases requiring laparotomy'. The proportion of patients in that category relative to the total number is twice as great in the unstimulated group (17 per cent) as in the stimulated group (7 per cent), but elimination of that category causes no significant change in the final result.

It is possible that acute illness may influence the tendency to venous thrombosis. *Table IV* shows the stimulated and unstimulated groups divided according to emergency or waiting-list admission. Emergency admission in this series is an indication of acute illness rather than the time of operation, most emergency patients being operated on after the day of admission. A greater proportion of waiting-list than of emergency patients were stimulated and the former have a slightly lower incidence of thrombosis. Statistical comparison of the corresponding groups, however, shows no significant difference: for emergencies $\chi^2 = 0{\cdot}36$, $P > 0{\cdot}05$; for waiting-list patients $\chi^2 = 2{\cdot}7$, $P > 0{\cdot}05$.

Although this was an uncontrolled survey the stimulated and unstimulated groups are comparable in important respects. Peroperative muscular stimulation does not appear to reduce the incidence of postoperative leg-vein thrombosis.

Table III.—DISTRIBUTION OF DISEASE/OPERATION COMPLEX WITH AGE IN UNSTIMULATED AND STIMULATED PATIENTS

DIAGNOSIS: OPERATION	UNSTIMULATED PATIENTS								STIMULATED PATIENTS							
Age (years)	10–	20–	30–	40–	50–	60–	70–	80–	10–	20–	30–	40–	50–	60–	70–	80–
Cancer of the colon	—	—	—	1	3	1	3	1	—	—	—	—	1	1	6	—
Diverticulitis	—	—	—	2	—	7	2	4	—	—	—	1	—	5	1	—
Cancer of the stomach	—	—	—	—	—	4	—	3	—	1	—	—	1	2	2	—
Peptic ulcer	—	1	4	7	7	6	7	—	—	1	4	7	4	2	2	—
Gall-bladder disease	3	3	5	—	4	5	1	3	—	2	4	4	5	5	1	—
Prostate disease	—	—	—	—	—	10	7	4	—	—	—	—	1	8	11	1
Complicated hernia	—	—	1	1	2	4	1	1	—	—	—	1	1	3	1	—
Renal or ureteric stone	—	—	1	1	1	—	—	—	—	—	—	1	1	2	—	—
Cancer of the breast	—	—	—	2	1	2	—	1	—	—	—	1	1	—	1	1
Other diseases with laparotomy	2	—	3	6	4	7	6	2	—	—	1	1	1	1	1	3
Other	—	1	3	1	1	2	7	—	—	—	—	2	2	1	2	1

Table IV.—INCIDENCE OF THROMBOSIS RELATED TO AGE AND TO EMERGENCY OR WAITING-LIST ADMISSION IN UNSTIMULATED AND STIMULATED PATIENTS

AGE	EMERGENCY ADMISSION				WAITING-LIST ADMISSION			
	Unstimulated		*Stimulated*		*Unstimulated*		*Stimulated*	
	Total No.	Thrombosis	Total No.	Thrombosis	Total No.	Thrombosis	Total No.	Thrombosis
10–	3	—	—	—	2	—	—	—
20–	1	1	—	—	4	—	4	1
30–	11	2	4	—	6	—	5	—
40–	13	3	3	—	8	—	15	2
50–	11	4	6	3	12	4	12	1
60–	27	9	12	—	21	3	18	3
70–	24	6	13	5	10	3	15	5
80–	9	4	2	1	10	4	4	1
Total	99	29	40	9	73	14	73	13
	29·3 per cent thrombosis		22·5 per cent thrombosis		19·3 per cent thrombosis		17·8 per cent thrombosis	
	Total emergency admissions = 139 Total venous thrombosis = 38 (27·3 per cent)				Total waiting-list admissions = 146 Total venous thrombosis = 27 (18·2 per cent)			

Table V.—THE TIME AFTER OPERATION OF THE ONSET OF CLINICAL VENOUS THROMBOSIS IN UNSTIMULATED AND STIMULATED PATIENTS

PATIENT	DAY AFTER OPERATION																							
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	27	28	60
Unstimulated	0	2	5	3	2	7	5	4	4	1	1	2	1	—	—	—	—	—	—	1	1	1	1	1	1
Stimulated	0	2	1	2	2	2	3	0	2	2	1	0	1	—	—	1	1	—	—	2	—	—	—	—	—
Total	0	4	6	5	4	9	8	4	6	3	2	2	2	—	—	1	1	—	—	3	1	1	1	1	1

The time of onset of clinically overt thrombosis is shown in *Table V*. Nearly all thromboses in both groups occurred within 9 days of operation. Thrombosis would be unlikely to occur, therefore, after a patient has been discharged from hospital.

DISCUSSION

In comparing statistically two groups of patients with regard to the effect of a form of treatment carried out in one of the groups, the important factor is that the groups should match in all other respects. Whether matching is done prospectively or retrospectively (or occurs fortuitously) matters less. Assessment of the two groups in the present series has shown them to be sufficiently alike for statistical comparison to be valid.

Investigation by phlebography and by ^{125}I-fibrinogen uptake has revealed that venous thrombosis is clinically overt in a third to a half of cases (Negus, Pinto, Le Quesne, Brown, and Chapman, 1968; Kakkar, 1969). However, these methods are time-consuming, expensive, especially if a large number of patients are involved, and occasionally dangerous. Clinical assessment reveals the incidence which would resemble that found should muscle stimulation become an established procedure. In practice the clinical determination of thrombosis will continue to be used (except in some specialized centres) until a practicable safe screening test is devised.

In the comparison of two similar groups of patients the partial incidence revealed by clinical diagnosis is satisfactory as long as the proportion of those with thrombosis diagnosed in each group is the same, and as long as the total number of patients in each group is large enough to obliterate any small differences. The clinical manifestations of thrombosis form a spectrum from non-existent to severe, and in large groups of patients the spectrum is likely to be fully covered and stable so that in each individual group the proportion of those with thrombosis which is clinically diagnosable will be similar. In the present study the range of the severity of symptoms and signs of thrombosis in each group were the same. If stimulation had reduced the incidence of venous thrombosis or only its average severity there would have been fewer cases diagnosed in the stimulated group because the spectrum of clinical manifestations would have shifted towards non-existence.

Doran, Drury, and Sivyer (1964) compared the legs of each patient, one leg only being stimulated, but although it is known that in conscious subjects voluntary exercise of one limb does not alter the blood-flow through the other three limbs (Lind, Taylor, Humphreys, Kennally, and Donald, 1964) it is not known whether the same applies to patients who are passively exercised and influenced by a combination of anaesthetic drugs. This difficulty in a within-patient trial is overcome by a between-patient trial, as carried out here.

Doran, White, and Drury (1970) found that leg raising to 15° appeared to have a similar effect to muscle stimulation in reducing the incidence of thrombosis, but in the present trial, however, the combination of stimulation and leg raising made no difference in the incidence of postoperative thrombosis.

No direct evidence has yet been produced (and would be difficult to obtain) that actual clots are formed during the time of operation, although changes leading to thrombosis are probably initiated.

We conclude that the exact cause and timing of deep-vein thrombosis are not known. If immobility during surgery was a major cause of postoperative thrombosis then our trial should have been successful. There must, therefore, be other more important aetiological factors, and we found no reason for persisting with the use of electrical stimulation of the muscles of the lower limbs during operation as a means of preventing postoperative leg-vein thrombosis and pulmonary embolism.

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SHORT NOTES OF RARE OR OBSCURE CASES

BILATERAL URETERIC OBSTRUCTION CAUSED BY BENIGN PELVIC LIPOMATOSIS

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SUMMARY

A second case of bilateral ureteric obstruction owing to diffuse pelvic lipomatosis is reported. The clinical features and possible aetiological factors are discussed. The condition may be mistaken for a pelvic neoplasm due to high fixation of the bladder and colon, but it is felt that the diagnosis can be made on the basis of characteristic radiological findings. Surgical intervention is unsuccessful in replacing the bladder and colon to their normal positions but may be necessary for relief of obstruction.

ENGELS (1959) first described a very unusual condition in which the bladder and sigmoid colon are surrounded, elevated, and compressed by seemingly normal but grossly excessive amounts of fat. Since then 6 other cases have been added by Leuzinger, Bahr, Miller, and Shipman (1961) and Fogg and Smyth (1968), and a case with some similar pathological features but without visceral displacement was reported by Bender and Kass (1970). The condition is rare and has hitherto been regarded as entirely innocuous. We report here a case with severe bilateral ureteric obstruction, the second example in the literature where the ureters have been affected (Bender and Kass, 1970).

The condition is quite different from pericystitis or retroperitoneal fibrosis and probably constitutes a separate disease entity related perhaps to other visceral lipodystrophies. It presents a number of difficulties in diagnosis and management which raise problems of unusual practical and theoretical interest.

CASE REPORT

D. B., a merchant seaman, aged 39 years, first began at the age of 26 (1956) to have attacks of vague central abdominal pain which became gradually worse. By 1960 he was getting recurrent attacks of low-grade fever, nausea, vomiting, headaches, frequency of micturition, and dysuria. He was constipated, producing ribbon-like stools surrounded by large amounts of mucus but no blood. In February, 1964, now aged 34, he complained of suprapubic tenderness and was found to have a large irregular tender mass arising from the pelvis. He was admitted to St. Peter's Hospital under Mr. D. M. Wallace. An I.V.P. at that time showed a high bladder, left hydronephrosis, and a normal right ureter. At cystoscopy, which was difficult because of the position of the bladder, there appeared to be a papilliferous change at the bladder neck, but biopsy of this showed only polypoidal cystitis and epithelial hyperplasia. At laparotomy on 21 Feb., 1964, the bladder and sigmoid colon were found to be displaced upwards by a large amount of fat filling the pelvis. Although the left ureter was distended, no definite obstruction could be found. On opening it, bougies were easily passed through the ureteric orifice into the bladder.

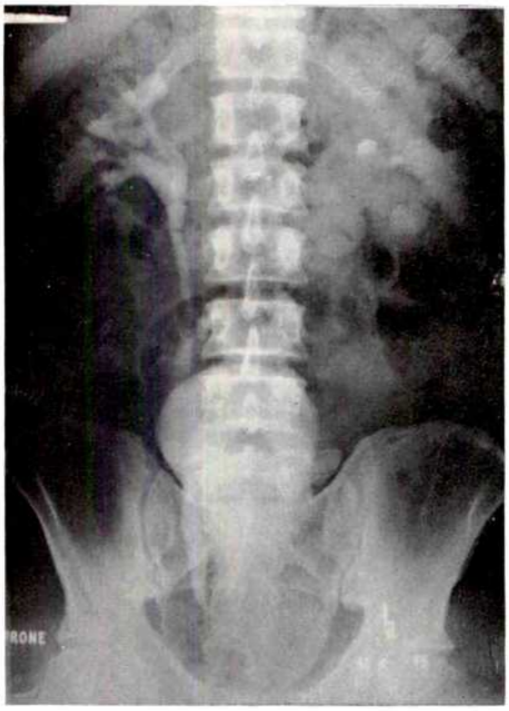

FIG. 1.—I.V.P. in June, 1964. The bladder is seen to be pear-shaped with its fundus projecting out of the pelvis. The collecting tract on the left side is grossly dilated and there is commencing dilatation on the right.

Following operation his former symptoms remained and, in addition, he began to suffer perineal ache and soreness. Four months after operation an I.V.P. showed some dilatation of the other (right) ureter and an increasing hydronephrosis of the left (*Fig.* 1). Cystoscopy in July, 1964, and September, 1965, demonstrated the left half of the bladder to be oedematous and swollen. He defaulted thereafter from St. Peter's.

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He came to the London Hospital in 1969 now complaining of flushing of the face, dysuria, perineal soreness, and nausea which were becoming unbearable. On examination he had marked clubbing of fingers and toes and a large tender suprapubic mass. Rectal examination was remarkable, the pelvis seeming surprisingly empty and the prostate impalpable. Investigations were as follows: haemoglobin, 14·5 G.; white-blood count, 4300; E.S.R., 22 mm. per hour; urea, 39 mg. per 100 ml.; creatinine clearance, 63 ml. per minute. Chest radiographs, lung function, and 5-hydroxyindolacetic acid (5-HIAA) excretion were normal. Specific complement-fixation tests for lymphogranuloma venereum were negative. The urine was sterile and contained neither cells nor casts.

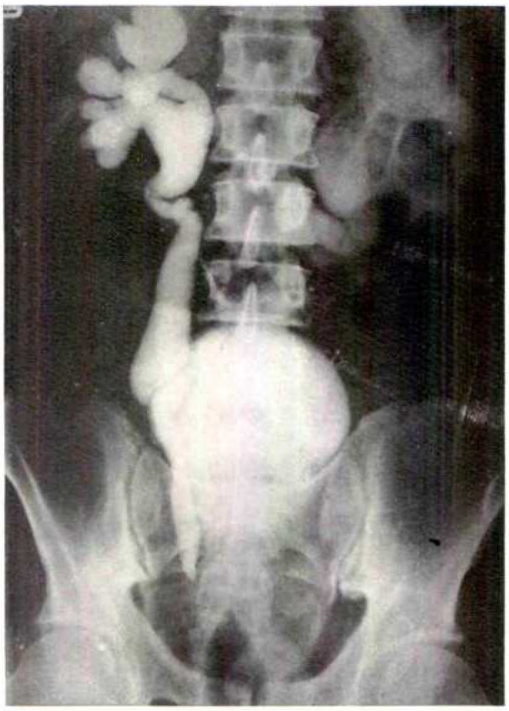

FIG. 2.—I.V.P. in April, 1969. There is gross dilatation of the collecting tract on both sides; the appearance of the bladder is unchanged.

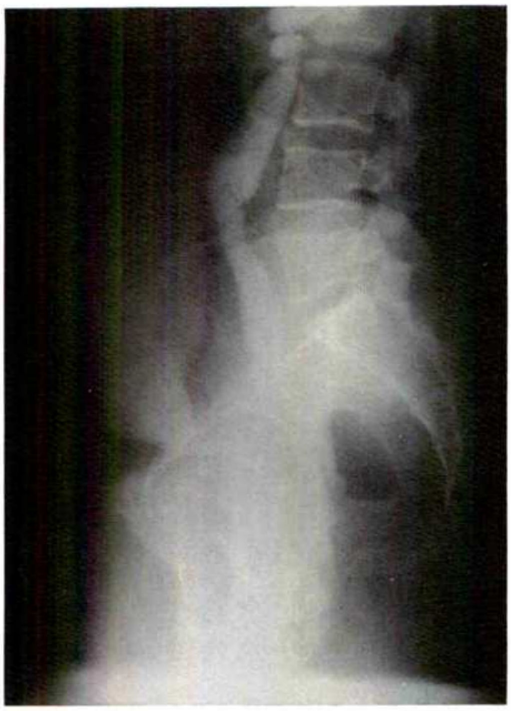

FIG. 3.—I.V.P. in April, 1969. Lateral view showing elevation of the base of the bladder with a uniform circumferential compression of its lower part. The ureter shown is seen to be dilated down to its point of entry into the bladder.

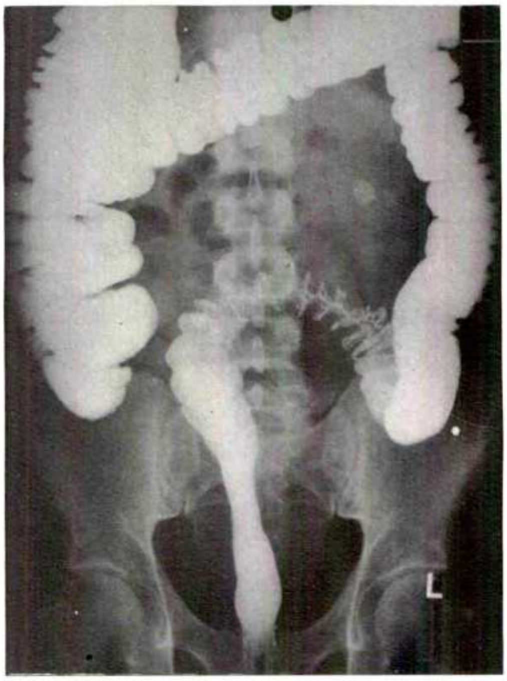

FIG. 4.—Barium enema showing a narrowing of the rectum and distal sigmoid colon which rises vertically from the pelvis.

Sigmoidoscopy revealed normal mucosa but an excess of mucus; the rectum appeared as if straightened out and showed none of the usual deviations or 'valves' of Houston. A rectal biopsy was normal. On cystoscopy the bladder wall was oedematous and the left wall of the bladder outlet was occupied by tissue not unlike the lateral lobe of the prostate. An I.V.P. (*Figs.* 2, 3) showed the bladder to resemble an inverted pear with its fundus high in the abdomen. The pelvi-caliceal systems and ureters were dilated down to the entry into the bladder. The appearances indicated a uniform extrinsic compression of the bladder, elevating its floor and narrowing its coronal and sagittal diameters. A barium enema (*Fig.* 4) showed that the rectum and sigmoid colon rose vertically from the pelvis, consistent with uniform extrinsic compression. A lymphangiogram showed normal pelvic and abdominal nodes with no evidence of lymphatic obstruction.

At operation the bladder was found to occupy the position of a 20-week-pregnant uterus. Both ureters were grossly distended, and distally they were encased in a mass of fibrofatty tissue which appeared to be obstructing them. The whole bladder was encased in a hood of fat which infiltrated the muscle-fibres of its posterior wall. The sigmoid colon was also surrounded by this tissue and was adherent to the fundus of the bladder. The fat was tough, dense, and firm and made it impossible to dissect the ureters free distal to the superior vesical vessels. They were, therefore, divided and reimplanted into the bladder using a tunnel-and-cuff technique. The large hood of fat around the bladder was removed with some difficulty, as was a large mass of fat lying between the left external iliac artery, ureter, and bladder. A thorough search of the abdominal contents and mesentery failed to show any other deposits of fatty tissue.

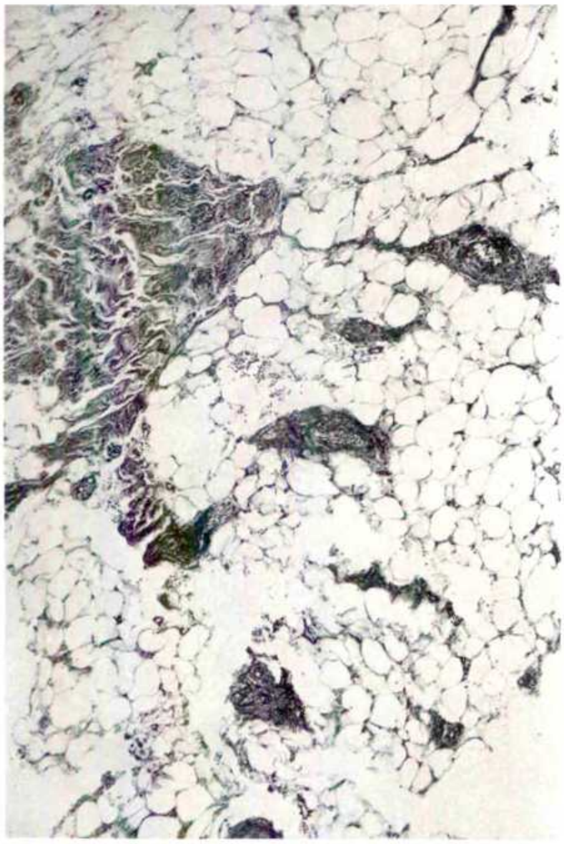

FIG. 5.—Normal fat and fibrous tissue which was removed from the fundus of the bladder and which was infiltrating the wall. Van Gieson. (× 16.)

Histologically the tissue was composed of normal-looking fat cells, with no evidence of inflammation or granulomata and only a few scattered areas of fibrosis. The fat was infiltrating the muscle-fibres of the bladder wall (*Fig.* 5).

Since discharge his symptoms have remained, but there has been no further deterioration in renal function as assessed by creatinine clearance and blood-urea. The bladder remains fixed in the same position and the sigmoidoscopic appearances are unchanged. A postoperative I.V.P. 1 month after operation showed that both ureters were less dilated (*Fig.* 6).

DISCUSSION

Twelve other cases of diffuse pelvic lipomatosis have appeared in the literature (Engels, 1959; Leuzinger and others, 1961; Fogg and Smyth, 1968; Bender and Kass, 1970). Some presented with symptoms of recurrent urinary-tract infection, low-grade fever, and suprapubic tenderness, whilst others had minimal complaints and were only found on routine investigation of unrelated conditions. Most cases complained of mild constipation, but mucus-covered stools have only been reported in the present case and in 1 of Engels's patients. A suprapubic mass resembling a pelvic neoplasm was found in 8 cases, and in some of these the prostate was not felt on rectal examination.

The radiographic appearances were similar in all cases except that of Bender and Kass (1970), but only 1 other case had hydronephrosis at presentation. The radiological features of the condition were (1) undue radiolucency of the soft tissues of the pelvis (Fogg and Smyth, 1968); (2) a high, pear-shaped bladder with circumferential compression of its base; (3) the rectosigmoid rising vertically from the pelvis, and (4) no evidence of loss of distensibility, contractility, emptying, or altered mucosal pattern in either the bladder or the rectum. Three cases had histological changes of chronic cystitis, but in all cases the rectal mucosa was normal.

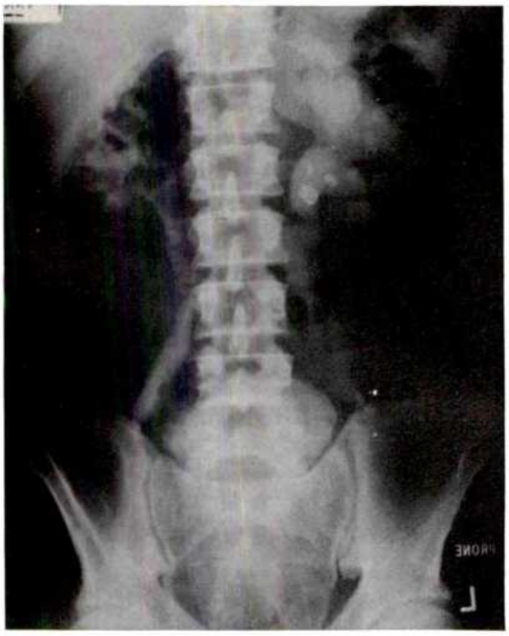

FIG. 6.—I.V.P. in June, 1969, showing the ureters to be less dilated but the appearance of the bladder remains unchanged.

All the patients who were explored were found to have excess fat distributed diffusely throughout the pelvis with the exception of the case of Bender and Kass (1970), where firm, non-tender masses were fixed to the lateral walls of the pelvis. In 4 out of 5 cases with fibrosis and adhesions, areas of chronic inflammation were seen in the adipose tissue. In all cases the fat cells have been histologically normal, although it is admittedly difficult to distinguish hyperplastic from benign fatty tissue and it is of interest that in our case the fat was found to be infiltrating the bladder wall despite its benign histological appearance.

The natural history of the condition is unknown as no long-term follow-up has been reported. However, in 3 cases there was evidence of progressive hydronephrosis. The aetiology is unknown. Engels (1959) suggested that the findings in most of his cases could be explained by the late and exaggerated results of chronic lower urinary-tract infection, accompanied by non-specific inflammation of the perivesical tissues. But many cases had neither adhesions nor urinary-tract infection, and such an excessive deposit of fat is not described as a consequence of infection elsewhere in the body. An isolated lipodystrophy was described by Crane, Aguilar, and Grimes (1955) and Rogers, Demetrakopoulos, and Hyams (1961) in patients whose mesentery was involved by tumour masses composed of nodules of structurally altered fat cells which were smaller than normal and were supported by a delicate reticular framework. The cells were abnormal, some were multinucleate and in others the nucleus was central, small, round, and hyperchromatic. None of these features was present in this case.

The recurrent relapsing inflammatory symptoms and tenderness recall the systemic variant of Weber-Christian disease (Steinberg, 1953; Ogden, Bradburn, and Rives, 1965). However, in these cases the visceral fat was confined to the mesentery, there was subcutaneous involvement, and characteristic lipid-laden macrophages were present in mesenteric fat.

Lipomas possess a definite capsule and those described in the pelvis are usually presacral, where they displace the colon anteriorly but cannot produce the characteristic bladder deformity seen in these cases.

Neither malignant nor granulomatous reactions were present excluding liposarcoma, traumatic fat necrosis, sclerosing lipogranuloma, and xanthogranuloma.

This condition seems to be a diffuse benign proliferation of normal fat cells in the pelvis from no known cause. It produces symptoms and signs because of pressure perhaps added to by fibrosis following the introduction of infection. Surgery may be needed in order to relieve obstruction or to establish a diagnosis. In none of the reported cases has it been feasible to remove enough of the fat to allow the displaced bladder and rectum to return to their normal position.

Acknowledgements.—We would like to thank Dr. J. Ellis, Mr. D. M. Wallace, and Professor J. Blandy for permission to publish this case, and Dr. J. Landells for reviewing the histology. We would also like to thank Mr. Ruddock, London Hospital Photographic Department, for the photographs.

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HYDROPNEUMOTHORAX COMPLICATING PERFORATED PEPTIC ULCER

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SUMMARY

A case of duodenal ulcer perforation complicated by hydropneumothorax, probably due to a congenital diaphragmatic defect, is described. No such case has previously been reported.

CASE REPORT

Mrs. B. D., aged 49, was admitted as an emergency with a diagnosis of pyloric stenosis. The patient had complained of epigastric pain for 1 week, had vomited, and had passed a melaena stool during the 24 hours prior to admission.

Peptic ulcer symptoms had been present for 12 years with exacerbations two or three times a year. Her twin sister also had peptic ulcer symptoms.

On examination the patient was pale and had a dry furred tongue. The pulse-rate was 90 per minute, regular, and of good volume; blood-pressure was 120/80. The abdomen was soft and without guarding and was neither distended nor rigid. There was no intra-abdominal mass but epigastric discomfort was present. On the day of admission a barium meal was carried out which confirmed the clinical diagnosis of pyloric stenosis (*Fig.* 1).

Thirty hours after admission the patient complained of sudden severe abdominal pain and right chest pain radiating to the right shoulder tip. Subsequently there was an episode of retching and she vomited a little barium.

The patient now showed the signs of generalized peritonism and an erect abdominal radiograph demonstrated free gas under the diaphragm. Furthermore, a chest radiograph taken at the same time showed a right-sided hydropneumothorax (*Fig.* 2).

Oesophagoscopy was performed under a general anaesthetic but an oesophageal lesion was not seen. A right chest tube was inserted and connected to an underwater seal. It immediately drained 500 ml. of dark brown fluid. A laparotomy was then carried out. Gas and free fluid were present in the peritoneal cavity. The lower oesophagus was normal. The stomach was very large. There was severe pyloric deformity and a 1·5-cm. perforation in the anterior wall of the duodenum. There was a small hole in the dome of the right hemidiaphragm to the right of the central tendon, about 2 mm. in diameter, through which the point of a haemostat could be passed into the pleural cavity. There was generalized inflammation of the peritoneum but this was not locally greater around the hole in the diaphragm.

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The diaphragmatic defect was closed, the duodenal perforation was oversewn, and a total vagotomy and gastro-enterostomy was carried out. After peritoneal toilet the abdomen was closed.

The patient made an uneventful recovery. She was given a course of ampicillin and neither chest nor abdominal sepsis was a problem. A right basal effusion resolved slowly and the patient was discharged from hospital on the twenty-first postoperative day.

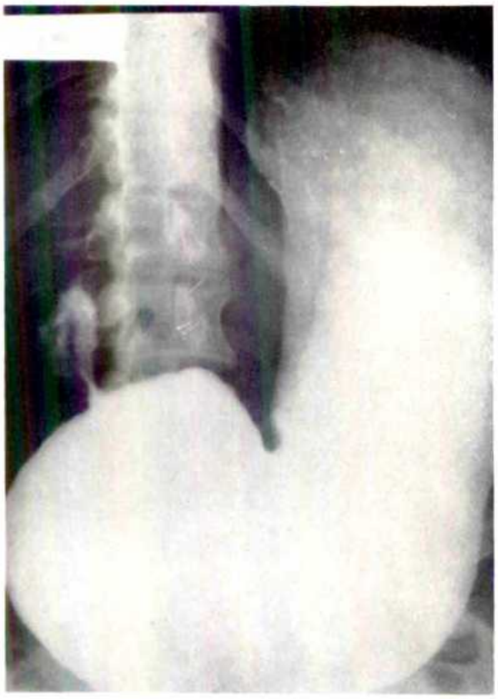

FIG. 1.—Barium meal showing pyloric stenosis.

DISCUSSION

A search of the *Index Medicus*, both manually and by Computer Medlar methods, and a review of the chest section of *Excerpta Medica* failed to find a reference to a similar case. Killen and Gobbel (1968), in their monograph, discuss spontaneous rupture of the oesophagus, in which spontaneous pneumothorax is a frequent finding. Perforated duodenal ulcer, however, is not listed as a cause, but only as part of the differential diagnosis of spontaneous pneumothorax. These authors also state that only 0·2 per cent of spontaneous pneumothoraces are due to subphrenic abscess. It is of note that inflammatory changes were not present around the diaphragmatic defect in our case.

Shapiro (1955) discussed the aetiology of spontaneous pneumothorax associated with pneumoperitoneum used in the treatment of pulmonary tuberculosis. Spontaneous pneumothorax is a rare complication of this technique and 36 cases were documented in his review. Only 5 of these patients developed spontaneous pneumothorax immediately after induction of the pneumoperitoneum. Shapiro postulated that a congenital hole in the diaphragm explained the aetiology in this small group. The larger group developed spontaneous pneumothorax at varying time intervals (i.e., a few days to months) after induction of pneumoperitoneum. In these cases Shapiro suggested that a muscular defect is present in the diaphragm bringing the pleura and the peritoneum into contact. The pressure gradient across the diaphragm causes herniation and bleb formation at this point; these blebs can be seen on radiographs and at thoracoscopy. A sudden rise of intra-abdominal pressure may cause bleb rupture and allow air to pass from the abdomen to the chest.

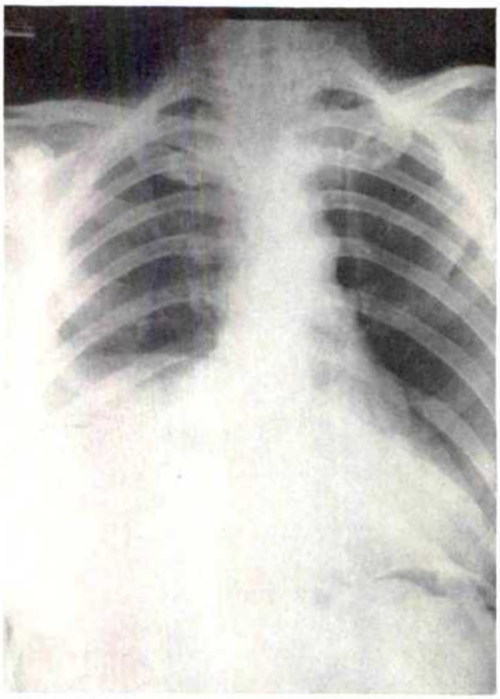

FIG. 2.—Chest radiograph showing air under the left hemi-diaphragm and right-sided hydropneumothorax.

Finn and Jowett (1970) reported 2 cases of hydrothorax developing acutely after the institution of peritoneal dialysis. These authors also said that chronic right-sided pleural effusions are not uncommon after repeated peritoneal dialysis. These two groups appear to parallel those described by Shapiro (1955). Finn and Jowett (1970) also state that pleural effusion, particularly right-sided, can complicate ascites and that post-mortem examinations have demonstrated small defects in the diaphragm in some cases.

These parallel clinical situations lead us to conclude that small defects in the diaphragm occur especially on the right side. Gas or liquid may traverse such a defect to occupy the pleural cavity.

Acknowledgements.—We would like to thank Miss M. P. Shepherd, F.R.C.S., and Dr. D. R. McPherson, F.F.R.

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A CASE OF RETROPERITONEAL HAEMANGIOMA

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SUMMARY

A case is reported of a retroperitoneal haemangioma occurring in a 26-year-old multiparous patient. The literature is reviewed and the pathology considered.

RETROPERITONEAL tumours are rare, only 0·2 per cent being so situated in a series of 60,000 tumours seen at the Memorial Hospital, New York, between 1926 and 1951 (Pack and Tabah, 1954a). The incidence of benign retroperitoneal tumours varies from 13 per cent (Braasch and Alberto, 1967) to 34 per cent (Pack and Tabah, 1954b). Of these very few are haemangiomas, fewer than 30 cases having been reported to date.

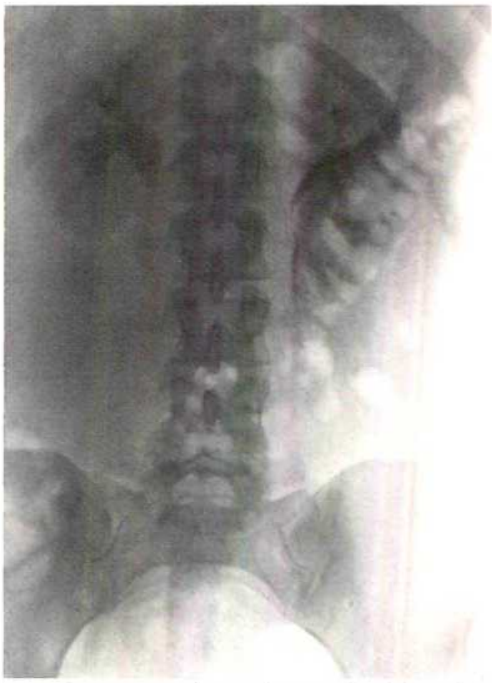

FIG. 1.—Intravenous pyelogram demonstrating hydronephrosis and displacement of the right kidney.

CASE REPORT

A 26-year-old woman, mother of 4 children, aged 7, 6, 2 years, and 10 months, when first seen gave a history of a painless abdominal swelling of 6 weeks' duration. She had not suffered any alteration of appetite or bowel habit, her weight remained unchanged, and, apart from the presence of a mass, she had no symptoms.

Physical examination showed the presence of a visible mass on the right side of her abdomen extending from the costal margin to the iliac fossa. The mass, which was firm and lobulated, was dull to percussion but not attached to the anterior abdominal wall. No other clinical abnormality was detected.

Laboratory investigations showed haemoglobin to be 86 per cent (12·6 g. per cent), white blood-count, 6000 per c. mm. with a normal differential count, and E.S.R., 28 mm. per hour. Urea, electrolytes, and liver-function tests were all within normal limits.

Intravenous pyelography (*Fig.* 1) showed a right hydronephrosis in a kidney which was displaced upwards. A soft-tissue mass was seen compressing and displacing the ureter medially, producing obstruction at the level of the 3rd lumbar vertebra.

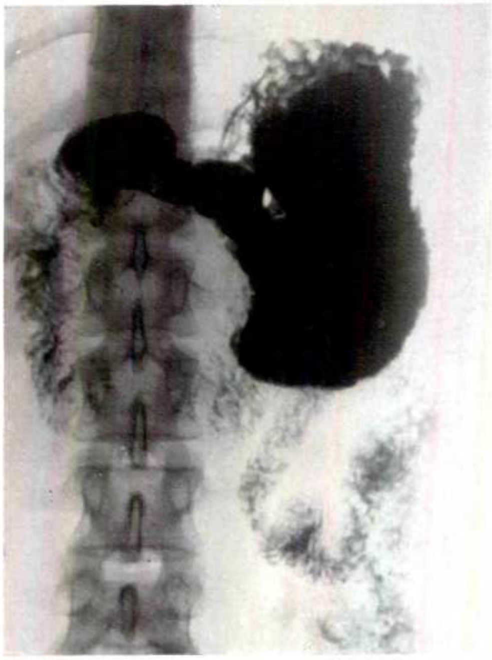

FIG. 2.—Barium meal showing upward displacement of the greater curvature of the stomach.

Barium meal and follow-through showed that the greater curvature of the stomach was displaced upwards (*Fig.* 2) and the hepatic flexure of the colon was displaced downwards (*Fig.* 3). There was no intrinsic lesion in the gastro-intestinal tract.

The diagnosis of a retroperitoneal tumour was made and a laparotomy performed. At operation a retroperitoneal tumour, 16–23 cm. in diameter, was found which was mobilized without undue difficulty, after reflecting the ascending colon medially and the duodenum upwards and freeing the mass where it was firmly attached to the head of the pancreas. The only remaining point of attachment was by a vessel, 0·75 cm. in diameter, running to the infrarenal inferior vena cava. After division of this vessel the mass was removed.

Postoperatively there were no complications and the patient was discharged on the fourteenth postoperative day.

Naked-eye examination of the specimen showed it to be a bosselated, smooth, cystic tumour, measuring

23 × 16 × 10 cm. (*Fig.* 4). The cysts varied in diameter, the maximum being 8 cm., and were filled with blood and thrombus of recent and older origin. The cut surface had a honeycomb appearance (*Fig.* 5), the lining of the cysts being smooth with focal areas of nodularity and the space between them consisting of fibro-fatty tissue. The venous connexions were demonstrated, but no major arteries were seen.

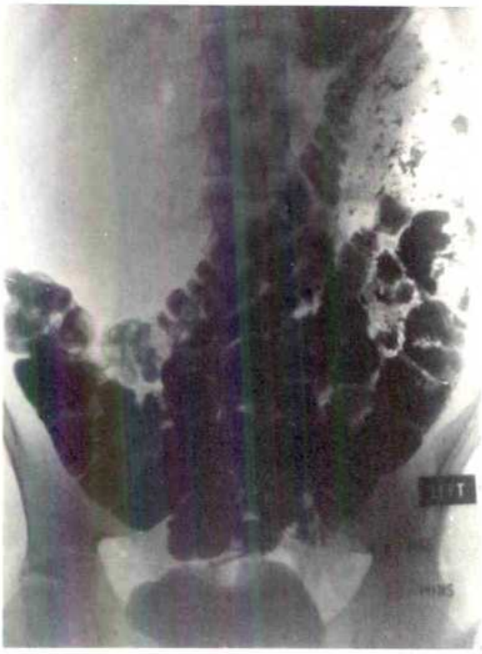

FIG. 3.—Barium follow-through showing displacement of the hepatic flexure.

Microscopically the tumour consisted of large vascular spaces lined by endothelium, beneath which were collections of smooth-muscle fibres, fragmented elastic tissue, and fibrous stroma. The smooth muscle frequently demonstrated discrete pads which projected into the lumen and some of these were covered by plaques of fibrous tissue. Haemosiderin-laden macrophages were seen in some of these fibromuscular pads, indicating an origin from organized thrombus. The intercystic stroma consisted of fibrous and adipose tissue together with smooth muscle and scanty lymphoid follicles.

DISCUSSION

The morphology and origin of the tumour confirm the clinical impression that the lesion was a venous haemangioma. The origin from below the right renal vein in the segment of the inferior vena cava derived from the postrenal segment of the right supracardinal vein (McClure and Butler, 1925) suggests the possibility that the tumour was derived from the remnants of the anastomosis between the supra- and post-cardinal veins, possibly in relation to anastomoses developing in the mesonephros.

The increase in size of the lesion is unlikely to be the result of active growth, even though pregnancy is known to be associated with the appearance or progression of angiomas. Haemangiomas are hamartomatous tumours (Willis, 1962) and, as such, rapid growth is unusual and may be an indication of malignancy, of which there is no evidence in this case. Indeed, it is possible that this tumour represents a variety of cirsoid aneurysm which, as Willis (1962) indicates, cannot be entirely separated from angiomata on morphological grounds. The probability is that the increase in size results from thrombosis and obstruction to the outflow of blood, with or without

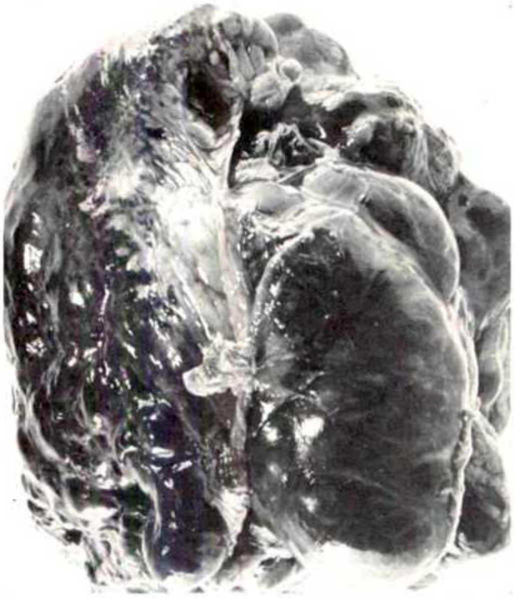

FIG. 4.—Smooth surface of the multicystic retroperitoneal tumour.

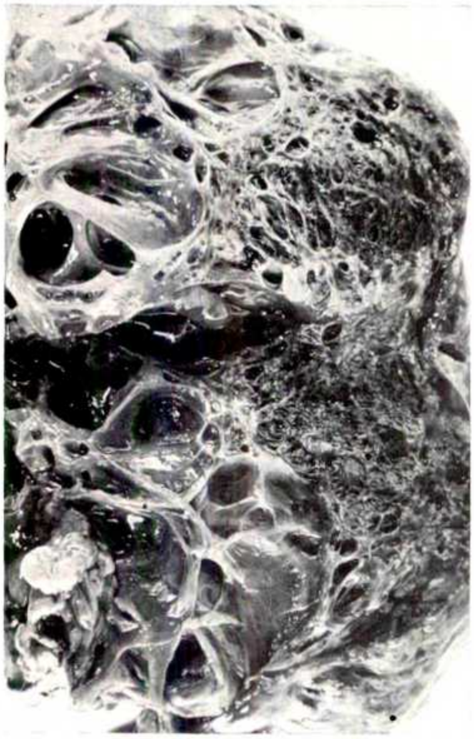

FIG. 5.—Cut surface of the tumour demonstrating multiple smooth-lined cysts.

the opening up of previously collapsed vascular channels.

That the tumour should present clinically soon after pregnancy yet be absent at delivery is significant, since in the puerperium there is an increased tendency to develop thrombotic episodes particularly in the venous system (Bonnar, Prentice, McNicol, and Douglas, 1970).

Acknowledgement.—We are grateful to Mr. V. S. Brookes, under whose care this patient was admitted, for allowing us to report this case.

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A SINGLE CONGENITAL ARTERIOVENOUS FISTULA OF THE HAND

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THE following case of an arteriovenous fistula of the hand had several unusual features; in particular, there was pain in the shoulder and axilla and the axillary artery was dilated.

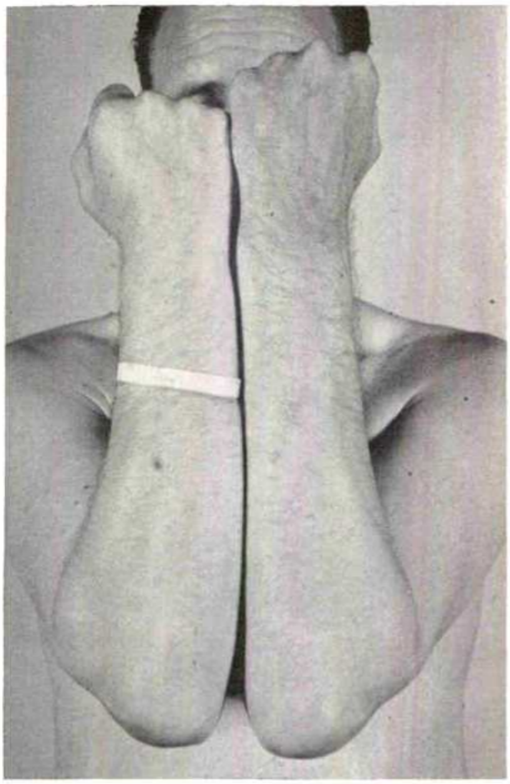

FIG. 1.—Photograph showing the increased length of the left forearm.

CASE REPORT

Mr. A. H., a laboratory technician aged 39, presented with pain in the left shoulder and a feeling of fullness in the left axilla, heaviness in the arm, and a throbbing pain in the hand whenever he exercised it. These symptoms had been getting steadily worse for 18 months. The shoulder pain radiated up the neck, across the chest, and down the arm. Although he was right-handed he had become incapacitated.

In 1946, when he was 16, a cricket ball struck the ulnar border of his left hand whilst he was batting: the hand became very painful, swollen, and discoloured. The symptoms subsided, but he was never quite free from trouble and, by 1950, the little finger became gangrenous and required amputation. In 1954 the ring finger became painful, swollen, and discoloured and an arteriogram showed an arteriovenous fistula. The left hand was explored and the ring finger was amputated. In 1960 the middle finger had developed a flexion deformity and was straightened by an operation on the skin.

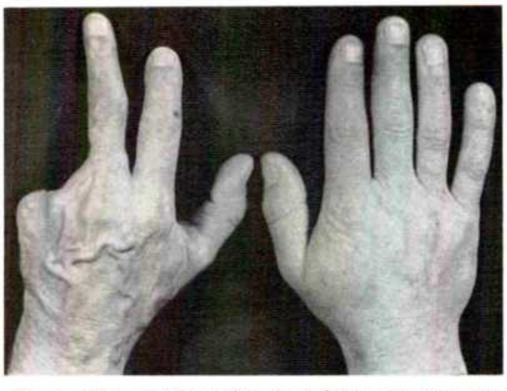

FIG. 2.—The condition before the definitive operation. Note the dilated veins on the dorsum of the hand. Compare with the normal right hand.

When first seen, general examination showed a fit man, the pulse-rate was 84 beats per minute and regular, and there was no cardiac enlargement or cardiac failure. The blood-pressure was 130/70 mm. Hg in all limbs. There were no abnormal neurological signs. Chest radiographs and electrocardiograms were normal.

Examination of the arms showed that the left forearm was 5 cm. longer than the right (*Fig.* 1) and that there were large dilated pulsatile veins on the dorsum of the left hand (*Fig.* 2). The ulnar border of the hand proximal to the site of the amputated fingers was purplish in colour. The

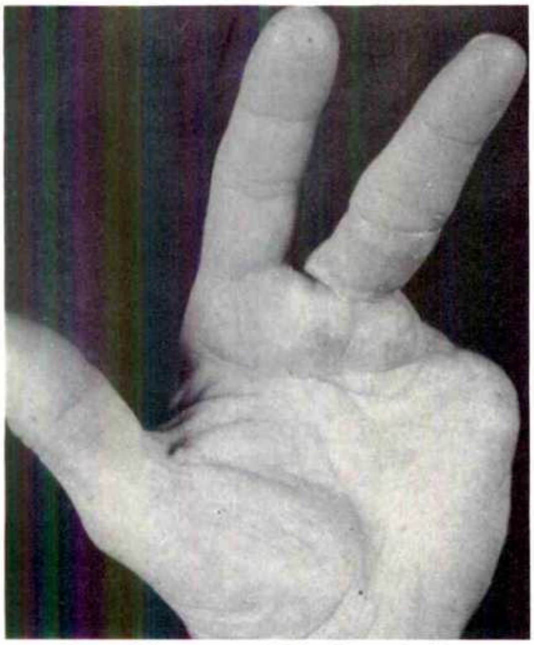

FIG. 3.—Palmar aspect of left hand shown in *Fig.* 2.

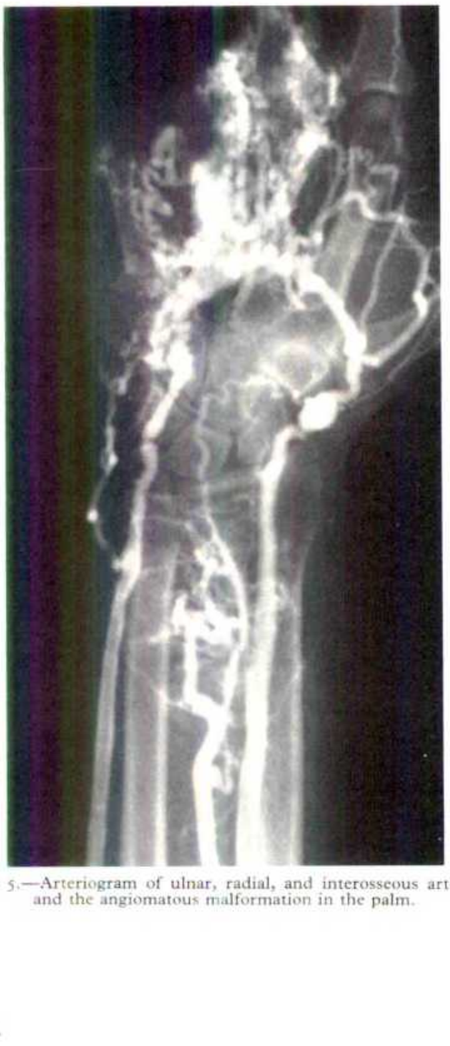

FIG. 5.—Arteriogram of ulnar, radial, and interosseous arteries and the angiomatous malformation in the palm.

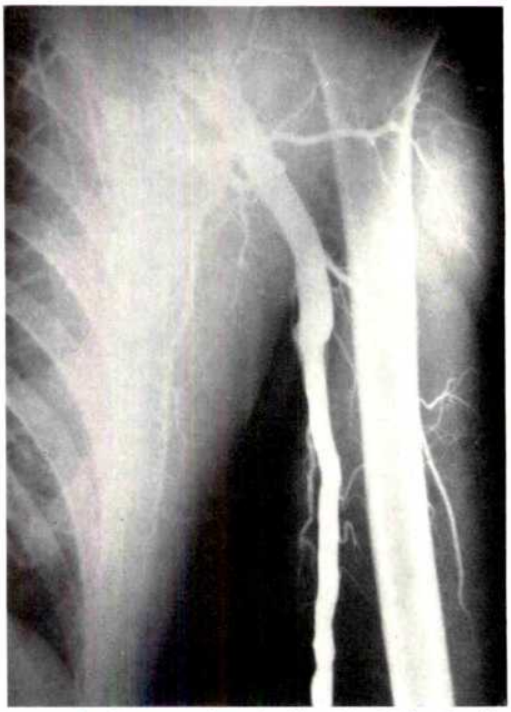

FIG. 4.—Arteriogram to show the dilated brachial and axillary arteries.

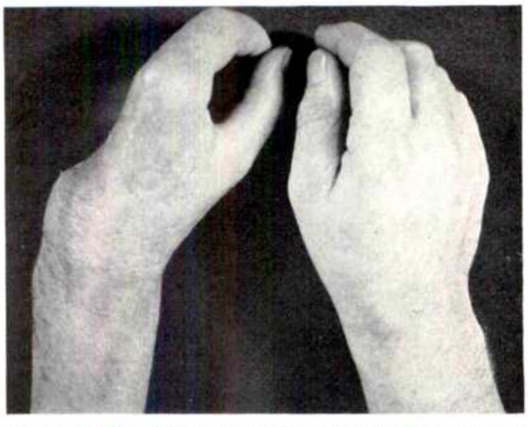

FIG. 6.—Results of ablative operation. Note the absence of veins on the dorsum of the left hand and the finger-to-thumb grip.

middle finger had a flexion deformity (*Fig.* 3) and was almost useless. The skin below the elbow was warmer on the left than on the right. There was a thrill from the hand to the axilla which corresponded to a buzzing machinery bruit, loudest over the third, fourth, and fifth metacarpals. Occlusion of either the radial artery or the ulnar artery reduced the intensity of the bruit in the hand, while occlusion of both of these vessels or of the brachial artery stopped the bruit and the pulsation of the veins on the dorsum of the hand. Occlusion of the brachial artery had no effect upon the heart-rate or the pulse pressure (negative Branham's sign).

Routine blood tests were normal. Analysis of blood from the right femoral artery, a vein on the right arm, and a dilated vein on the dorsum of the left hand showed partial arterialization of that from the dilated veins (*Table I*).

Radiographs of the thoracic inlet, left shoulder, and cervical spine were normal. The arch aortogram showed that the left subclavian and axillary arteries were dilated (*Fig.* 4) and that the radial and ulnar arteries flowed into an arteriovenous malformation in the hand (*Fig.* 5). There were no signs of arteriovenous fistulae elsewhere.

OPERATION.—A combined operation was performed by a vascular and a plastic surgeon. A longitudinal incision was made from the flexor aspect of the wrist into the palm and then continued proximally up the forearm. The ulnar and interosseous arteries were tied in the forearm and the radial artery was left intact. The useless middle finger and the third, fourth, and fifth metacarpals were excised together with the arteriovenous fistula which was closely related to these bones (*Fig.* 5). Thus the transverse head of adductor pollicis, the hypothenar muscles, and some interossei were necessarily divided. The median and ulnar nerves were identified and spared. The dorsal flap of skin was mobilized and the wound closed (*Fig.* 6). After the operation the throbbing pain in the hand and the symptoms in the shoulder and axilla disappeared. Despite vigorous physiotherapy the index finger lost 30° of extension after 5 weeks. At this stage a second operation was done to free fibrous bands in the palm, and an abdominal wall pedicle flap was attached to provide extra skin in the palm. The inset was completed 4 weeks later. Healing was excellent and the patient was able to extend the index finger fully and to grip between the index finger and the thumb.

Table I.—ANALYSIS OF BLOOD

BLOOD	*p*H	P_{O_2} (mm. Hg)	P_{CO_2} (mm. Hg)	STANDARD BICARBONATE (m*N*)	BASE EXCESS (mEq.)
Normal values					
Arterial	7·33–7·45	80–100	36–44	23–28	—
Venous	7·27–7·43	20	46	24–29	—
Present case					
Right femoral artery	7·40	70	42	26	−1
Right-arm vein	7·37	35	45	25	−0
Left-hand dorsum vein	7·42	58	39	25	+1

DISCUSSION

Despite the history of trauma at the age of 16 years there are three reasons for considering that the fistula was congenital (Holman, 1937; Flanc, 1968).

First, the left forearm was 5 cm. longer than the right. Secondly, the arteriogram (*Fig.* 5) showed a bizarre vascular pattern suggestive of a congenital malformation. Thirdly, histological examination showed fibro-elastic intimal thickening with fragmentation of the internal elastic laminae of the feeding arteries, and so was reminiscent of the 'arteriovenous angioma' described by Malan and Puglionisi (1965). This type of congenital arteriovenous fistula has also been variously called 'red angioma' by Broca (1869), 'arterial cavernous angioma' by Virchow (1876), and 'arterial racemose angioma' by Aschoff (1914). Malan and Puglionisi (1965) reported 16 cases of arteriovenous angioma of which 4 had an extensive arteriovenous shunt and 12 were hypoactive. Only 1 of the 4 active arteriovenous angiomas was in the hand.

In the present case the shoulder pain and axillary 'fullness' were attributed to the dilated main arterial trunk (*Fig.* 4). It was envisaged that this was perhaps nipped between the scalene muscles and the first rib. If the shoulder pain had not subsided after resection of the fistula, scalenotomy would have been considered but fortunately was not necessary.

Acknowledgements.—We wish to thank Professor R. B. Welbourn for help in preparation of this paper and Mr. Peter Martin for allowing us to record his patient.

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SPONTANEOUS RUPTURE OF THE STOMACH IN AN ADULT

BY CHRISTOPHER D. JEFFERISS*

WEST DORSET GROUP HOSPITALS

SUMMARY

A case of spontaneous rupture of the stomach in an adult is described following retching with pyloric stenosis. A table of the more recent of the 47 cases described in the world literature is given with references to all the reported cases.

SPONTANEOUS rupture of the stomach in an adult is a rare occurrence and the case to be reported is only the forty-seventh in the world literature. This case is also of interest in that the rupture happened shortly after admission to hospital so that the nature of the emergency was rapidly recognized and treated.

A brief review of the literature will be given covering the cases which have been reported since Albo, de Lorimier, and Silen reviewed all the cases that they found up to 1963, although of their 44 cases, 5 should be considered traumatic.

CASE REPORT

E. G. V., a housewife aged 58 years, was admitted to Dorset County Hospital on 19 Oct., 1968, with a 6-day history of epigastric pain, vomiting, and diarrhoea. For 4 months she had subsisted on a diet of semolina, Complan, and Benger's food for relief of classic peptic ulcer symptoms which had been diagnosed as 'hiatus hernia' and which had gradually progressed to copious foul-smelling vomits and eructations. Fourteen years previously she had had similar symptoms diagnosed as 'colitis', for which no treatment had been given after a negative contrast enema.

On admission she was dehydrated with a distended tympanitic abdomen (increase girth, 16 cm.) but had no pain. There was no succussion splash and no visible peristalsis. The rectum was empty. A tentative diagnosis of small-bowel obstruction was made but plain radiographs showed a grossly distended stomach containing air and fluid, indicating a marked and long-standing pyloric stenosis (*Fig.* 1). There was no pneumoperitoneum.

Shortly after the radiographs were taken the patient started to retch, suddenly developing severe abdominal pain and rigidity. She was hypotensive, slightly cyanosed, and markedly dyspnoeic. A diagnosis of perforation of the stomach was made and after 3 litres of saline had been infused intravenously laparotomy was performed.

The peritoneum was opened with a rush of air and foul free fluid revealing a collapsed but enormous stomach. There was a tear 18 cm. long on the lesser curve, of which 7 cm. was through all layers and the rest only through the serosal layer. The tear was sutured in one layer with difficulty owing to the friable nature of the gastric wall, and

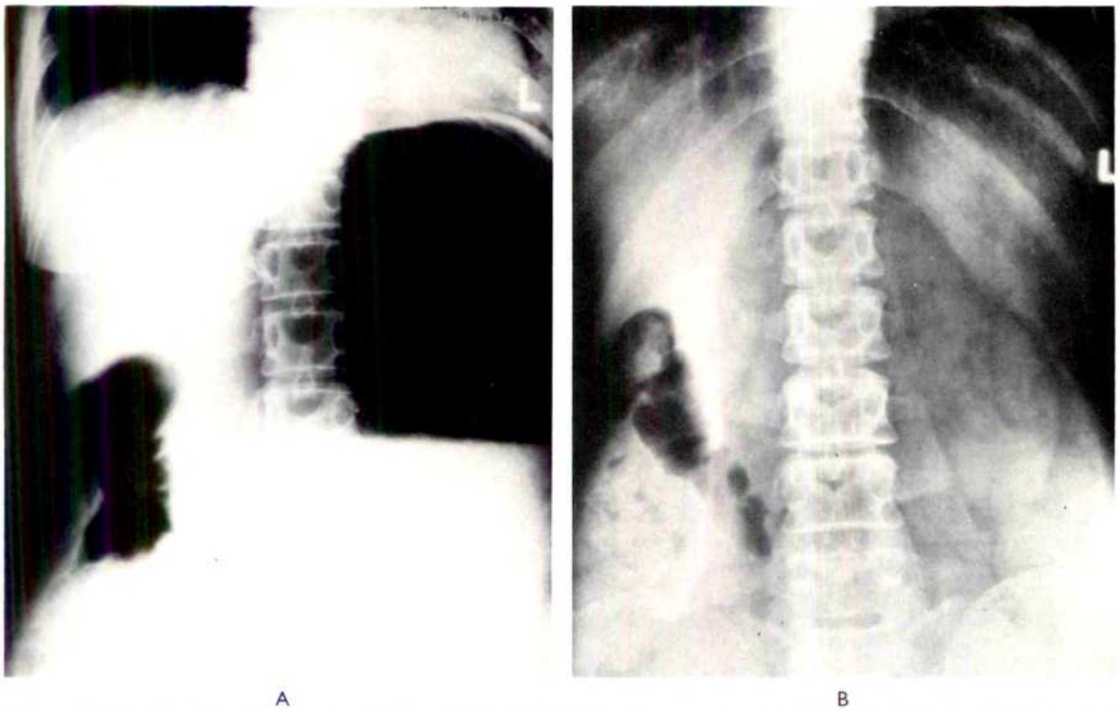

FIG. 1.—Radiographs taken on admission showing a grossly distended stomach containing air and fluid. A, Erect view. B, Supine view.

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then vagotomy with anterior gastrojejunostomy was performed. The peritoneal cavity was cleaned and noxythiolin, 2·5 g. in solution, instilled with drains left to the pelvis and the site of the rupture.

The patient was ambulant and commenced a normal diet on the third postoperative day, being discharged home on the fourteenth postoperative day. At 1 month she was very well and only complained of occasional looseness of stools to direct questioning. She remained well until readmission to hospital with a short history of intestinal obstruction 6 months later, when she was found at laparotomy to have a carcinoma of the caecum from which she later died, peritoneal deposits being present at this time.

DISCUSSION AND REVIEW

The diagnostic criteria for rupture of the stomach according to Millar, Bruce, and Paterson (1957) are severe abdominal pain, tympanitic distension with rigidity, subcutaneous emphysema, and 'shock'. Many of the cases described lack subcutaneous emphysema, especially when diagnosis and laparotomy have been early. In the present case the suddenness of the onset of 'shock' was dramatic and was probably related to both the gross contamination of the peritoneum and to tension pneumoperitoneum, which might have been rapidly relieved by a needle, as reported by Olsen and Foley (1961) in the treatment of a similar condition occurring in children after tonsillectomy.

Table I.—SUMMARY OF 8 CASES REVIEWED IN THE LITERATURE SINCE 1963

AUTHOR AND YEAR	AGE AND SEX	COMMENTS	TIME BEFORE OPERATION	OPERATION	RESULT	SITE OF TEAR
Cronin, 1959	61 M.	Large meal, gastritis	Over 5 hours	Suture of tear	Died	Lesser curve
Shaldon, 1961	49 F.	10 years' peptic ulcer	Not stated	Suture of tear	Lived	Lesser curve
Mirsky and Garlock, 1965	40 F.	Vomiting	11 days	Suture of tear	Lived	Anterior wall
Fleming, Horton, and Wagget, 1966	45 F.	Pyloric stenosis	2 hours	Vagotomy and gastrojejunostomy	Lived	Anterior wall
Zakrys, Pawlowski, and Rajtar, 1966	64 M.	Pyloric stenosis, barium meal	Not stated	Total gastrectomy	Lived	Near lesser curve
Schwartz, 1966	65 F.	Effervescent alkalis	5 hours	Suture and gastrostomy	Died	Lesser curve
Gue, 1970	64 M.	In inguinal hernia	Not stated	Suture of tear	Died	Lesser curve
Jefferiss, 1971	58 F.	Pyloric stenosis	2 hours	Vagotomy and gastrojejunostomy	Lived	Lesser curve

The mechanism of rupture has been discussed by many authors including Cronin (1959) in his review of alimentary tract ruptures. It seems to be due to a closed-loop type of obstruction in the stomach associated with a sudden rise in intraluminal pressure caused by either attempts at vomiting or ingestion of bicarbonate for relief of ulcer symptoms. The usual cause of distal obstruction in the stomach is pyloric stenosis due to peptic ulceration, but Gue (1970) describes a case where the distal obstruction seemed to be caused by the stomach being contained within an inguinal hernia. Some of the cases previously recorded as spontaneous rupture of the stomach have resulted from the administration of oxygen by the nasal route to patients with normal stomachs, or have followed endotracheal [*sic*] intubation. These cases, 3 by Walstad and Conklin (1961), 2 by Baglio and Fattal (1962), and 1 described by Foex (1962), should be considered as traumatic as would a compressed-air injury of the rectum.

The site of rupture is commonly along the lesser curve or on the anterior wall. A mucosal tear is followed by dissection in the deeper layers of the stomach and a longer tear in the serosa. It seems that the site is determined to some extent by the relative fixity and poor distensibility of the gastro-oesophageal junction. The tears are usually described as being difficult to suture, and in the cases where organic outflow obstruction was present from peptic ulceration, vagotomy and gastrojejunostomy seem to have been successful when used. Certainly any surgical procedure should be done early, possibly preceded by paracentesis abdominis to relieve tension.

The condition was first described by Boerhaave in 1724 but was only separated later by Cruvelhier (cited by Glassman, 1929) from the common perforation of a peptic ulcer. In the further 8 cases which I have traced (*Table I*) since Albo and others (1963) reviewed the literature, the preponderance of females continues and there is an increasing number of survivors as early operative measures are undertaken. In the case described by Mirsky and Garlock (1965) there was a delay of 11 days before surgery but the patient had an anterior perforation which had sealed itself off, which would seem an unlikely event with an extensive lesser-curve rupture.

Acknowledgement.—My thanks are due to Mr. W. A. L. Tucker, O.B.E., F.R.C.S., for allowing me to publish this case.

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REVIEWS AND NOTICES OF BOOKS

Frozen Section in Surgical Diagnosis. By ANDREW A. SHIVAS, T.D., M.D., F.R.C.S.E., D.P.H., F.R.C. Path., and SUZANNE G. FRASER, A.I.M.L.T., University of Edinburgh. 8½ × 5½ in. Pp. 261 + ix. Illustrated. 1971. Edinburgh: E. & S. Livingstone. £6.

THIS is a book which surgeons the world over have been looking for. It will fill a very definite gap in the literature of pathology and surgery. The beautiful 204 colour illustrations prepared by that expert, the late T. C. Dodds, will be an ever-ready reference file for surgeons, pathologists, and students.

The modern surgeon, especially one who deals with neoplasia, will welcome this book; it will be his constant reference volume.

After a chapter on technical notes, the authors, who have devoted many years of their lives in perfecting their own techniques, deal with the common conditions in the breast, thyroid, and lymph-nodes, and finally consider other sites in the body where frozen sections often give a definite diagnosis of the condition. Sir John Bruce, who writes a foreword to this important monograph, says: 'This short, beautifully illustrated, and instructive book leaves clinicians with little excuse for unseemly approaches in the future and provides a basis on which the pathologist and his surgical confreres can meet on common ground.' We thoroughly endorse these candid remarks.

An excellent production.

Hepatic Encephalopathy. By FREDERICK STEIGMANN, M.D., and BERNARD F. CLOWDUS, II, M.D., Cook County Graduate School of Medicine, Illinois. 8¾ × 6 in. Pp. 201 + xii. 1971. Springfield, Ill.: Charles C. Thomas. $13.50.

THE authors of this monograph make use of the term 'hepatic encephalopathy' instead of the usual one of 'hepatic coma' because they consider that many patients with hepatic insufficiency demonstrate only an altered state of consciousness, intellect, and personality.

The authors have a matured clinical background which spans a period of over 35 years, and their clinical acumen is to be seen in this book.

This volume contains a wealth of material and provides a concise review of the established fundamental physiological, pathological, and biochemical factors involved in the production of hepatic encephalopathy. The various clinical manifestations of this condition are well described, including the neurological and psychiatric findings.

The diagnosis and prognosis are discussed in some detail.

The treatment, including prophylactic, general care, and specific treatment, is considered at length.

A bibliography at the end of the book contains 699 references.

As a reference volume this book could not be bettered.

Orthopädische Therapie. By G. CHAPCHAL, Nijmegen, and D. WAIGAND, Biberach. 10 × 7 in. Pp. 533 + xvi, with 299 illustrations. 1971. Stuttgart: Georg Thieme Verlag. DM.98.

THIS is a new book on orthopaedic treatment. The volume attempts to cover the whole field of orthopaedics and includes extensive chapters on physiotherapy and hydrotherapy. Most orthopaedic conditions are covered in this book, but an outstanding omission is the entire and now-important problem of the orthopaedic aspects of spina bifida. On the other hand, the management of varicose veins is described in considerable detail. Fractures and joint injuries are dealt with very briefly, but the various operative procedures are given in great detail.

The book contains a fair number of oversimplified line drawings, virtually no X-rays, and no clinical or operative photographs. The diagrams have been so simplified that they cannot really be followed unless the text is very carefully studied. The lack of fuller illustrations will undoubtedly limit the use of this volume which otherwise is beautifully printed and produced.

Principles of Medical Statistics. Ninth edition. By SIR AUSTIN BRADFORD HILL, C.B.E., D.Sc., Ph.D., Hon.D.Sc., M.D., F.R.C.P., F.R.S., Professor Emeritus of Medical Statistics in the University of London. 8¼ × 5¼ in. Pp. 390 + ix. Illustrated. 1971. London: The Lancet Limited. £1·25.

THIS is a book which should be in every medical library, for it is invaluable to every clinician and medical research worker who wishes to make a statistical review of cases.

The first edition appeared in 1937 and many of the subsequent editions have been reprinted, some more than once. These facts speak for themselves and reveal the importance and popularity of the book.

The author covers the difficult problems of medical statistics in a very comprehensive way. The collection and sampling of statistics and the presentation of statistics are all explained in a lucid manner. Clinical trials and clinical research are discussed at some length.

This book should be read by all medical students, for it will give them a sound idea how medical statistics are formulated.

The price of the book is most moderate.

Les Analgésiques et la Douleur. By G. VOURC'H, J. DE CASTRO, P. GAUTHIER-LAFAYE, J. F. GIUDICELLI, and P. VIARS. 9⅖ × 7 in. Pp. 583 + xx, with 96 illustrations. 1971. Paris: Masson et Cie. 150F.

A COMPREHENSIVE survey is given of the well-known and the recently developed analgesic drugs. The drugs are evaluated by the classic pharmacological methods. Though one chapter is dedicated to the antipyretic analgesics, salicylates, para-aminophenol derivatives (phenacetin), pyrozole and quinoline derivatives, the central analgesics, i.e., morphine and morphinomimetic substances, including the antimorphiates, cover the main part of the book.

One is amazed by the number of substances that are more powerful than morphine, but toxic side-effects like respiratory depression, circulatory collapse, muscle hypertonia, vomiting, and addiction are evident in nearly all of them. Demerol (pethidine, dolantine), though weaker, shows all the side-effects of morphine; its popularity does not seem justified. The authors are fairly satisfied with the antimorphiate pentazocine, where addiction should be slight; here one hesitates to agree. The extremely powerful analgesics like dextromoramide, fentanyl, and phenoperidine are very toxic as well, respiratory depression being a striking effect, but they are revolutionary ingredients in anaesthesia where controlled respiration offers no problem. In neuroleptanalgesia (1962) only moderate quantities of fentanyl are used; in analgesic anaesthesia and sequential analgesic anaesthesia (1969) larger doses of fentanyl or dextromoramide replace barbiturates and inhalation anaesthesia.

The antimorphiates like nalorphine show analgesic effects but cause uncomfortable psychic sensations, even hallucinations; their application is restricted to antidotal action in cases of respiratory depression.

The book is to be recommended.

Anaesthetics, Resuscitation and Intensive Care. Third edition. By WALTER NORRISS, M.D., F.F.A.R.C.S., and DONALD CAMPBELL, M.B., Ch.B., F.F.A.R.C.S., D.A., Consultant Anaesthetists, Glasgow Royal Infirmary. 8⅓ × 5⅓ in. Pp. 282 + xi. Illustrated. 1971. Edinburgh: E. & S. Livingstone. £1·50.

THE third edition of this small paperback will be as popular with students and resident medical officers as the former ones, for it gives them the information they require regarding anaesthetics, resuscitation, and intensive care.

This book is clear and concise and it is well illustrated with lucid drawings, diagrams, and photographs.

Recent Advances in Haematology. Edited by A. GOLDBERG, M.D., D.Sc., F.R.C.P., Regius Professor of Materia Medica, University of Glasgow, and M. C. BRAIN, D.M., F.R.C.P., Professor of Medicine, McMaster University, Ontario. 9 × 6 in. Pp. 387 + vi, with 43 illustrations. 1971. London: J. & A. Churchill. £4.

HAEMATOLOGY today is a large and separate branch of pathology and as the years go by it increases in importance. Haematology concerns many branches of medicine and surgery and for this reason this book will interest a wide variety of medical men.

Each of the ten chapters in the book covers in a very comprehensive way some subject which has practical importance to the clinician. To mention only a few: megaloblastic anaemias, disorders of iron metabolism, abnormal haemoglobins, treatment of malignant blood diseases, and leucocyte groups in man and their relation to transplantation antigens.

At the end of each chapter there is a very complete list of references from the world literature on that particular subject.

The 43 illustrations are excellent and enhance the value of the text.

This is an excellent book of reference on haematology.

Pathologie du Pied. Fourth edition. By JEAN LELIÈVRE, Paris. 9⅖ × 6⅕ in. Pp. 868 + xi, with 673 illustrations. 1971. Paris: Masson et Cie. 140F.

CONSIDERABLE time elapsed before surgery of the foot began to arouse the same interest as was accorded to surgery of the hand. In recent times several good books have appeared which deal with this particular branch. One of these is Jean Lelièvre's near classic, the fourth edition of which is now before us. Comparison with previous editions shows that numerous passages have undergone considerable alteration. Noteworthy among these is the section on orthopaedic shoes and their manufacture, still to most physicians a practically uncharted territory. A conspicuous feature is the frequent use of diagrammatic drawings, inspired as the author acknowledges in his preface by the artist Lesbouvit. Besides the common disorders one finds descriptions of practically all affections that may occur in the foot, resulting in an excellent book of reference. Surprisingly enough the book remains eminently readable, thanks to the easy and logical arrangement of the subject-matter. The disorders are described in the orthodox textbook way, but the actual surgical technique is treated in a special chapter at the end of the book; many procedures appear to be original. Unfortunately, some of these descriptions are too short for the uninitiated; the extensive accounts of the pathology and diagnosis, however, more than compensate for this.

One brief criticism: it seems fair that those specializing in foot surgery should also deal with foot fractures, but few will agree with the author that his territory ought to include the fractures of the ankle, however eloquently he pleads his case.

Technique des Plâtres et Corsets de Scolioses. By MARC OLLIER, Lyon. 9½ × 6¼ in. Pp. 130, with 132 illustrations. 1971. Paris: Masson et Cie. 48F.

THIS handy book is a technical manual for making casts and braces in the treatment of scoliosis, as practised in Stagnara's well-known centre in Lyon.

Marc Ollier, the chief physiotherapist, and obviously a master of his craft, has given a most detailed account of how to construct the various types of plaster casts. But he has not confined himself to the mere technical aspects—for each type of cast the indications and complications are clearly discussed. Very interesting is the comparison between the 'Lyon brace', with its more solid support of the trunk and freedom of the head and neck, and the dynamic corrective, but perhaps more cumbersome, Milwaukee brace. The author has tried to establish the indications for each. This well-produced book with its many photographs and line drawings is certainly 'a must' for those who treat their patients along the lines of Stagnara. In addition, anyone making plaster casts for scoliosis can find many tips not specific for the system described but of more general application.

The Continuing Education of the Surgeon. Edited by HAROLD G. BARKER, M.D., New York. 9 × 6 in Pp. 121 + x. Illustrated. 1971. Springfield, Ill.: Charles C. Thomas. $11.75.

THIS book contains the transactions of the Twelfth Annual Meeting of the Allen O. Whipple Surgical Society.

The various papers stress the value of continual education of practitioners, and advise the more constant use of postgraduate lectures and demonstrations in hospitals.

The use of a tumour registry is supported by most surgeons.

The nine contributors to this volume stress the value of organized co-operation and not healthy competition. It is the discussions at the end of each paper that make this book of real interest.

Surgical Anatomy. Vols. 1 and 2. Fifth edition. By B. J. ANSON, M.A., Ph.D.(Med. Sc.), Chicago, and C. B. MCVAY, Ph.D., M.D., F.A.C.S., South Dakota. 10⅕ × 7⅕ in. Pp. 1282 + xl. Illustrated. 1971. London W. B. Saunders Company Ltd. £19·15.

THERE is a tendency today to cut short courses in anatomy and to lessen the hours spent in the complete dissection of the human body. This being so, it is essential that the medical student should have a very comprehensive course on surgical anatomy in his final-year studies.

This large two-volume work has become a world classic; since the first edition was published in 1933 it has gone from strength to strength and the new fifth edition, dedicated to that master surgeon Loyal Davis, will enjoy an international reputation.

One of the features of this work is the originality and clearness of the illustrations, over 3000 in number. With the ever-widening sphere of modern surgery, so the importance of surgical anatomy becomes more evident.

Surgeons the world over will wish to have these two important volumes in their personal library for ready reference.

Cardiovascular Surgery, 1969. Edited by EARLE B. MAHONEY, M.D., New York. 10 × 7⅝ in. Pp. 178. Illustrated. 1970. New York: The American Heart Association, Inc. $5.

THIS is the American Heart Association's Monograph Number 30, and it contains the papers which were presented at the Scientific Sessions held at Dallas, Texas, in November, 1970.

There is much to interest the cardiac surgeon as well as cardiologists. As one would expect, there are many papers on valve replacements. The internal mammary artery implantation seems to have come into its own and long-term 'follow-up' results are now published.

An interesting paper on congestive heart failure in infancy treated by early repair of ventricular septal defect is of real practical value.

It is interesting to note that the enthusiasm for cardiac transplantation of the past few years appears to be in abeyance.

There are papers on peripheral arterial and venous problems, and the coverage of cardiac surgery is excellent.

Urology and Renal Medicine. By J. E. NEWSAM, M.B., Ch.B., F.R.C.S., Consultant Urological Surgeon, Western General Hospital, Edinburgh, and J. J. B. PETRIE, B.Sc., M.B., Ch.B., M.R.C.P., Senior Medical Registrar, Renal Unit, Royal Infirmary, Edinburgh. 7⅝ × 4⅞ in. Pp. 259 + v, with 72 illustrations. 1971. Edinburgh: E. & S. Livingstone. £1·25.

THERE is much to be said for a joint authorship by a surgeon and a physician in a book on urology, because the coverage should thereby be more complete.

This paperback, intended primarily for undergraduates, is written in a clear concise manner and is illustrated with some excellent line drawings, halftones, and telling diagrams.

The chapters on disorders of the Renal Parenchyma, Renal Failure, and Dialysis and Transplantation are very good indeed.

This book will be of real value to students and those postgraduates who are preparing for higher medical and surgical diplomas.

Handbuch der Experimentelle Pharmakologie. Anticoagulantien. Edited by F. MARKWARDT. 9¾ × 6¼ in. Pp. 598 + xiv. Illustrated. 1971. Berlin: Springer-Verlag. DM.198.

THIS is the twenty-seventh volume of a Handbook of Experimental Pharmacology. This volume deals with anticoagulant therapy and includes the works of six authors from four different countries. The entire problem of the physiology and biochemistry of blood coagulation is discussed. The various drugs available for influencing and indeed diminishing blood coagulation are reported in the various chapters in great detail and the action of individual drugs on individual parts of the coagulation system are discussed. Each chapter has a very extensive list of references, and there are also extensive indexes to authors and subject-matter. There is no doubt whatever that this volume will become a standard work on anticoagulant therapy, but its price will limit the distribution to medical libraries rather than to individuals. It is hoped that the volume will appear in the English language as it really is a most comprehensive account of anticoagulant therapy, its indications, and its problems.

Venous Thrombosis and Pulmonary Embolism. By MICHAEL HUME, M.D., Boston, SIMON SEVITT, M.D., M.Sc., F.R.C. Path., F.R.C.P.I., Birmingham, and DUNCAN P. THOMAS, M.D., B.Sc., D.Phil., Boston. 9¼ × 6 in. Pp. 456 + xiii. Illustrated. 1970. London: Oxford University Press. £7·50.

THIS is an excellent monograph on a most important subject; it is the combined effort of a physician, a surgeon, and a pathologist. All three have had much to do with the problem of pulmonary embolism as a complication of venous thrombosis and therefore write from clinical experience.

The whole subject of venous thrombosis and pulmonary embolism is considered in a comprehensive manner. The pathological findings and experimental observations, together with circumstances associated with the disease, are critically examined.

The clinical features of pulmonary embolism are surveyed in a very practical way, while the use of radiology and lung scanning in the diagnosis of pulmonary embolism is stressed.

The problem of prevention of venous thrombosis and pulmonary embolism is discussed in some detail.

Medical and surgical treatments are surveyed.

An excellent bibliography is given at the end of each chapter.

As a reference book on this important problem this volume could not be bettered.

Shaw's Textbook of Gynaecology. Ninth edition. By JOHN HOWKINS, M.D., M.S., F.R.C.S., F.R.C.O.G., and GORDON BOURNE, F.R.C.S., F.R.C.O.G., St. Bartholomew's Hospital, London. 9 × 6 in. Pp. 823 + viii. Illustrated. 1971. Edinburgh: E. & S. Livingstone. £4·50.

THE ninth edition of this well-known textbook of gynaecology will in our opinion prove as popular as the long list of former editions. Nine editions, many of them reprinted, in 33 years proves the value and popularity of the work.

The name of Gordon Bourne appears for the first time and it would please Wilfred Shaw to know that one of his pupils was helping in the new edition of his book.

This book is printed in an attractive style and is well illustrated with good and telling illustrations, and, what is more, it is easy to read.

It should prove of real value to students and practitioners alike, and its price is moderate.

Simultaneous Prostatectomy and Inguinal Herniorrhaphy. By SIDNEY R. WEINBERG, M.D., F.A.C.S., New York, ALBERT KOVETIZ, M.D., U.S. Air Force, and STEPHEN M. LAZARUS, M.D., Brooklyn. 9 × 6 in. Pp. 51 + ix. Illustrated. 1971. Springfield, Ill.: Charles C. Thomas. $6.75.

IN this small monograph the authors advocate a combined operation in which a retropubic prostatectomy is performed through a curved suprapubic incision. This incision is continued in a curved direction so as to afford access to the inguinal canal, and a radical cure of the inguinal hernia is carried out.

The authors maintain that the operation of simultaneous prostatectomy and inguinal herniorrhaphy does not represent any innovation in the physiological principles of surgery or surgical techniques. The bladder is drained by means of a Foley catheter and the retropubic space is also drained.

The clinical result and 'follow-up' seem to be very satisfactory.

This combined operation, while saving the patient an additional surgical procedure, does not materially increase the mortality and morbidity of simple abdominal prostatectomy.

Orthopédie Traumatologie. By SOCIÉTÉ FRANÇAISE DE CHIRURGIE ORTHOPÉDIQUE ET TRAUMATOLOGIE. 8¾×7 in. Pp. 233. Illustrated. 1969. Paris: Expansion Scientifique Française. 68F.

IN this volume twelve topics of interest are presented in the form of seminars. Each one is of value to the trainee orthopaedic surgeon as well as to the established practising clinician. The reviewer is struck by the meticulous thoroughness of the presentations.

Two subjects are outstanding in this collection of papers: club-foot and leg-lengthening. There is an excellent and practical description of the soft-tissue release operation for club-foot, with important technical details seldom found in standard writings.

A similar exhaustive and immensely practical description of the leg-lengthening procedure will be of great value to the surgeon who intends to do the operation and who has no previous experience of the technique or who is not satisfied with the results he has so far obtained.

The Scientific Basis of Medicine. Annual Reviews, 1971. Edited by IAN GILLILAND, M.D., F.R.C.P., and JILL FRANCIS, University of London. 8⅝×5⅝ in. Pp. 397+ix. Illustrated. 1971. London: The Athlone Press. £3·50.

THIS book has much for the specialist and general practitioner, for it gives the most recent advances on a wide range of medical and surgical topics.

Such topics as immunity to malignant disease in man, understanding of the muscle spindle, experimental cholelithiasis, the ageing eye, and new concepts of the function of the lymphatic system in the swollen leg are but a few of the excellent articles in this book.

It is a great advantage to all medical men to have an up-to-date book, each year, which gives them the results of scientific advance in the field of medicine.

Human Organ Support and Replacement. Edited by JAMES D. HARDY, M.D., F.A.C.S., Mississippi. 9¾×6¾ in. Pp. 453+xiii. Illustrated. 1971. Springfield, Ill.: Charles C. Thomas. $30.50.

THIS large volume with its twenty-five contributors, mostly from America and Canada, covers a very important subject in a very comprehensive way. It is surely time that the world recognized that artificial devices and transplants have reached a level in which great progress has been made over the past decade. Following the success of renal transplantation it must be obvious that other organs will eventually be transplanted with equal success.

This book covers the whole subject of organ transplantation in a very practical way. It covers such diverse topics as histocompatibility typing, immunological modalities used in clinical allografting, organ storage, transplantation of the kidney, liver, stomach, small intestine, thyroid, parathyroid, adrenals, ovary, pancreas, spleen, lung, and heart. It also considers blood-vessel replacement and limb replacement.

A very complete list of important references is given at the end of each chapter. The illustrations throughout the book are clear and well chosen.

This book will be the reference volume on this important subject for many years to come.

Myoplastic Amputation, Immediate Prosthesis and Early Amputation. By MARIAN WEISS, M.D., Wierzejewskiego, Poland. 9×5⅘ in. Pp. 245+xii. Illustrated. 1971. Bethesda, Maryland: National Library of Medicine. $2.50.

THE operation of an amputation of the lower limb goes far back into history, but the experience of the two World Wars and the increase in accidents on the roads have advanced our knowledge of the best methods of amputation.

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In this book the types of amputation of the lower limbs, the immediate fitting of a prosthesis and early walking by the patient, and postoperative care are discussed in detail. Some patients are encouraged to walk the same day as the operation. These new methods are said to eliminate neuroses and other psychopathological conditions.

This new method certainly warrants a trial in this country.

International Encyclopedia of Pharmacology and Therapeutics. Section 8: Local Anaesthetics. Edited by P. LECHAT, Paris. 9×6 in. Pp. 377+ix. Illustrated. 1971. Oxford: Pergamon Press Ltd. £6.

THIS volume covers the field of local anaesthesia in a very complete and comprehensive way. The various contributors to the ten chapters come from different clinics and institutes in Sweden, Switzerland, United States, West Germany, and France.

The blocking effects of some local anaesthetics commonly used in clinical practice are considered in detail. The absorption, distribution, metabolism, and excretion of local anaesthetics are discussed.

The toxicity and irritancy of local anaesthetics are described in a lucid manner.

Every facet of the subject of local anaesthetics has been covered in this book, and this being so it makes the book a useful reference volume on this subject.

Surgical Treatment of Coronary Arteriosclerosis. By RENE G. FAVALORO, M.D., Ohio. 10×6¾ in. Pp. 132+xvi. Illustrated. 1971. Edinburgh: E. & S. Livingstone. £6·75.

THIS is a useful monograph on the surgical treatment of coronary arteriosclerosis, an all-too-common condition in these modern times.

The author gives a very practical and interesting account of the preoperative evaluation and distribution of the severity of the coronary obstruction.

Preoperative preparation, anaesthesia, and postoperative care are stressed.

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This is a book which all cardiac surgeons will wish to possess, and postgraduate students who are studying for higher degrees or diplomas will find it most useful.

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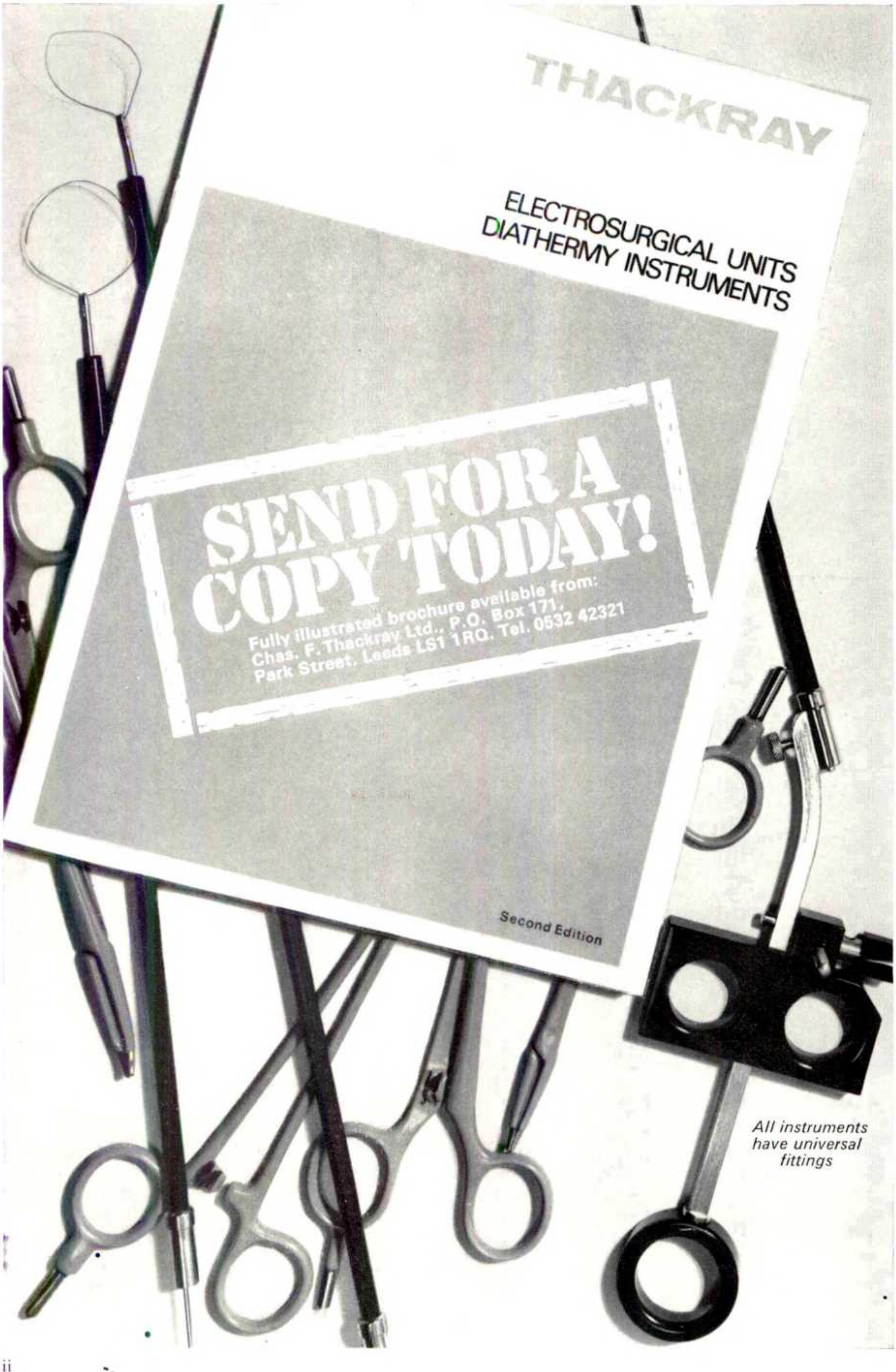
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CONTENTS

PAGE

ORIGINAL PAPERS

The Response to Therapy of Skeletal Metastases from Mammary Cancer *C. S. B. Galasko and F. H. Doyle* 85
Carcinoma of Aberrant Breast Tissue - - - - *G. M. R. Smith and W. P. Greening* 89
Glomus Tumour - - - - - - - - *J. Strahan and H. W. C. Bailie* 91
The Effect of Environmental Temperature and Nutritional Intake on the Metabolic Response to Abdominal Surgery - - - - - - *John Spivey and Ivan D. A. Johnston* 93
The Effect of a Single-dose Parenteral Antibiotic in the Prevention of Wound Infection *A. V. Pollock and D. S. Tindal* 98
A Modified Technique of Colostomy - - - - - - - *L. R. Abeyatunge* 99
The Local Effects of Intra-arterial Injections of Sodium Tetradecyl Sulphate (S.T.D.) 3 per cent *W. A. L. Mac Gowan, P. D. J. Holland, Hyacinth I. Browne, and Dermot P. Byrnes* 101
Giant Hydronephrosis in a Solitary Crossed Ectopic Kidney - *A. J. Yates-Bell and D. A. Packham* 104
Inhibition of the Growth of Tumour Cells in Culture by Noxytiolin - - - *C. W. Jamieson* 108
Perianal Gas-producing Infection of Non-clostridial Origin - - - *Terence Brightmore* 109
Primary Skin-grafting in the Treatment of Chronic Osteomyelitis - *A. Naylor and D. J. Crockett* 117
Hyperkalaemia following Temporary Occlusion of the Portal Vein and Hepatic Artery *R. R. Hall* 125
Omental Reinforcement of Intestinal Anastomoses *D. C. Carter, D. H. R. Jenkins, and H. N. Whitfield* 129
The Routine Use of Ultrasound for the Diagnosis of Postoperative Deep-vein Thrombosis in a District General Hospital - - - - - - - - - - - - *R. F. McIlroy* 133
Extrahepatic Biliary Drainage in Experimental Liver Injury - - - - *Irwin Faris* 136
A Technique for detecting Rejection Episodes in Human Transplant Recipients using Radioactive Fibrinogen - - - - - - - - - - *John R. Salaman* 138
Abdominal Wound Infections and Plastic Wound Guards *J. Alexander Williams, G. D. Oates, P. P. Brown, D. W. Burden, Jane McCall, A. G. Hutchison, and Lorna J. Lees* 142
Treatment of Arteriovenous Malformation by Endarterial Electrocoagulation *A. M. N. Gardner and I. A. Stewart* 146

SHORT NOTES OF RARE OR OBSCURE CASES

Prolapse of the Ileum through the Rectum and Anal Canal - *J. H. Hall and W. J. D. Bradfield* 149
Bowel Herniation through a Defect of the Broad Ligament - *I. G. M. Cleator and W. M. Bowden* 151
Idiopathic Pseudomembranous Colitis successfully treated by Surgical Excision *B. T. Jackson and C. J. Anders* 154
A Case of Diaphragmatic Hernia, Absent Pericardium, and Hamartoma of Liver *A. A. Deutsch, K. N. Brown, N. V. Freeman, and D. A. Stanley* 156
Perforation of a Peptic Ulcer in Duplicated Ileum - - - - - *C. D. Collins* 159

REVIEWS AND NOTICES OF BOOKS

Malignant Tumours in Organ Transplant Recipients—*I. Penn.* Manuel d'Osteosynthèse. Technique A.O.—*M. E. Muller, M. Algöwer, and H. Willenegger.* Cardiovascular Surgery, 1970—*Earle B. Mahoney.* Surgeons' Decisions—*H. L. Duthie.* Psychiatric Aspects of Organ Transplantation—ed. *Pietro Castelnuovo-Tedesco.* Gathorne Robert Girdlestone—*J. Trueta.* Progress in Pediatric Surgery—ed. *P. P. Rickham, W. Ch. Hecker, and J. Prévot.* Engineering and Living Systems. Interfaces and Opportunities—*D. R. Rutstein and M. Eden.* Basic Practical Surgery—*C. Barrie Williams.* Fractures of the Mandible—*H. C. Killey.* Full Dentures. The Treatment of the Edentulous Patient—*Alan Mack.* Fractures of the Middle Third of the Facial Skeleton—*H. C. Killey.* Anatomy of the Brain and Spinal Medulla—*Neville G. Sutton.* Plastic and Reconstructive Surgery—*ed. J. T. Hueston.* Oral Diagnosis. Oral Medicine—*David F. Mitchell, S. Miles Standish, and Thomas B. Fast.* Diseases of the Breast—*C. D. Haagensen.* Transperikardiale Operationen an den Hauptbronchien und Lungengefassen—*L. K. Bogusch, A. A. Travin, and J. L. Semenenkow.* The Immunobiology of Transplantation—*Rupert Billingham and Willys Silvers.* Atlas of Ear Surgery—*William H. Saunders and Michael M. Paparella.* Modern Trends in Surgery, 3—ed. *W. T. Irvine.* Amputees and their Prostheses—*Mohinder A. Mital and Donald S. Pierce.* Glossaire d'histopathologie des tumeurs humaines—*Réne Gerard-Marchant.* The Structure and Support of Contemporary Residency Programs in Surgery—ed. *Harold G. Barker.* Nephron Failure: Conservation, Substitution, Replacement—*John B. Dossetor and M. Henry Gault.* Surface and Radiological Anatomy—ed. *W. J. Hamilton, G. Simon, and S. G. Ian Hamilton.* 161

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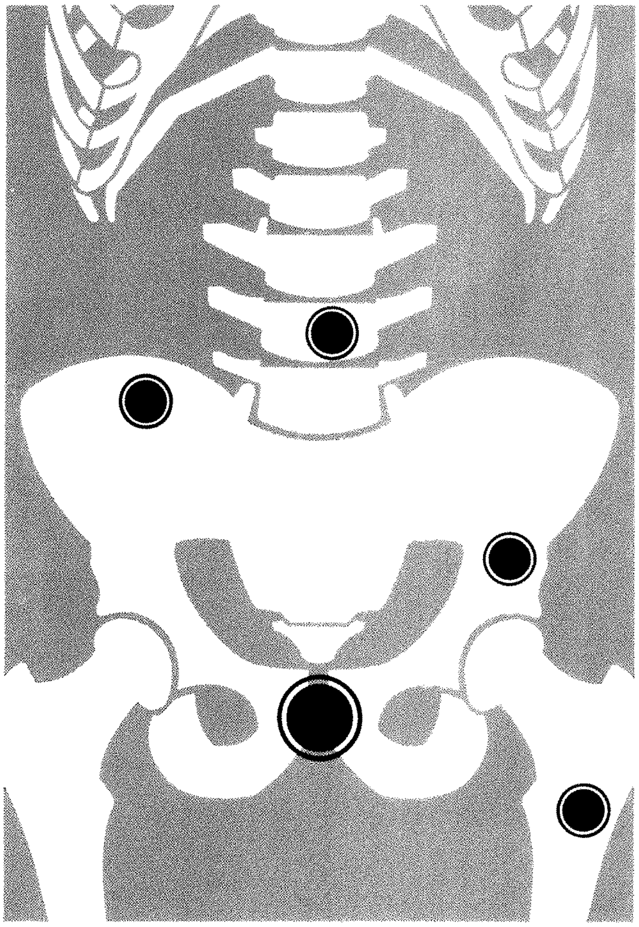

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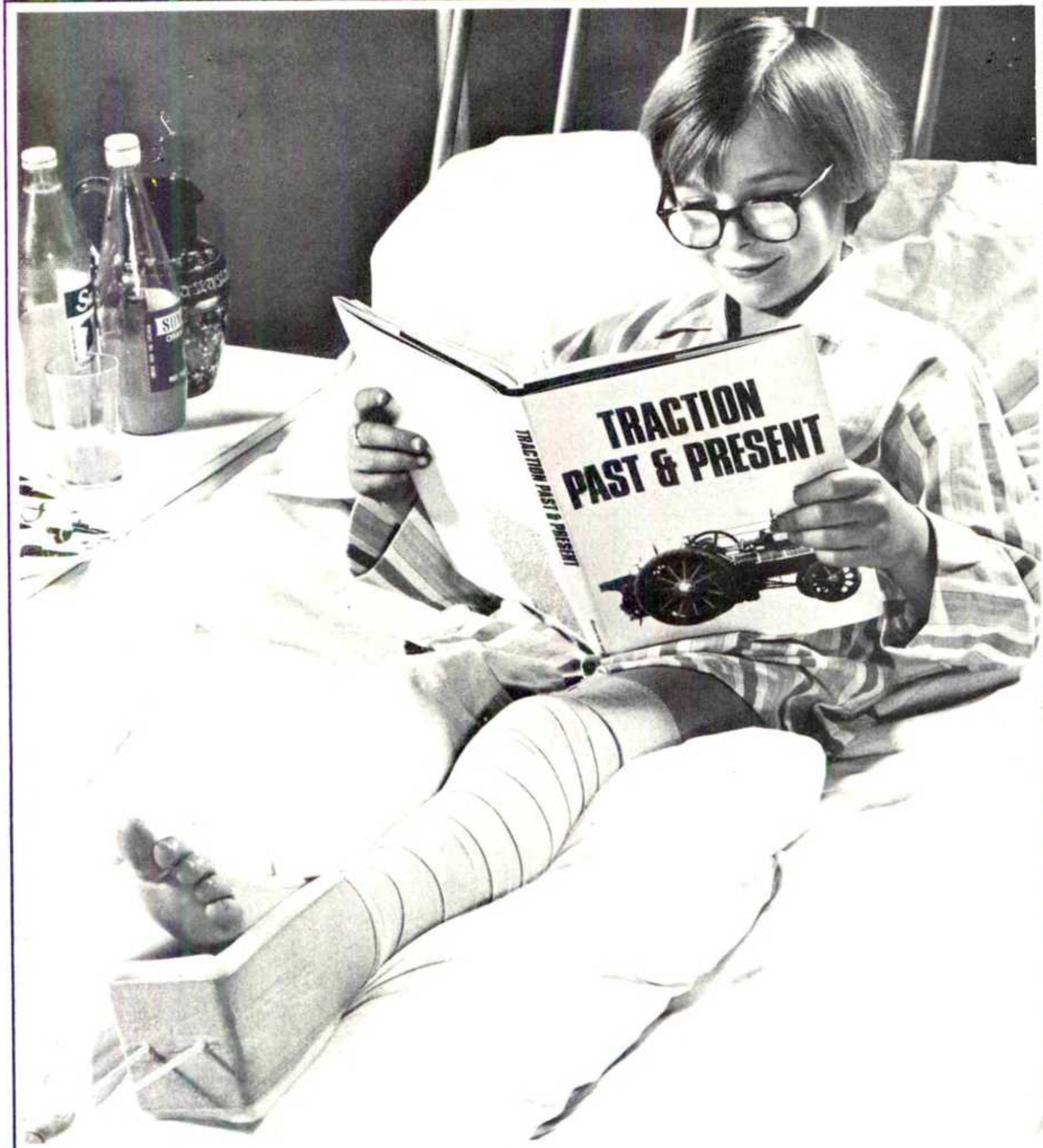

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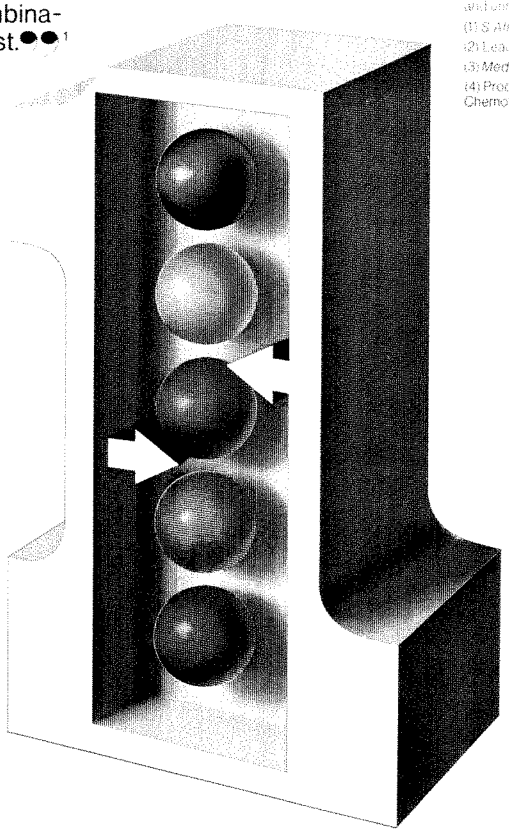

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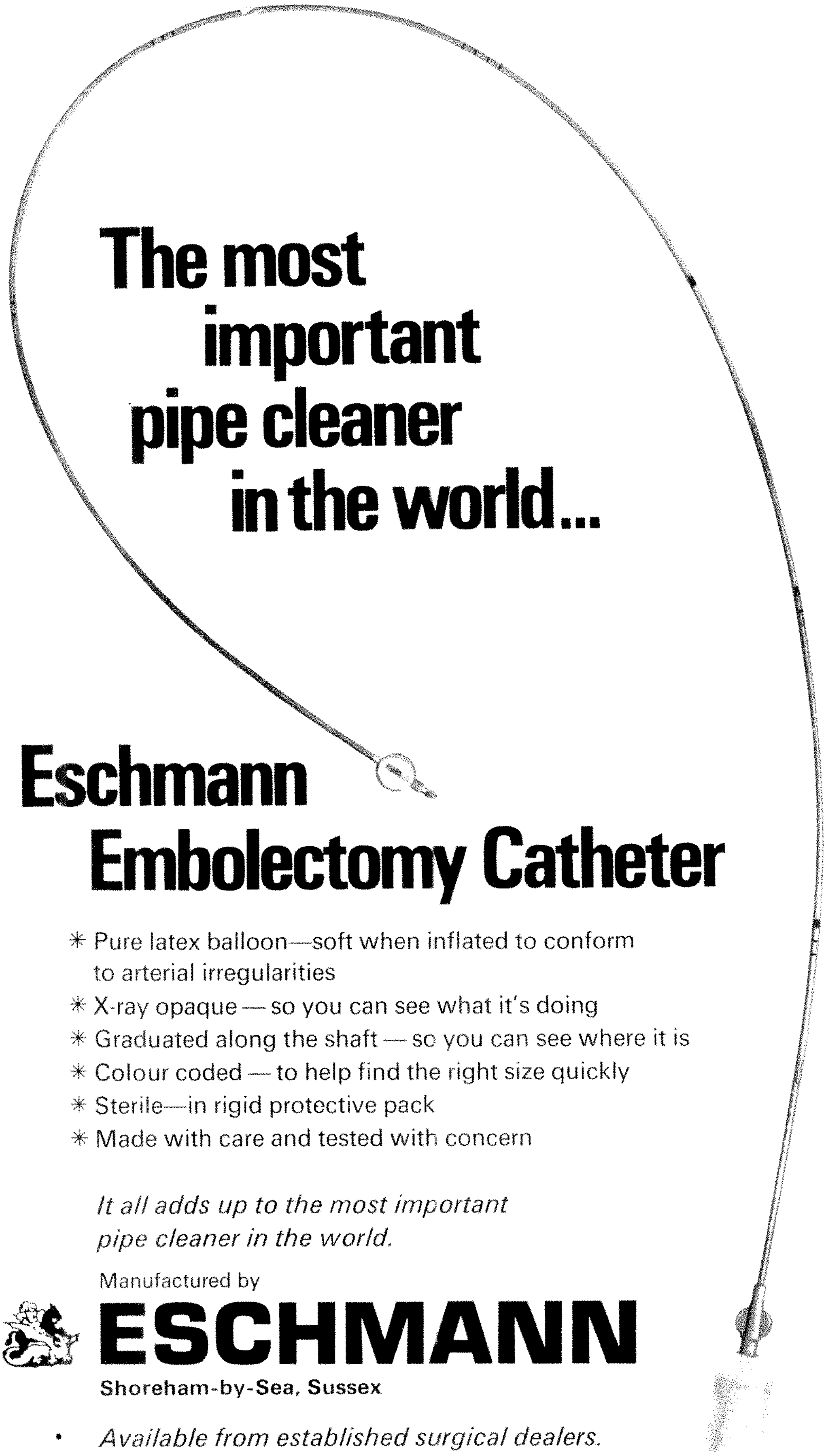

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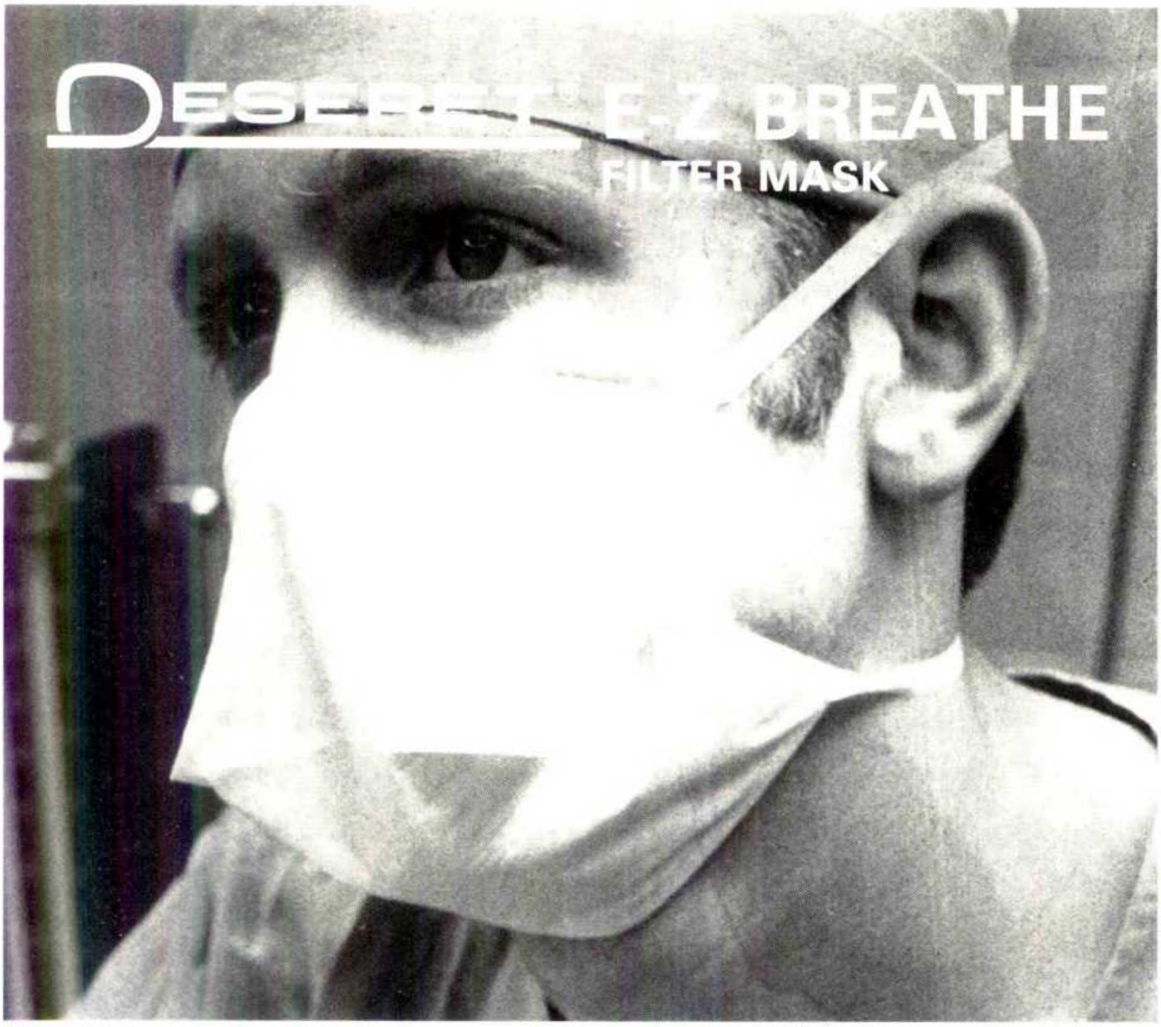

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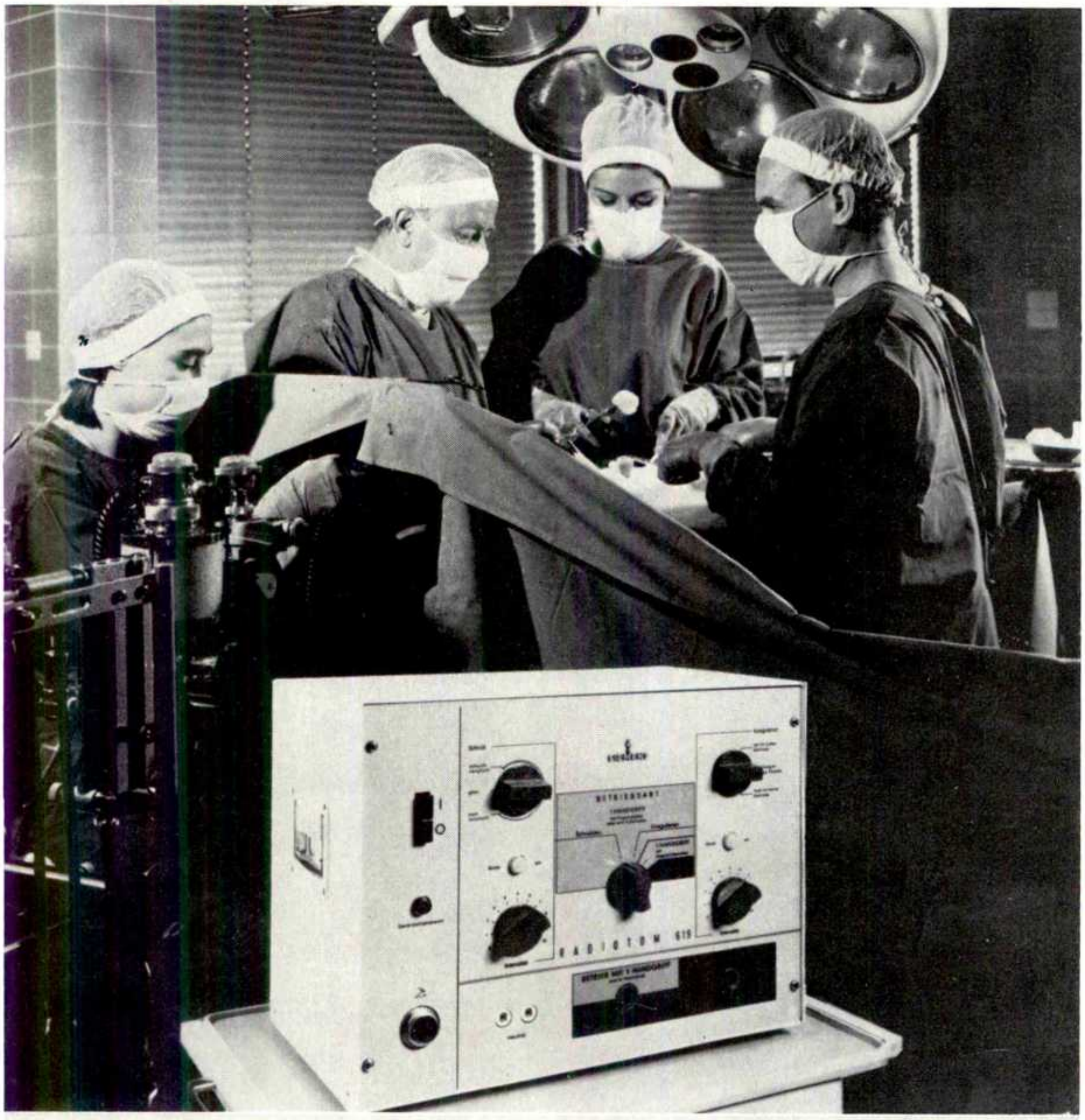

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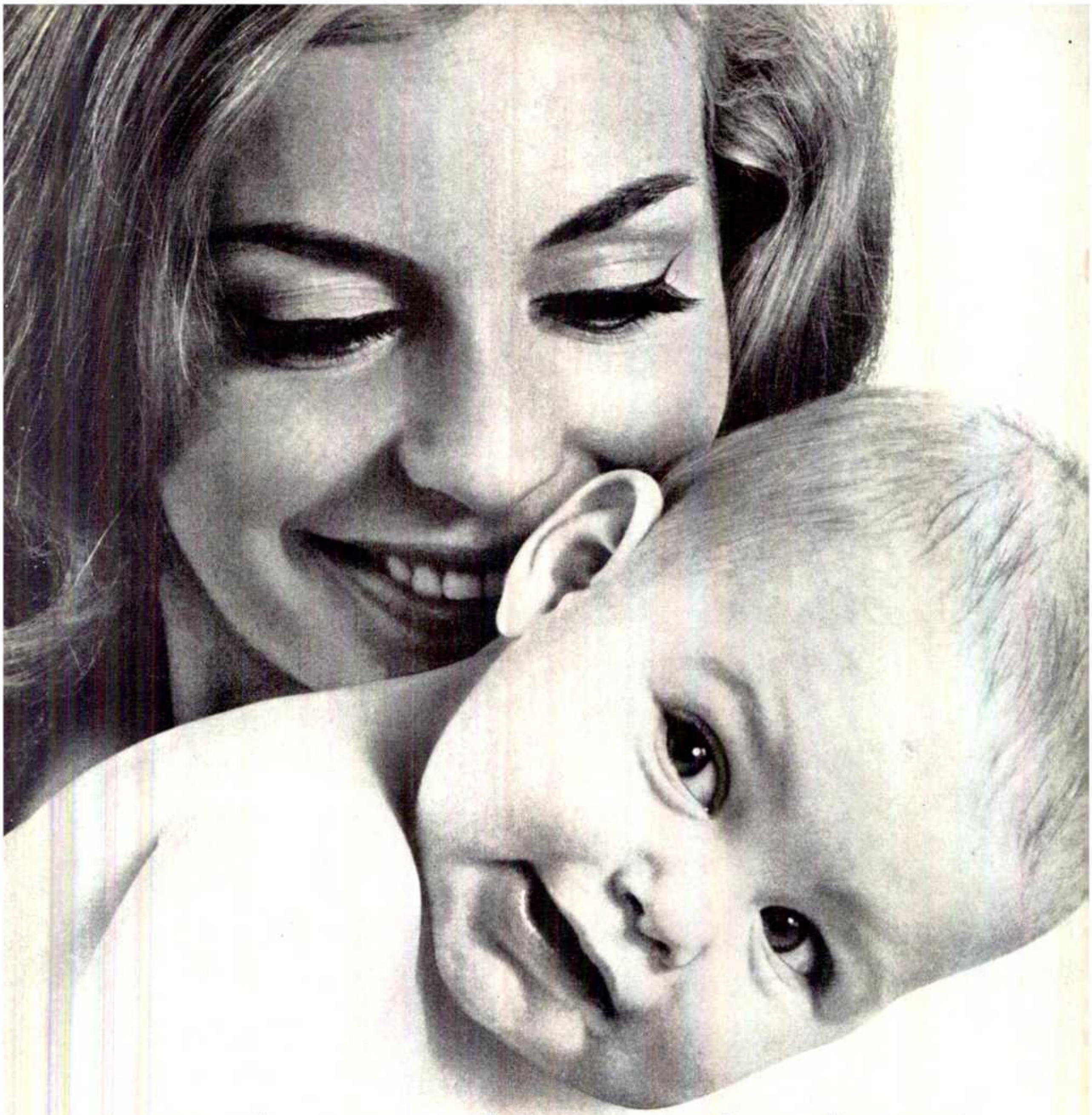

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ORIGINAL PAPERS

THE RESPONSE TO THERAPY OF SKELETAL METASTASES FROM MAMMARY CANCER

ASSESSMENT BY SCINTIGRAPHY*

BY C. S. B. GALASKO† AND F. H. DOYLE

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SUMMARY

Clinical, radiological, and scintigraphic methods were used to assess the response of 30 patients undergoing treatment for advanced mammary cancer. Scintigraphy provided more information than radiology in 13 patients. In 2 patients scintigraphy indicated that sclerotic metastases which had not altered radiologically following treatment were probably 'healing'. In another 4 patients who developed apparently 'new' sclerotic metastases on serial radiographs the scintigrams indicated that these lesions probably represented 'healing' of lesions which had been too small for identification on the original radiographs.

A VARIETY of treatments for advanced mammary carcinoma, ranging from simple hormonal therapy to major ablative endocrine surgery such as pituitary ablation, hypophysectomy, and adrenalectomy, is available. The treatment is usually staged, progressing from simple hormonal therapy to major surgery. Response to a particular form of treatment should be assessed quickly and objectively so that if the patient has failed to respond, therapy can be altered. Obviously if a remission has been induced then the treatment should be continued.

The commonest site for distant metastases from mammary cancer is the skeleton (Willis, 1948; Ackerman and del Regato, 1954; Haagensen, 1956). In patients with untreated metastatic involvement of bone the lesions are commonly lytic and rarely sclerotic. A mixture of lysis and sclerosis is sometimes seen. The response of skeletal metastases to treatment is often difficult to assess. With remission of disease, bones with lytic metastases may radiologically return to normal or the lytic areas may become sclerotic (Graham, 1965). The development of new lytic lesions or the enlargement of existing ones indicates progression of the disease. From radiographs it is impossible to differentiate sclerotic lesions due to progression of disease from those due to 'healing' (Joplin, 1965). The clinical assessment of response is also unreliable as many metastases are asymptomatic (Galasko, 1969a.) The pain of skeletal metastases may be relieved by endocrine treatment even though the lesions continued to enlarge on serial radiographs.

In 1961 Gynning, Langeland, Lindberg, and Waldeskog reported on 3 patients whose advanced mammary cancer had responded to hormonal treatment. Their skeletal metastases, which had been present on their initial radiographs and which had concentrated strontium-85, lost their avidity for the isotope after treatment. The scintigraphic examination of these patients was limited to a specific area of the skeleton. The use of scintigraphy of the axial skeleton in the assessment of response to treatment has not previously been reported. We have compared serial scintigrams, radiographs, and clinical findings in the assessment of the response to treatment of patients with advanced mammary cancer.

MATERIALS AND METHODS

Skeletal scintigrams were obtained in 30 patients before treatment for their advanced mammary cancer was started and again after an interval of 3–4 months. The method of scintigraphy has previously been described (Galasko, Westerman, Li, Sellwood, and Burn, 1968; Galasko, 1969b). One and a quarter hours after the intravenous administration of 1·5 m.c. of fluorine-18 each patient was examined with a gamma-camera (Pho-Gamma Mark II, Nuclear Chicago). The fluorine-18 was obtained from the Medical Research Council Cyclotron Unit, Hammersmith Hospital. In all cases the camera was used with a 11·4-cm. collimator, which was obtained by bolting 7·6-cm. and 3·8-cm. multichannel collimators together.

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* Based on a paper presented to the Surgical Research Society in July, 1970. Some of the material was presented by C. S. B. G. to the University of the Witwatersrand for the degree of Master of Surgery.

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With the patient seated, pictures were taken of the left, right, and posterior aspects of the skull, the cervical, dorsal, and lumbar spines, the left and right

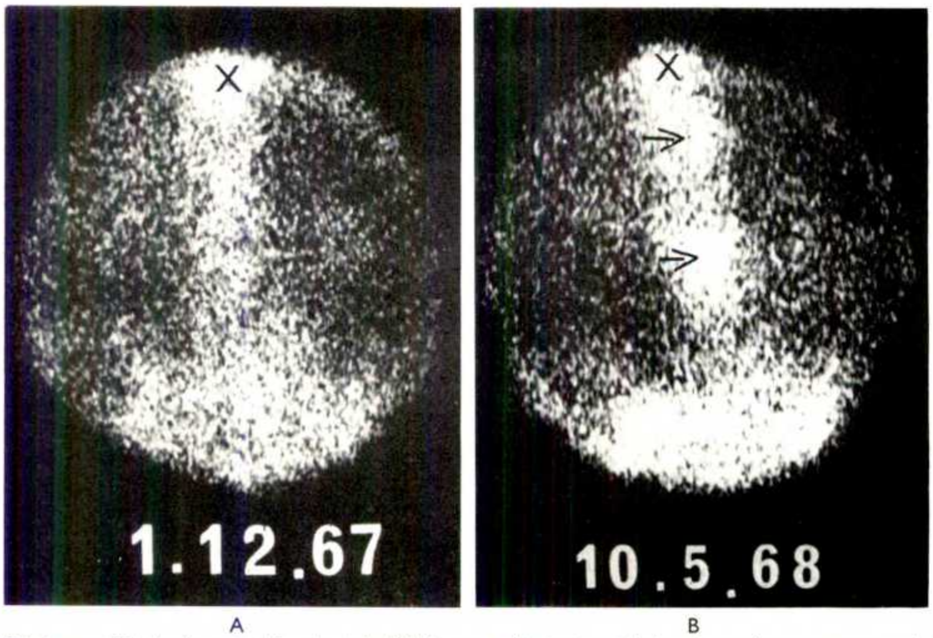

FIG. 1.—Scintigrams of the lumbar spine of a patient who failed to respond to treatment for her advanced mammary cancer. A, Scintigram before treatment for advanced mammary cancer was begun. No definite lesion can be seen. B, Scintigram obtained 5 months later. Lesions can be seen in two lumbar vertebrae (arrowed). The area of apparently increased uptake (X) is due to an 'edge effect' of the crystal.

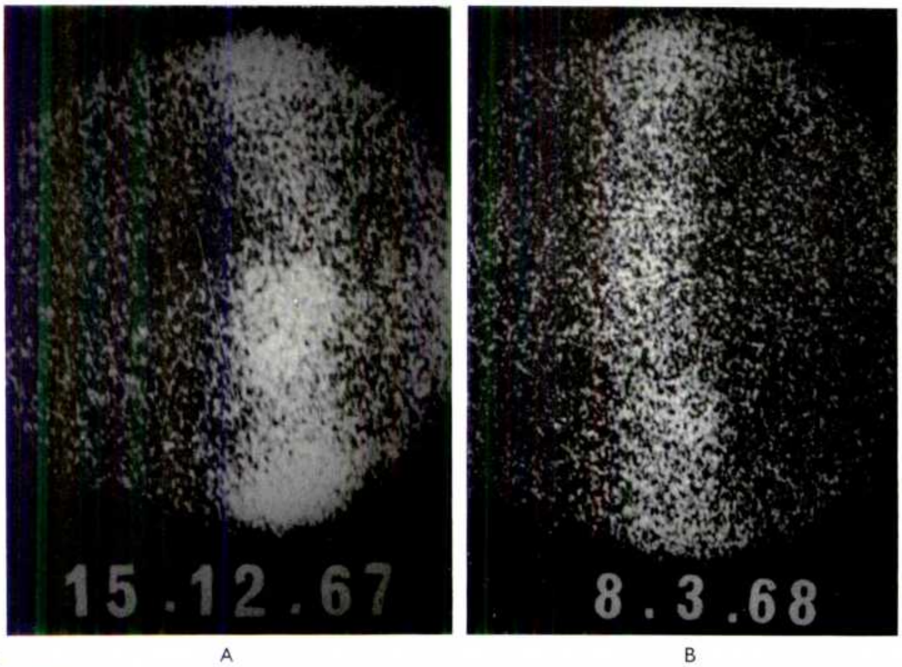

FIG. 2.—Scintigram of the dorsal spine in a patient whose mammary cancer responded to therapy. A, Multiple lesions can be seen in the scintigram which was obtained before therapy was commenced. B, Three months later the scintigraphic appearance of the dorsal spine had virtually returned to normal.

shoulder regions (including the proximal humeri), the left and right rib cages, and the posterior aspect of the pelvis. The patient then emptied her bladder (fluorine-18 being excreted in the urine) and a series of supine pictures were taken. These included the central, right, and left anterior aspects of the pelvis, the left and right proximal femora, and the sternum. These seventeen pictures constituted the axial skeletal scintigram.

Within a few days of the scintigram being taken each patient had a radiographic skeletal survey. This consisted of a lateral radiograph of the skull, antero-posterior and lateral views of the cervical, dorsal, and lumbar spine, and postero-anterior and antero-posterior radiographs of the chest and pelvis respectively.

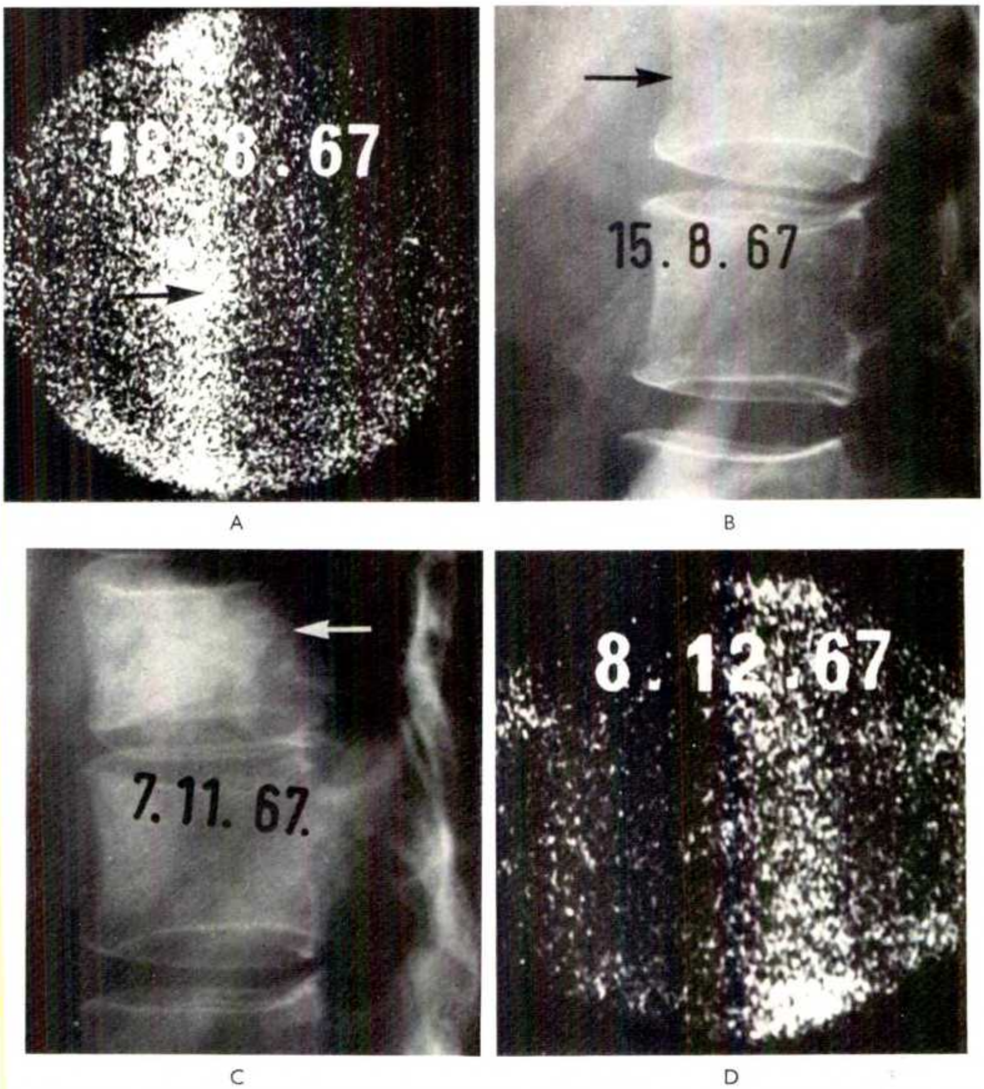

FIG. 3.—A patient who developed 'new' sclerotic metastases which were visible on the radiographs. Scintigrams and radiographs of the 11th and 12th dorsal vertebrae taken before treatment for advanced mammary cancer was started and repeated 3 months later. A, On the initial scintigram a lesion can be seen (arrowed). B, The initial radiograph was normal. C, Three months later diffuse sclerosis of the 11th dorsal vertebra was apparent (arrowed). D, The lesion was no longer apparent on the scintigram.

RESULTS

A summary of the results is given in *Table I*. Two patients with inoperable local tumours had no skeletal metastases. The primary tumours disappeared with treatment and their radiographs and scintigrams remained normal. In 10 patients the scintigraphic, radiological, and clinical findings were in agreement. Nine patients had deteriorated (*Fig*. 1) and 1 had gone into remission (*Fig*. 2). In 5 patients the scintigraphic and radiological findings indicated progression of the disease, even though all 5 had experienced some relief of pain. In 9 patients the scintigrams provided more information than the serial radiographs. Six patients had deteriorated and 3 had gone into remission. The details of these patients are shown in *Table II*. The only 2 patients whose lesions were initially sclerotic are included in this group. Both went into remission. Although the radiographic appearance of the lesions did not alter they diminished in number and size on the scintigram.

In 4 patients the findings were particularly interesting. In all 4 the primary breast tumour disappeared with treatment. Three of the patients had had lytic lesions on their initial radiographs and these had sclerosed with treatment. Following treatment each patient had developed apparently 'new' sclerotic lesions. In all 4 patients the apparently 'new' sclerotic lesions had been identified on the initial scintigram and had disappeared with treatment. On the initial scintigram, lesions which had not been radiologically present had been demonstrated in each patient (*Fig.* 3). With treatment these lesions had disappeared.

Table I.—SUMMARY OF RESULTS

No. of Patients	*Comparison of Scintigraphic, Radiological, and Clinical Findings*
2	Did not have skeletal metastases but local mammary tumour regressed on treatment
10	Scintigraphy, radiology, and clinical impression in agreement
5	Scintigraphy and radiology in agreement; clinical impression fallacious
9	Scintigraphy proved more informative than radiology
4	Apparently 'new' sclerotic metastases on radiographs; 'healing' on scintigram

Table II.—DETAILS OF 9 PATIENTS IN WHOM SCINTIGRAPHY PROVIDED MORE INFORMATION THAN RADIOGRAPHY

NO. OF PATIENTS	CLINICAL IMPRESSION	RADIOLOGICAL FINDINGS	SCINTIGRAPHIC FINDINGS
3	Deterioration	No lesions	Further lesions
2	No change	No lesions	Further lesions
1	Improvement (temporary)	No lesions	Further lesions
1	Remission	No lesions	Fewer lesions
2	Remission	No change of sclerotic lesions	Fewer lesions

The scintigram gave additional information, not otherwise available, in 13 (43 per cent) of the 30 patients (*Table I*).

DISCUSSION

We interpret our findings as follows. The majority of skeletal metastases evoke an osteoid reaction in the invaded bone (Milch and Changus, 1956; Galasko, 1971a). This osteoid has a high avidity for 'bone-seeking' isotopes (Charkes and Sklaroff, 1965; Galasko, 1971b). Charkes and Sklaroff (1965) suggested that when metastatic lesions remitted the osteoid calcified, matured, and lost its increased avidity for isotopes. In our view the loss of avidity for fluorine-18 by skeletal metastases, lytic or sclerotic, indicates healing. This confirms the observations of Gynning and others (1961). The apparently 'new' sclerotic lesions which were shown radiologically by patients on treatment represent healing of the lesions which, although detected scintigraphically, were too small to be recognized radiologically. Skeletal metastases have been recognized scintigraphically many months before their radiological detection (Corey, 1962; Charkes, Sklaroff, and Young, 1966; Spencer, Herbert, Rish, and Little, 1967; Galasko, 1969b). Our findings are in agreement with the observations of Joplin (1965), who stated that it was impossible on radiological grounds to differentiate sclerotic metastases due to progression of the disease from sclerotic lesions which occurred as a result of 'healing'. With scintigraphy we now may be able to differentiate these two different types of sclerotic lesions.

We believe that skeletal scintigraphy is not only an important diagnostic tool in the investigation of patients with mammary cancer but is also of considerable value in the assessment of response to treatment. Radiographic skeletal surveys, on their own, may be misleading in that undeclared lesions may sclerose on treatment.

Acknowledgements.—The authors wish to thank Professor J. F. Fowler for providing facilities in the Department of Medical Physics at the Royal Postgraduate Medical School, London, Mr. D. D. Vonberg and his staff of the Medical Research Council Cyclotron Unit, London, who supplied the isotope, and Professor R. B. Welbourn and Mr. J. I. Burn under whose care these patients were admitted.

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CARCINOMA OF ABERRANT BREAST TISSUE

A REPORT OF 3 CASES

By G. M. R. SMITH and W. P. GREENING
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Summary

Three cases of carcinoma of aberrant breast tissue are described and the literature is briefly reviewed. It is suggested that subcutaneous nodules of uncertain origin around the periphery of the breast should be viewed with suspicion and treated by early excision.

The incidence of accessory breast tissue is probably about 1–2 per cent (Speert, 1942; Cogswell and Czerny, 1961), and it is approximately twice as common in females as in males (Geschickter, 1945).

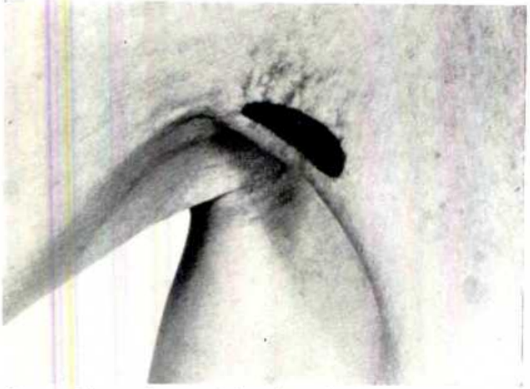

Fig. 1.—*Case* 1. Scar marked to show the site of excision of the tumour.

Copeland and Geschickter (1950) have suggested that a useful distinction may be drawn between supernumerary breasts, which usually have a nipple or areola in association with persistent or atrophic glandular tissue, and aberrant breast tissue, which is without a nipple or areola. Supernumerary breasts are most commonly present along the site of the embryological milk-line, running from axilla to groin, but may also occur in other situations, including the cheek, neck, shoulder, midline of chest or abdomen, flank, hip, thigh, and buttock (Cutler, 1961). Aberrant breast tissue, in contrast, is found in proximity to the normal breast, and consists of accessory fragments of breast tissue beyond the periphery of the gland. It may occur in the axillary, sternal, infraclavicular, or epigastric regions. The axillary site is the most common.

Tumours of aberrant breast tissue are rare. Carcinoma occurs more frequently than benign tumours (Geschickter, 1945). Copeland and Geschickter (1950) described 9 cases. Seven of these occurred in the axilla and 2 in the sternal region. Chiari (1958) collected 57 cases of carcinoma of aberrant breast tissue from the literature and added 3 of his own. Forty-three of these occurred in the axilla, 6 in the infraclavicular region, 6 in the sternal area, and 5 in the epigastrium, close to the xiphisternum.

CASE REPORTS

Case 1.—A woman, aged 43 years, was seen in 1957 with a small, painless nodule of recent origin in the right axilla. On examination a soft, subcutaneous swelling, measuring 1 cm. in diameter, was present on the anterior axillary fold. Axillary lymph-nodes were not enlarged, and no masses were palpable in the breasts. The swelling was thought to be a lipoma or sweat-gland tumour and was excised (*Fig.* 1). Histological examination showed that it was an anaplastic carcinoma of the breast.

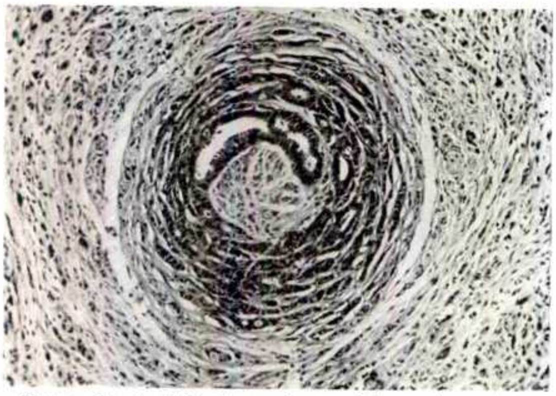

Fig. 2.—*Case* 2. Infiltrating carcinoma of aberrant breast tissue. H. and E. (× 80.)

Postoperatively, she received a course of radiotherapy to the axilla and supraclavicular region (5050 rad). She remains recurrence-free 13 years later.

Case 2.—A Turkish woman, aged 54 years, first noticed a nodule in the right axilla in 1958. Excision-biopsy was advised but she refused this. By 1966 the swelling had grown larger and was fixed to overlying skin. It was excised in Turkey. Histological examination revealed a carcinoma of indeterminate origin. Re-excisions for local recurrence were done in 1968 and in May, 1969. Histological examination now showed the features of carcinoma of the breast.

In July, 1969, she was seen in England. A firm nodule, measuring about 1 cm. in diameter, was present in the right axilla, adjacent to the previous scar. At least two enlarged lymph-nodes were palpable deep to the nodule. No masses were present in the breasts. The nodule was widely excised with the surrounding fat and lymph-nodes. Histological examination showed an infiltrating carcinoma of the breast (*Fig.* 2) with secondary deposits in three lymph-nodes.

Postoperatively, she received a course of radiotherapy to the right axilla and supraclavicular region (4500 rad).

When last seen, in September, 1970, she was recurrence-free.

Case 3.—A woman, aged 49 years, was seen in July, 1970, with a painless swelling in the right axilla. This had been present for about 6 weeks. On examination a subcutaneous nodule, measuring 1·5 cm. in diameter, was present in the upper lateral part of the right axilla. Axillary lymph-nodes were not enlarged, and no masses were palpable in the breasts. The swelling was thought to be an epidermoid cyst or sweat-gland tumour. Excision-biopsy was done. Histological examination showed an infiltrating, intraduct and intralobular carcinoma of mammary origin. A few duct and lobular structures of breast type were also present.

Three days later the wound was widely excised with the axillary fat and lymph-nodes. Histological examination showed a small amount of residual carcinoma together with aberrant mammary tissue. No secondary carcinoma was seen in 18 lymph-nodes.

Postoperatively she received a course of radiotherapy to the axilla and supraclavicular region. When last seen, in November, 1970, she was recurrence-free.

DISCUSSION

Carcinoma of aberrant breast tissue is a rare condition. Chiari (1958) found only 3 cases in a series of 918 patients who were operated on for carcinoma of the breast over a 10-year period, and several equally large series have included no cases. The condition is, therefore, likely to be misdiagnosed unless it is borne in mind whenever an unusual swelling is seen in the area around the breast. The cases described here demonstrate this, for in each instance the correct diagnosis was not made until the tumour had been excised and examined histologically. This serves to emphasize that any subcutaneous nodule in the area around the periphery of the breast, and especially in the axilla, should always be viewed with suspicion and treated by early excision.

The presence of aberrant breast tissue is often noticed only when breast engorgement takes place during pregnancy and lactation, or when tumour formation occurs within it (Razemon and Bizard, 1929). There is no convincing evidence that this tissue is more prone to malignant change than normal breast parenchyma, and excision of aberrant breast tissue which is not causing symptoms and contains no tumour is, therefore, not normally indicated (de Cholnoky, 1951).

Carcinoma of aberrant breast tissue may be treated by wide local excision (Cogswell and Czerny, 1961) or by radical mastectomy (Copeland and Geschickter, 1950; Chiari, 1958). De Cholnoky (1951) advocates wide local excision with the removal of adjacent lymph-nodes as the treatment of choice and suggests that the breast should only be removed if any suspicious nodules are palpable within it. If mastectomy is not done, particularly careful follow-up is, of course, necessary to exclude any later manifestation of an occult primary neoplasm in the breast.

It has been suggested that the prognosis of carcinoma of aberrant breast tissue may be worse than that of carcinoma of the normal breast, because these tumours metastasize early to lymph-nodes (Cogswell and Czerny, 1961). Copeland and Geschickter (1950) noted that only 1 of their 9 cases survived for more than 5 years, and several other reported cases have shown a rapid progression to death. However, Chiari (1958), in a review of 60 cases, came to the conclusion that the clinical characteristics of carcinoma of aberrant breast tissue were the same as those of carcinoma of the breast, and he was unable to confirm that the prognosis of the two conditions differs significantly.

The present 3 cases were treated by local excision of the tumour, with the additional removal of the axillary lymph-nodes in 2 cases. The breast was not removed. Postoperatively each patient received a course of radiotherapy to the axilla and supraclavicular region. Follow-up to date has revealed no tumour recurrence, in 1 case 13 years after treatment.

Acknowledgements.—We wish to thank Dr. N. F. C. Gowing, Consultant Pathologist, Royal Marsden Hospital, and Dr. P. M. Peters, Royal Northern Hospital, for the histological reports. Thanks are also due to the Department of Photography, Royal Marsden Hospital, for the illustrations.

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GLOMUS TUMOUR

A REVIEW OF 15 CLINICAL CASES

By J. STRAHAN* and H. W. C. BAILIE
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SUMMARY

Fifteen cases of glomus tumour are recorded. Twelve patients presented with a solitary limb lesion. One patient had a glomus arising in a pilonidal sinus. Two members of one family had multiple lesions.

Complete surgical removal is curative, and malignancy is not a hazard. It is important to make a preoperative diagnosis, so that at operation a capsule can be looked for carefully. If no capsule is found an *en bloc* excision is imperative.

It is suggested that pain may sometimes be initiated by trauma, by thrombosis, or by the vascular congestion associated with menstruation and pregnancy.

GLOMUS tumours have been described in almost every part of the body. The typical clinical picture of the painful, bluish, circumscribed, skin nodule is now familiar to most clinicians. This condition was known as early as the eighteenth century, but the first clear clinical description was probably given by William Wood of Edinburgh (1812), who employed the term 'painful subcutaneous tubercle'. In 1924 Paul Masson published a description of the histological features which remains valid today.

Table I.—SUMMARY OF 15 CASES OF GLOMUS TUMOUR

CASE	SEX	AGE OF ONSET	SITE OF TUMOUR
1 (E. McG.)	F.	9	Left pretibial region
2 (A. M.)	F.	50	Calf of left leg
3 (E. S.)	F.	66	Subungual right middle finger
4 (M. H.)	F.	19	Subungual right thumb
5 (G. McF.)	F.	57	Plantar surface of right foot
6 (M. K.)	F.	33	Plantar surface of left foot
7 (S. E. M.)	F.	54	Pulp of right index finger
8 (M. O'H.)	F.	25	Plantar surface of right foot
9 (M. M.)	F.	64	Base of right thumb
10 (J. C.)	M.	77	Tip of left index finger
11 (P. M.)	F.	22	Pilonidal sinus
12 (J. M.)	M.	31	Left elbow
13 (J. McW.)	M.	29	Subungual left big toe
14 (H. A)	F.	26	Multiple (56)
15 (D. A.)	F.	28	Multiple (5)

The tumour is usually solitary, and typically it is found in the limb extremities where there is normally a concentration of glomus tissue, but no part of the body surface is exempt. Skeletal and visceral examples are rare. A wide spectrum of both histological and clinical features is now recognized in glomus tumours. The vascular glomus, resembling an angioma, differs greatly from the cellular tumour, but in all cases the hall-mark of histological diagnosis is the recognition of the characteristic 'glomus' cell in the vessel walls. The tumour usually has a well-defined capsule.

CLINICAL STUDY

Fifteen patients were seen at Coleraine Hospital in Northern Ireland over a period of 16 years (*Table I*). A histological confirmation of glomus tumour was obtained in 14 cases, there being no indication for surgical interference in the other. Thirteen patients were reviewed during 1969. Of the other 2 patients, 1 had died and the other had emigrated.

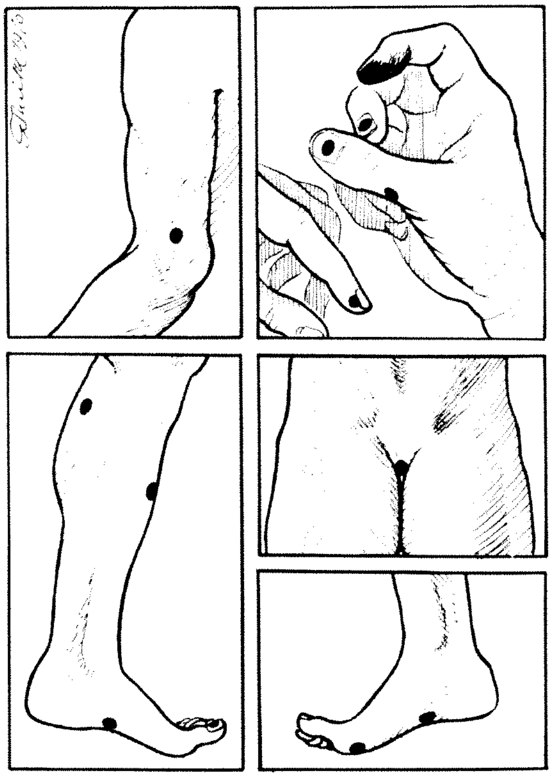

FIG. 1.— The site of the tumour in 13 patients with solitary glomus tumour.

There were 3 males and 12 females, with ages on presentation ranging from 19 to 77 years. Thirteen of the patients had a single lesion but multiple tumours occurred in 2 members of one family. The site of the tumour in the 13 patients with a single lesion is shown in *Fig.* 1.

Pain was the presenting symptom in 14 of the 15 patients. One female patient with a painless tumour of her thumb (*Case* 9) attended because she was worried about malignancy. Where pain originated in the digit it often radiated as far up as the trunk during severe paroxysms. The duration of the pain in this series varied from 4 to 20 years.

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Seven of the cases meriting separate description are detailed below.

CASE REPORTS

Case 7.—A 55-year-old female patient first attended a surgical clinic in August, 1963. She was then known to have myxoedema and was on maintenance thyroid therapy. She had moderately severe angina with pain radiating to both arms which was helped by glyceryl trinitrite. Disk degeneration of the lower cervical spine had also previously been diagnosed. Her complaints were of paroxysms of severe pain in the tip of her right index finger, accompanied by a less severe 'soreness' radiating to her right ear. The patient appeared distressed and said that she was 'distracted', 'muddled', and 'could not concentrate'. There was a localized point of extreme tenderness in the index finger-tip, and although there was no sign of a tumour the tender area was explored. At operation no recognizable tumour was found, but a small biopsy was taken and histology showed definite overdevelopment of glomoid structures under a thickened epidermis. The pattern was diffuse without any evidence of encapsulation. Her symptoms persisted after this exploration, and a wider excision was carried out 1 month later. This again was not curative, and 10 months later the finger-tip was amputated through the distal interphalangeal joint. Histology again showed a widespread increase in glomoid structures.

The patient was not seen again until this present review. She was still having paroxysms of pain in the amputation stump of her right index finger, radiating proximally and precipitated by light touch, cold, and dependency of the hand. The pain was eased by elevation or heat. On close examination of the part there was one pinhead-sized nodule with slight adjacent bluish discoloration which was very sensitive to light touch. Both the patient and her daughter (who is a nursing sister) insisted that during these paroxysms of pain there was an obvious red blush of the finger-tip.

Case 8.—During her third pregnancy a 27-year-old housewife found a painful nodule in the sole of the right foot. The pain disappeared after her confinement but recurred with the next pregnancy 18 months later. The nodule also increased in size and she was referred to the surgical clinic in the 26th week of pregnancy. There was a tender bluish swelling, 2 × 2 cm., on the sole of the right foot. Surgical exploration was deferred until 5 weeks after delivery, when a pale-pink, lobulated, fatty tumour, superficial to the plantar fascia, was dissected out. There was no evidence of a capsule. Histology showed fibrofatty tissue in which there was a prominence of vascular spaces with glomus cells. Following this operation she was symptom-free for 2 years, but pain returned with her fifth pregnancy. The pain was aggravated by weight-bearing and she noticed a bluish discoloration in the operation site. After delivery, symptoms again improved.

When seen at review a pinhead-sized nodule with a bluish flare around it was noted in the scar line. She said that her pain, though not now severe, was always worse during the week before menstruation.

Case 10.—A 77-year-old-man with one arm went to his doctor with a painful index finger, saying that he had run a nailbrush bristle under the nail. He was referred to hospital, and on examination the finger-tip was red and extremely tender to light touch. Under anaesthesia the nail was trimmed and a small incision was made in the pulp when a bead of pus was obtained. Four weeks later, in spite of antibiotic therapy, the finger was still painful and the patient was very short in temper. A small pout of granulations had grown at the site of the incision. Radiographs of the finger showed no bony abnormality. At a further exploration a narrow tract led to a small encapsulated glomus tumour of the pulp on the tip of the bony phalanx. Removal of the tumour produced complete relief of symptoms and a restoration of confidence.

Case 11.—After 3 years of recurrent inflammation and discharge from a pilonidal sinus, a 25-year-old clerk was referred to the surgical clinic. Pain was mentioned in her history, but this was considered to be due to attacks of inflammation. At operation an *en bloc* dissection of the sinus was performed with primary closure. Histology revealed a large glomus in the wall of a chronically inflamed sinus.

When seen at review she was very pleased with the results of the operation and was completely free from pain. Only then did she reveal that before the operation, pain was such that she often had to sit with a book under one buttock to relieve it, and sometimes it had been so intense that she could not sit at all.

Case 13.—A 27-year-old bus driver purchased a new pair of shoes for his wedding day. He wore them on that day and then put them aside as he thought that they were too loose. Eighteen months later he tried them on again but found that the 'left shoe hurt his big toe'. Within the next few months he obtained five different pairs of shoes but each hurt the left big toe. The pain in the toe became more severe and often occurred at night. A light touch was sufficient to cause a paroxysm of severe pain spreading up to the instep. When examined closely, a minute area of discoloration was seen under the nail which was very sensitive to touch. It was explored on two occasions through a window, but only in the second biopsy specimen were glomus elements detected. There was no sign of encapsulation.

At review 6 months later he still had pain.

Case 14.—A 26-year-old girl was referred to a consultant dermatologist following an eruption of purpuric-like spots on the limbs and trunk. She had no symptoms apart from menorrhagia with no obvious cause. A diagnosis of multiple haemangiomata was suggested and was supported by biopsy of a nodule from the left thigh. No treatment was undertaken.

Some months later she was referred for a surgical opinion with a painful nodule in the back of the neck near the hairline. The nodule measured 1·5 cm. in diameter and was bluish to red in colour. Multiple similar lesions (56 were counted) were widely scattered over the face, trunk, and limbs. These varied in size from tiny impalpable and completely collapsible lesions of less than 1 mm. to raised palpable nodules which were only partly compressible. The painful nodule was excised. It was encapsulated and pink in colour. Histologically, it resembled a cavernous haemangioma, but in many areas glomus cells were arranged in the walls of dilated vascular spaces. There was one area of thrombosis proceeding to organization. On review of the earlier biopsy it was possible to recognize glomus cells but no thrombosis in the vascular spaces. Apart from menorrhagia the patient was symptom-free.

Case 15.—The 31-year-old elder sister of *Case* 14 had five widely distributed skin nodules which had first been noticed at the age of 28. At review two of the nodules were slightly painful on deep pressure. No surgical treatment was offered.

DISCUSSION

Fourteen patients have had surgical excision of their tumours, but there was no indication for surgical interference in *Case* 15. All those patients in whom an encapsulated tumour could be shelled out at operation have had a very satisfactory result. Patients with unencapsulated tumours have had further trouble. The results of treatment are shown in *Table II*.

The glomus tumour is regarded not as a neoplasm but as a hamartoma because of its organoid structure. Malignancy is not a hazard and so-called 'recurrences' are almost certainly always incomplete removals of unencapsulated tumours. As the review of the cases described here has made clear, incomplete removal is all too frequent. Once it is recognized that the tumour does not possess an obvious capsule the surgeon should be prepared to change his approach and to carry out *en bloc* excision rather than to persist in any attempt to dissect out the tumour. As it is impossible to be certain before operation that the tumour has a capsule, care should be taken not to have the excision treated as a minor procedure. Linked to this is the obvious importance of an accurate preoperative clinical diagnosis. Many mistakes were made and delays in cure occasioned by misleading histories, as in *Case* 10, or by complete failure to recognize the condition and the possibility of surgical treatment, as in *Case* 4, who suffered severe pain for 5 years before she was referred for a surgical opinion. At this point we would emphasize the importance of warning the pathologist of the possibility of a glomus tumour.

Table II.—RESULTS OF TREATMENT RELATED TO PATHOLOGY

PATHOLOGY	NO. OF PATIENTS	RESULTS OF TREATMENT
Encapsulated	9	All cured by simple enucleation of the tumour
Uncapsulated	5	2 operations—cured 3 operations—cured 3 operations—residual symptoms 1 operation—residual symptoms 2 operations—residual symptoms
Total	14	

Case 11 appears to be the first recorded instance of a glomus tumour in a pilonidal sinus. It also seems to be a happy if unplanned example of the proper treatment of a glomus tumour.

Glomus tumours can be present for a long time without pain. Why they become painful is not at all certain, and attempts to correlate the histological picture with the presence or absence of pain have failed to show any constant characteristic. For example, the relationship between pregnancy, menstruation, and pain in *Case* 8 was striking. Also, in a further patient (*Case* 14) a painful lesion showed an organizing thrombus where a painless lesion showed no such pathology. Pathologists often describe sclerosis in these tumours which could well represent organized thrombus. Trauma may be the initiating factor in the onset of pain (Lendrum and Mackey, 1939). This occurred in only 1 patient in this series (*Case* 10). The presence of severe pain with a very localized and sensitive trigger-point should lead to the suspicion of a glomus tumour, even when there is no apparent swelling or discoloration. We suggest that there should be less reluctance in exploring such trigger-points.

When multiple lesions occur there is often a family history (Gorlin, Fusaro, and Benton, 1960; Hueston, 1961). These multiple tumours are often of the painless variety, although pain can erupt in a previously asymptomatic nodule.

Acknowledgements.—We would like to thank Mr. I. H. Greer who contributed 2 cases to this series, and also Dr. J. E. Morison for his most helpful advice and criticism.

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THE EFFECT OF ENVIRONMENTAL TEMPERATURE AND NUTRITIONAL INTAKE ON THE METABOLIC RESPONSE TO ABDOMINAL SURGERY*

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SUMMARY

Ambient temperatures of 29° C. had no effect on the nitrogen balance after elective abdominal surgery in 15 well-nourished men compared with 29 similar patients nursed at 24° C. The catabolic response as measured by nitrogen balance is small following operation of moderate severity and can be abolished by an increased intake of nitrogen and calories.

SURGICAL operations of moderate severity are followed by an increased excretion of nitrogen in the urine and a negative nitrogen balance which lasts for 4 or 5 days. The losses of nitrogen are due in part to a reduction in the intake of food over the period of injury (Cuthbertson, 1936). Patients who are well nourished prior to operation lose more nitrogen than nutritionally depleted subjects. The nitrogen

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[*] Based on a paper read to the Surgical Research Society in January, 1969.

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balance may be improved after injury by giving adequate sources of energy and nitrogen, but an obligatory catabolic response appears to persist in spite of apparently adequate intakes (Johnston, Marino, and Stevens, 1966).

Environmental factors have also been shown to diminish the metabolic response to injury. Caldwell (1962) showed that rats on a moderately restricted dietary intake excreted less urinary nitrogen when they were maintained at a temperature of 30° C. Barr, Burke, Liljedahl, and Plantin (1968) reported that, following severe burns, patients who were nursed at 32° C. in dry air had a reduced consumption of oxygen and maintained their nutritional state fairly easily.

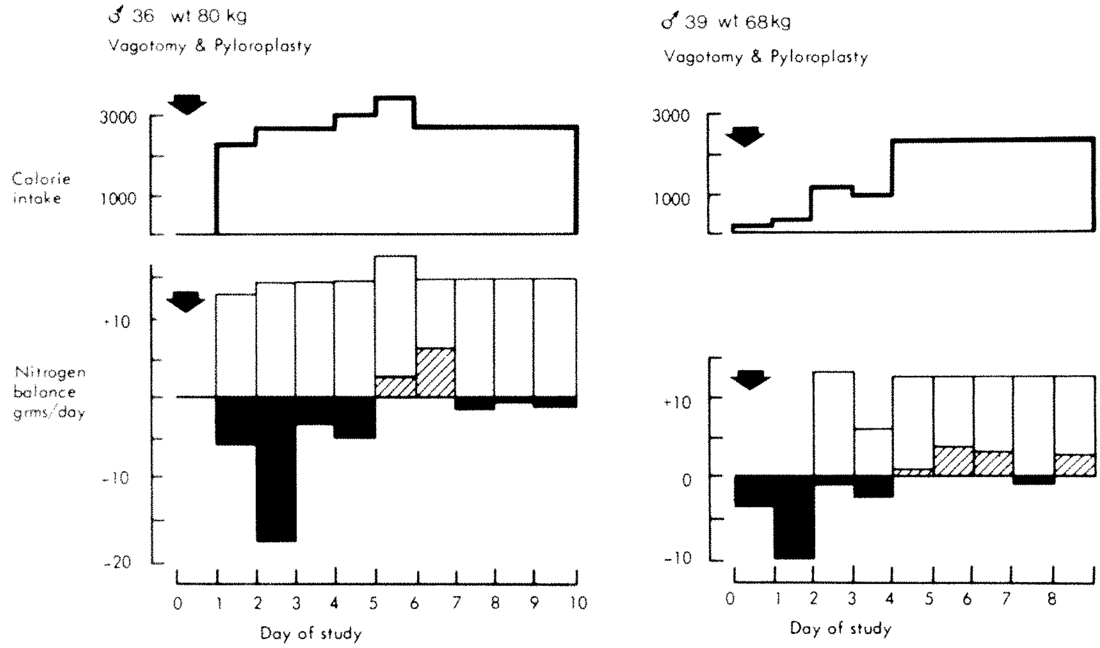

FIG. 1.—The calorie intake and nitrogen balance after vagotomy and pyloroplasty in 2 men of different weights receiving different intakes of food.

Davies and Liljedahl (1970) have subsequently shown that nitrogen losses in the urine of burned patients are reduced at high ambient temperatures of about 30° C. Cuthbertson, Smith, and Tilstone (1968) reported a similar reduction in urinary nitrogen in patients with closed limb fractures who were nursed at 30° C., and they suggested that high temperature reduces heat loss by the body, inhibits heat production, and thus reduces the breakdown of body protein to provide energy substrates.

Calorie intake and energy production are also closely related, and because of this an investigation was planned to study the effect of a high ambient temperature of about 30° C. on the metabolic response to surgical procedures of moderate severity in well-nourished men who were given varying calorie intakes in the postoperative period.

MATERIALS AND METHODS

Forty-four male patients aged between 21 and 67 years who were within 10 per cent of their standard weight, calculated in relation to sex, height, and age (Kemsley, 1952), were selected for study and were divided into two groups. The first group (29 patients) was nursed throughout at an ambient temperature of 24 ± 1·5° C., with a relative humidity of between 40 and 50 per cent. The second group (15 patients) was nursed at a temperature of 29 ± 1° C., with a relative humidity of 35 per cent for the first 3 days after operation. These patients were then transferred to the normal ward environment.

Table I.—DETAILS OF THE STUDY

FEATURE	GROUP 1	GROUP 2
Temperature of the environment (° C.)	24	29
Relative humidity (per cent)	40–50	35
No. of patients studied	29	15
Age range (years)	22–67	21–62
Mean age (years)	46·4	44·1
Weight range (kg.)	49–100	55–92
Mean weight (kg.)	70·3	69·9

Thirty-seven patients had vagotomy and pyloroplasty or gastro-enterostomy, 5 had partial gastrectomy, 1 had vagotomy alone, and 1 had a hiatal hernia repair. The age and weight of the patients and other details of the study are shown in *Table I.* Nitrogen balance studies were commenced on the day of operation and were continued for 8 days. The intake of nitrogen ranged from 0 to 272 mg. per kg. body-weight per day, and was maintained at a constant level in each patient. High intakes of nitrogen and calories in the postoperative period were achieved by using casein hydrolysate solution (aminosol, 10 per cent), soya bean oil emulsion (intralipid, 20 per cent), and sorbitol, 30 per cent. A potassium supplement of 80 mEq. per day was added to the parenteral intake. Parenteral feeding was replaced with nutritious fluids by mouth on the fourth postoperative day, and all the patients were given solid food on the fifth day. A constant intake was then maintained for the remainder of the study. The ratio of calories to nitrogen was maintained at about 200 calories to 1 g. of nitrogen at all times. The calorie and nitrogen intake during oral feeding was calculated from the tables of McCance and Widdowson (1964).

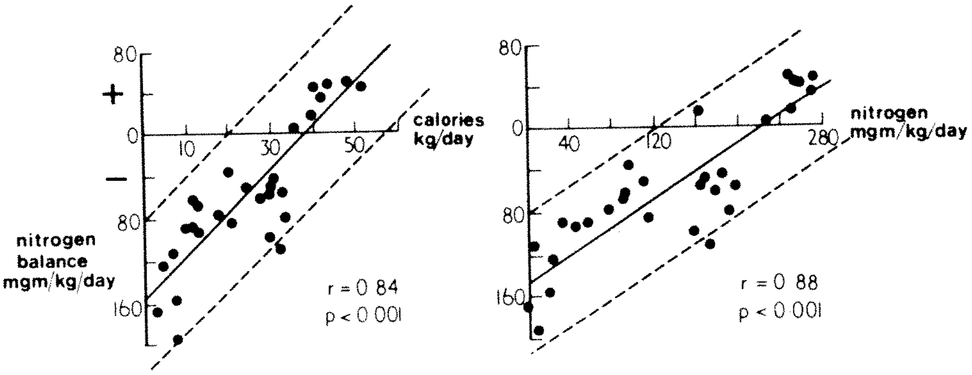

Fig. 2.—Regression analysis of the mean daily intakes of calories and nitrogen and the nitrogen balance in patients who were nursed at 24° C. (normal ward temperature) for the first 3 days after operation.

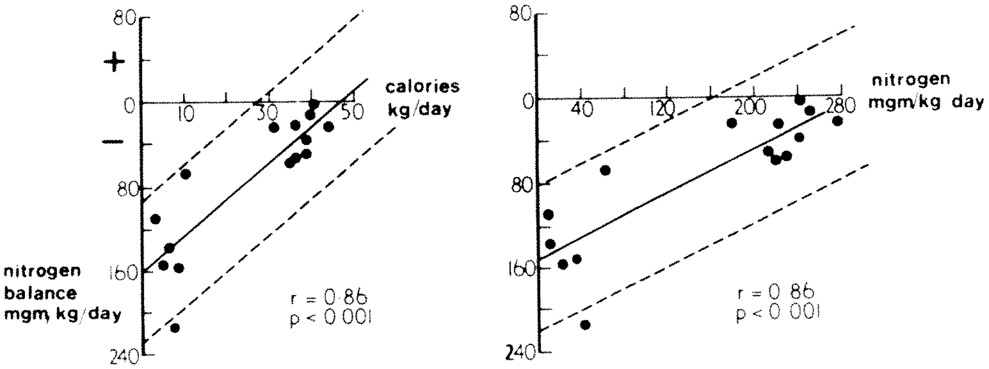

Fig. 3.—Regression analysis of the mean daily intake of calories and nitrogen and the nitrogen balance in patients who were nursed at 29° C. (high ambient temperature) for the first 3 days after operation.

Urinary nitrogen was measured in each 24-hour collection by the micro-Kjeldahl technique. The daily urinary creatinine output was estimated, and if the cumulative creatinine excretion after 3 days varied by more than 10 per cent from the excretion in the subsequent 3 days a collection error was assumed and the balance was discarded.

RESULTS

The postoperative balance studies from 2 patients of different weights are shown in *Fig.* 1. One patient had a low postoperative intake of calories and nitrogen while the other had a high intake. The balances of nitrogen are negative in both patients, and the nitrogen losses are greater in the heavier patient on a high intake. The obvious difficulty of comparing daily balance data from patients of different body-weight receiving different intakes of food was overcome by expressing all intakes and balances in terms of kg. body-weight.

The results are expressed as mean daily intakes and balances for each patient for the periods 1–3 and 5–7 days after operation.

The mean intake of calories and nitrogen was plotted against nitrogen balance, which was also expressed in terms of body-weight. The values for the 29 patients who were maintained at $24 \pm 1\cdot5^\circ$ C. are shown in *Fig.* 2. The balance of nitrogen remains negative when the intake is low and changes to positive as the intake rises. A regression analysis indicates that zero balance is achieved at a mean intake of 38 cal. per kg. per day and 223 mg. nitrogen per kg. per day ($P < 0\cdot001$). The 95 per cent confidence limits for the regression have been plotted.

The results for the 15 patients who were nursed at the higher temperature ($29 \pm 1^\circ$ C.) are shown in a similar fashion in *Fig.* 3. The relationship between intakes of calories and nitrogen and nitrogen balance is again significant ($P < 0\cdot001$). A regression analysis indicates that balance is achieved at an intake of 47 cal. per kg. per day and 296 mg. nitrogen per kg. per day. The observations for these patients, with the exception of 1 patient on a low intake, all fall within the 95 per cent confidence limits of the previous group. There is thus no evidence that after elective abdominal surgery of moderate severity, exposure to a temperature of 29° C. modifies the postoperative nitrogen loss during the first 3 days. A number of the patients who were nursed at high temperatures found the conditions uncomfortable.

The results for the period 5–7 days after operation have been analysed in the same way (*Fig.* 4). The patients were eating normally and most had a positive nitrogen balance at this time. A mean intake of 30 cal. per kg. per day and 152 mg. nitrogen per kg. per day was now sufficient to maintain nitrogen balance. The correlation between intake and balance remains significant ($P < 0.001$).

A comparison of the regression lines for the immediate and late postoperative periods shows a shift to the left in the period 5–7 days after operation (*Fig.* 5). This difference may represent the extent of

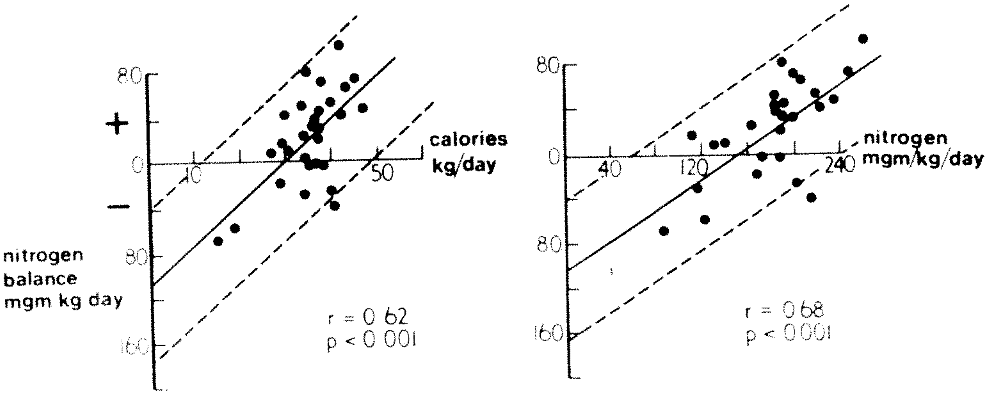

FIG. 4.—Regression analysis of the mean daily nitrogen and calorie intake and the nitrogen balance in patients 5–7 days after operation.

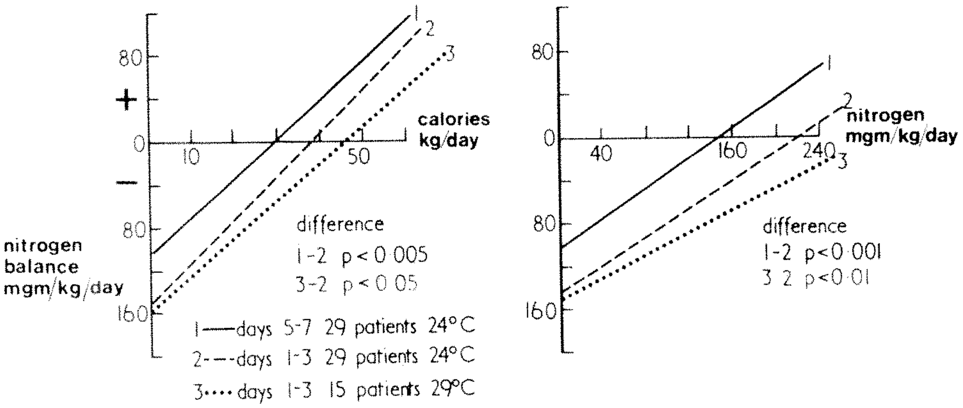

FIG. 5.—A comparison of the regression analyses of the intake/balance relationships in the early and late postoperative periods.

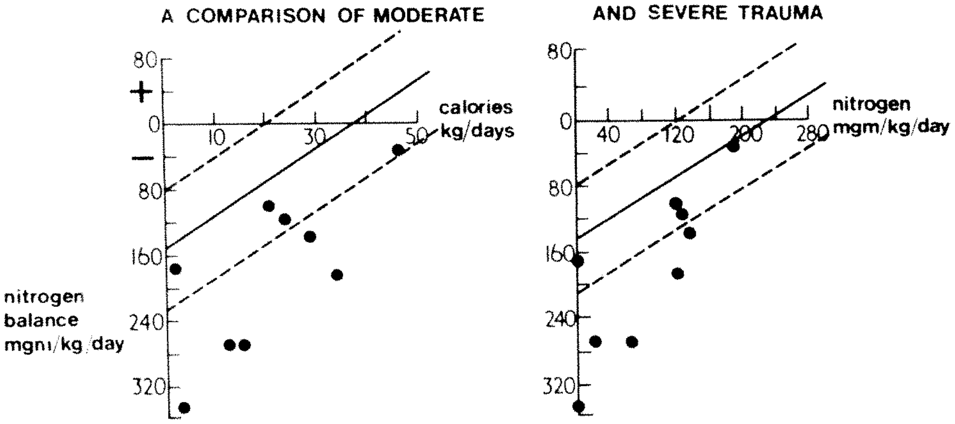

FIG. 6.—The relationship between calorie and nitrogen intakes and nitrogen balance after major trauma (each dot represents 1 patient) plotted against the regression analysis of data from patients after elective surgery of moderate severity.

the catabolic response in the postoperative period. The differences between the regressions was analysed using the formula:—

$$\frac{\text{Distance between slopes}}{\text{Standard error of distance}},$$

with n_1-2 and n_2-2 degrees of freedom. The difference was found to be significant (*Fig.* 5).

It was considered that if changes in body catabolism can be detected by this method of regression analysis then data from patients after major trauma should show a more marked shift to the right.

The mean daily intake, output, and balance data from 9 patients following multiple fractures, chest injury, and major neck and abdominal surgery for malignant disease were calculated from the second to the fourth day after injury or operation, and these results are shown alongside the regression analysis of the data obtained 1–3 days after elective surgery of moderate severity (*Fig.* 6). All the results fell below the regression line for the moderate injury group, and 5 results fell outside the 95 per cent confidence limits. These results indicate that very high intakes would be required to achieve a positive balance in such patients.

DISCUSSION

The results of this investigation have failed to show any reduction of postoperative nitrogen loss in the first 3 days after operations of moderate severity when the ambient temperature was raised to 29° C. Cuthbertson and others (1968) studied patients with closed fracture which is recognized as producing a more profound catabolic response than the operation in this study.

The present investigations show that the catabolic response following elective, uncomplicated abdominal operation is very small in terms of total nitrogen turnover, when allowances are made for diminished intake immediately after surgery. It may be that only the response to more major injury is affected by high ambient temperatures.

The results indicate that the negative nitrogen balance following moderate surgical trauma can be overcome by an increase in the calorie and nitrogen intake in the postoperative period. The required increase over resting requirements is modest and amounts to not more than 8 cal. per kg. per day and 70 mg. nitrogen per kg. per day in well-nourished men.

The nitrogen losses after major injury are much greater, so that the intakes necessary to achieve balance cannot be reached easily. These results suggest that the calorie and nitrogen requirements for balance after major injury are related mainly to the severity of the trauma.

It may be that in patients after major trauma the combination of high intakes and an increase in the ambient temperature will be an effective method of reducing the nitrogen losses. High-temperature nursing will clearly be of greater value when a component of energy expenditure such as evaporative heat loss is present after injury, as in severe burns. However, in patients with closed injuries or after major surgery where excessive evaporative heat loss does not occur but where the resting metabolic expenditure may be increased by up to 40 per cent (Kinney, Long, and Duke, 1970), problems of heat distribution might develop within the body. It is important also to determine why some patients could not tolerate the high temperature of their surroundings.

These studies show that the catabolic response to the moderate trauma of abdominal surgery is small in terms of calorie requirements and is not influenced in the first 3 days by changes in ambient temperature. Severe injury, on the other hand, is associated with much greater losses of nitrogen, and the calorie and nitrogen requirements to achieve balance are very great.

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THE EFFECT OF A SINGLE-DOSE PARENTERAL ANTIBIOTIC IN THE PREVENTION OF WOUND INFECTION

A CONTROLLED TRIAL

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SUMMARY

In a series of 349 operations a single dose of 500 mg. of ampicillin was given immediately preoperatively to 164 patients selected at random. There was no significant reduction in the wound-infection rate in cases given ampicillin compared with the controls.

THE incidence of postoperative infections in sutured surgical wounds has concerned us for some years (Jackson, Pollock, and Tindal, 1971a, b). We have shown in a series of 921 operations (Jackson and others, 1971a) that the most important determinant of wound infection is the nature of the operation performed. The incidence of infection in clean wounds was 4·4 per cent, in potentially contaminated wounds (largely operations on hollow muscular organs) 14·9 per cent, and in actually contaminated wounds 43·1 per cent. These differences were significant when subjected to χ^2 analysis. Similar results have been reported by other authors (e.g., Jepsen, Larsen, and Thomsen, 1969). In our series a plastic adhesive drape applied before skin incision had no effect in reducing the rate of wound infection.

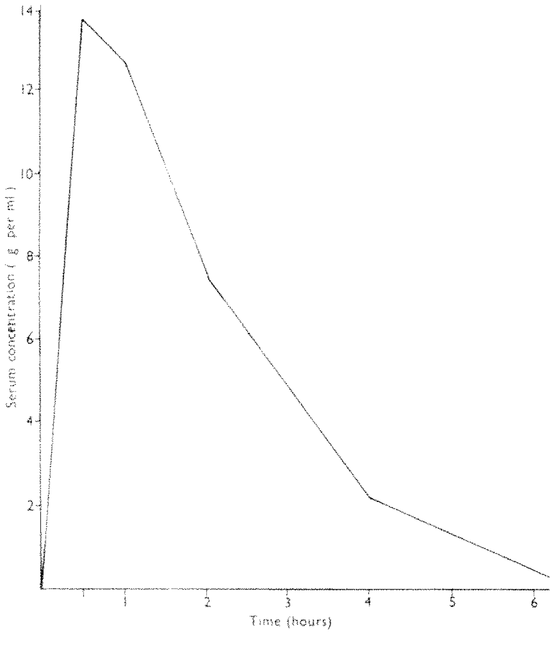

FIG. 1.—Serum concentration following intramuscular injection of ampicillin, 500 mg. (*By courtesy of Beecham Research Laboratories.*) Dr. E. A. P. Croydon of Beecham Research Laboratories has kindly sent us figures for serum concentration after intravenous injection of ampicillin, 250 mg. These show a higher level during the first hour, and thereafter a decline corresponding to the graph after intramuscular injection.

In a second trial (Jackson and others, 1971b) 704 wounds were studied and random cases were sprayed with a bacitracin–polymyxin–neomycin spray. We found that this spray produced no statistically significant improvement in the wound-infection rate.

We then turned our attention to the possibility of reducing wound infections by the prophylactic use of a single parenteral dose of an antibiotic. Our purpose was to flood the tissues with blood containing a high concentration of the antibiotic during the time of possible contamination of the wound (*Fig.* 1). We chose to use ampicillin (500 mg.) as this is a broad-spectrum antibiotic which can easily and safely be injected intravenously by the anaesthetist at the time of induction of anaesthesia.

The use or non-use of the antibiotic was decided by the spin of a coin. All patients were observed for a minimum of a month and wound infections were recorded by one of us, without knowing whether ampicillin had been used or not. We have defined a wound infection as the discharge of pus from the wound and have divided the cases into major and minor wound infections based on the presence or absence of constitutional disturbance, particularly pyrexia, and delay in discharge from hospital.

Each patient was asked about penicillin sensitivity and no one was included in the survey who gave such a history. No patient was excluded on the grounds that antibiotics were already being used, nor was the postoperative use of antibiotics in any way altered. Children under the age of 10 years were excluded.

RESULTS

We stopped the present investigation after 349 operations as we found that the results were not encouraging. In this group there were 172 clean, 155 potentially contaminated, and 22 contaminated operations. In 83 of the clean operations ampicillin was used and 3 wound infections occurred (3·6 per cent). Of these, 2 were minor and 1 was major. In the other 89 clean operations no ampicillin was used and there were 4 wound infections, which were all major (3·4 per cent). The difference is not statistically significant ($\chi^2 = 0{\cdot}085$).

Of 155 potentially contaminated operations, 70 were given prophylactic ampicillin and there were 13 wound infections (18·6 per cent), 11 of which were major. Eighty-five patients were not given ampicillin and 14 wound infections occurred (16·5 per cent), 11 of which were major. The difference is not statistically significant ($\chi^2 = 0{\cdot}118$).

Twenty-two contaminated operations were included, and these were equally divided between the two treatment groups. Six patients who had been given ampicillin and 7 who had had no treatment became infected. The difference is not statistically significant ($\chi^2 = 0{\cdot}188$).

DISCUSSION

The majority of postoperative infections in clean stitched wounds arise as a result of endogenous contamination during the period of operation. When, on the other hand, the wound is left open or is drained, ward infections are probably of greater significance (Davidson and Smith, 1969; Jepsen and others, 1969). The contribution of unsterile instruments, surgeons' hands, or airborne infection during operation has been shown to be of very little significance unless the operating-theatre personnel have obvious symptomatic infections (Todd, 1968; Seropian and Reynolds, 1969).

It should be possible to reduce the rate of wound infection by diminishing the contamination of the open wound from the patient's own sources and by increasing his resistance to infection. Studies are in progress on the latter aspect, but in the present survey we have been concerned only with the possibility of lessening the bacterial contamination of the wound by the use of a prophylactic antibiotic.

There are three ways in which antibiotics may be used: the wound may be sprayed or sprinkled with the active substance, it may be irrigated with a solution of the drug, or the antibiotic may be introduced into the blood-stream whence it will be shed into the new wound. The results of all these methods of prevention have been equivocal. Topical application has been shown to be of value in experimental wounds (Hopson, Britt, Sherman, and Ledes, 1968) and in patients with general peritonitis (Noon, Beall, Jordan, Riggs, and de Bakey, 1967). Our own results with an antibiotic spray failed to show a significant improvement in the rate of wound infection (Jackson and others, 1971b).

The alternative method, using a prophylactic parenteral antibiotic, gives equally controversial results. Fekety, Chiff, Sabiston, Seidl, Smith, and Thoburn (1969) failed to show any effect in cardiac surgery using penicillin and methicillin. Altemeier, Culbertson, and Hummell (1968) suggested that the incidence of wound infection with preoperative or prophylactic antibiotics was greater than the infection rate of wounds in patients not treated with them. On the other hand, Polk and Lopez-Mayor (1969) found a significant reduction in the rate of wound infection in patients undergoing gastro-intestinal operations who were given one dose of cephaloridine before and two immediately after operation. Our own results show that a single preoperative dose of ampicillin affords no protection against wound infections. Further work on antibiotic prevention of wound infection is planned.

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A MODIFIED TECHNIQUE OF COLOSTOMY

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SUMMARY

A modified technique of colostomy is described which avoids the disadvantages of the more widely used technique employing a glass rod and rubber tube. The use of a rubber drain, instead of a glass rod, which is brought out through two small stab incisions allows the immediate fitting of a bag, thus avoiding contamination of the main incision.

MANY techniques of doing a colostomy have been described (Gabriel and Lloyd-Davies, 1935; Cattell, 1942), each one having its own advantages and disadvantages. Obviously, problems arise with the decompression type of colostomy rather than with the diverting colostomy.

For a colostomy to be effective it must (*a*) decompress the bowel of faeces and flatus adequately, (*b*) be a suitable distance away from the main incision, if any, and (*c*) preferably have a disposable colostomy bag fitted immediately in order to avoid contamination of the main wound.

The most widely used method of colostomy employs a glass rod with a rubber tube connected to its ends to anchor the colon to the abdominal wall. The glass rod is usually kept in position for 7 to 10 days before it is removed, and it is therefore impossible to fit a disposable bag snugly around the colostomy opening. A bulky dressing has to be applied which is very uncomfortable to the patient and also inevitably leads to contamination of the main wound, and occasionally there are attendant complications such as wound dehiscence, incisional hernia, etc.

In 1968 Lee described a method in which he used a sturdy rubber tube instead of a glass rod to anchor the loop of colon. The tube was sutured to the skin at its ends. This method is very effective indeed, except in obese patients where the loop of the colon is under tension and pressure necrosis of the loop of the colonic bridge can occur, leading to retraction of the bowel and the spillage of faeces.

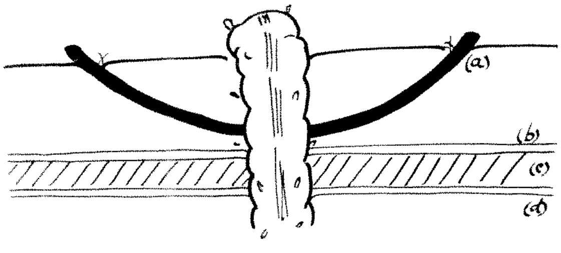

FIG. 1.—a, Rubber tube traversing a subcutaneous tunnel. b, Anterior rectus sheath. c, Rectus muscle. d, Posterior rectus sheath and peritoneum.

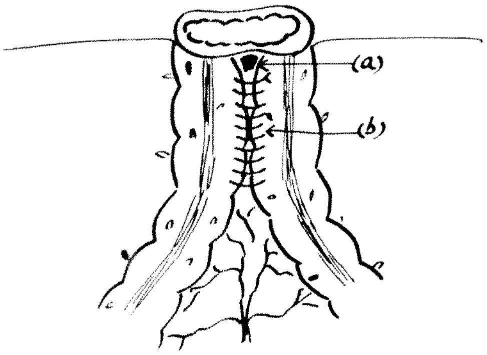

FIG. 3.—a, The site for the rubber tubing through the transverse mesocolon. b, Approximating the taenia coli to form a spur prevents small-bowel inclusion when the enterotome is applied.

The author has found the following modification helpful in overcoming most of the disadvantages of the routine technique.

TECHNIQUE

The loop of colon is brought out of the colostomy incision after separating the omental attachment (in the case of the transverse colon). A 2·5-cm. rubber drain (either a corrugated drain or a Penrose drain) is passed through an avascular area in the mesentery, and is brought out through two small (1·8-cm.) stab incisions on either side of the colostomy incision. This drain traverses a subcutaneous tunnel and is sutured to the stab incisions at either end (*Fig.* 1). The colostomy is opened at the end of the operation. Some surgeons make the incision along the anterior taenia coli, while others make a cruciate incision. Both these methods do not allow a sufficient 'opening-out' of the two stoma, resulting in a wide bridge along which a significant amount of faeces can leak into the distal colon. For this reason the author prefers to make the incision around two-thirds of the circumference of the colon (*Fig.* 2). This allows a more complete 'opening-out' of the stoma, making the bridge narrower (*Fig.* 3). Once this has been done and haemostasis has been achieved there is no real necessity to suture the colon to the skin. With the colostomy thus completed, a disposable colostomy bag can be fitted snugly. The rubber drain is removed in about 7–10 days.

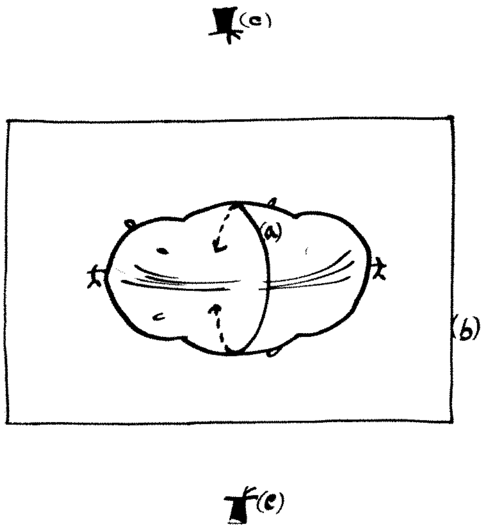

FIG. 2.—a, Line of incision for opening the colon. b, Area for the colostomy bag. c, Rubber tubing outside the colostomy bag.

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THE LOCAL EFFECTS OF INTRA-ARTERIAL INJECTIONS OF SODIUM TETRADECYL SULPHATE (S.T.D.) 3 PER CENT*

AN EXPERIMENTAL STUDY

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SUMMARY

The accidental intra-arterial injection of the commonly used sclerosant sodium tetradecyl sulphate (S.T.D.) 3 per cent during the treatment of varicose veins can affect seriously the blood-supply to the limb, and gangrene may follow.

Intra-arterial injection of S.T.D. into the limb arteries of dogs chemically disintegrates the blood in the slow-moving stream of the capillaries and converts it into a thick sludge which obstructs the circulation locally, resulting in necrosis of the extremity.

THE inadvertent intra-arterial injection of sodium tetradecyl sulphate (S.T.D.) 3 per cent in the treatment of varicose veins can be dangerous. Patients have developed acute ischaemic changes and gangrene of the foot following this accident. For example, a patient aged 20 years developed gangrene of the foot within 2–3 days of injection of S.T.D. into a perforating vein on the medial aspect of the leg. The posterior tibial artery was injected inadvertently, resulting in loss of the forefoot.

An animal investigation was planned to examine the results of injecting the sclerosant S.T.D. into arteries and to determine whether its effect was due to spasm of the artery, to intimal irritation resulting in thrombosis (as in veins), or to denaturing of the blood.

MATERIALS AND METHODS

Greyhound dogs, weighing approximately 25 kg., were used in the experiments. S.T.D. 3 per cent in a sterile aqueous solution containing 2 per cent benzyl alcohol and buffered to *p*H 7·6 was used as a sclerosant (Pharmaceutical Research Limited, Hereford). The effects of 2 per cent benzyl alcohol had already been investigated by Fegan (1967), who found that this substance had no effect when injected intravenously in a similar dosage and situation to the intravenous injection of sodium tetradecyl sulphate. Therefore, it was assumed that the effect of S.T.D. 3 per cent was due to its constituent sodium tetradecyl sulphate, a salt of an alkali metal and a long-chain fatty acid (sodium 1-isobutyl-4-ethyloctyl sulphate).

A total of 18 limbs were examined in 13 dogs; 2·5 ml. of the solution (0·1 ml. per kg. body-weight) were injected into the main femoral artery in the thigh. Arteriograms were performed with 20 ml. of 76 per cent Urografin (Schering) as the contrast medium and using an Elema Schonander cassette changer at a speed of 2 films per second. Arteriograms were carried out immediately after injecting the S.T.D. Further arteriograms were carried out 15 and 30 minutes after the injection of S.T.D. Arteriograms were also performed 1 and 2 weeks after the sclerosant injection. The main arteriographic change noticed was the immediate loss of pad vessels. There was no evidence of narrowing or obstruction in the main lower limb vessels. There was, however, a blurred appearance in the region of the pad (*Fig.* 1). Clinically, the animals who showed loss of pad vessels had limb and paw swelling for up to 2 weeks after the injection.

The animals were killed at 18 hours, 1 week, and 3 weeks after the injection of S.T.D. The complete leg vessels from the site of injection were dissected out with the intact foot pad. Representative areas of the blood-vessels and pad were examined histologically. The most constant histological change was an unusual form of paravascular necrosis of the muscle pad (*Fig.* 2). There was no evidence of any intimal damage or irritation in the vessels, even up to 3 weeks after the injection. This injection, however, did not produce gangrene in the dog's limb. Although the limb became swollen it usually returned to normal in 2 weeks. Even when preliminary compression of the femoral artery for 60 seconds (as suggested by Engler, Freeman, Kanavage, Ogden, and Moretz, 1964) was applied prior to the injection, gangrene was not produced. When the dose of S.T.D. was increased to 4 ml. in one injection, death occurred within 48 hours.

Attempts were made to determine whether the animals could be protected from the local effects of S.T.D. Four dogs were injected intra-arterially with 2·5 ml. S.T.D. followed immediately by 40 mg. of Papaverine HCl solution into the same vessel. The effects were compared with the contralateral limb in which the artery was injected with 2·5 ml. S.T.D. alone. In 2 of the 4 animals there was clinical, histological, and arteriographic evidence that some protection had been achieved.

Lumbar sympathectomy was performed on 2 animals, and on full recovery 2 weeks later 2 ml. S.T.D. were injected into the femoral artery, but again there was limb swelling and obvious pain. Loss of pad vessels was demonstrated on an arteriogram in 1 of the animals. Both animals had recovered fully by 2 weeks. It was not possible to draw any conclusions regarding the value of sympathectomy from these experiments.

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* Based on a communication to the Surgical Research Society at Hammersmith Hospital, London, in January, 1971.

The results suggested that the lesions were due to occlusion of the smaller vessels of the pad. A further investigation was planned to investigate the effect in small vessels by an experiment *in vivo* using a rabbit's ear chamber. Lop rabbits, weighing approximately 3 kg., on whom a Perspex ear chamber had been inserted 3 months previously were used. The central auricular artery at the base of the ear was injected with 0·3 ml. S.T.D. (based on a dose of 0·1 ml. per kg. body-weight). The events in the ear chamber were observed using a microscope with an oil-immersion lens at low- and high-power magnifications and were filmed in colour. A large arteriole was visualized in the centre of the field. The S.T.D. was seen to enter this vessel. No spasm was noted either in this arteriole or in the capillaries, but within a few minutes the red cells became distorted and broken and formed a central homogeneous thrombus, which appeared to be an intravascular aggregation of destroyed and fragmented red cells without fibrin

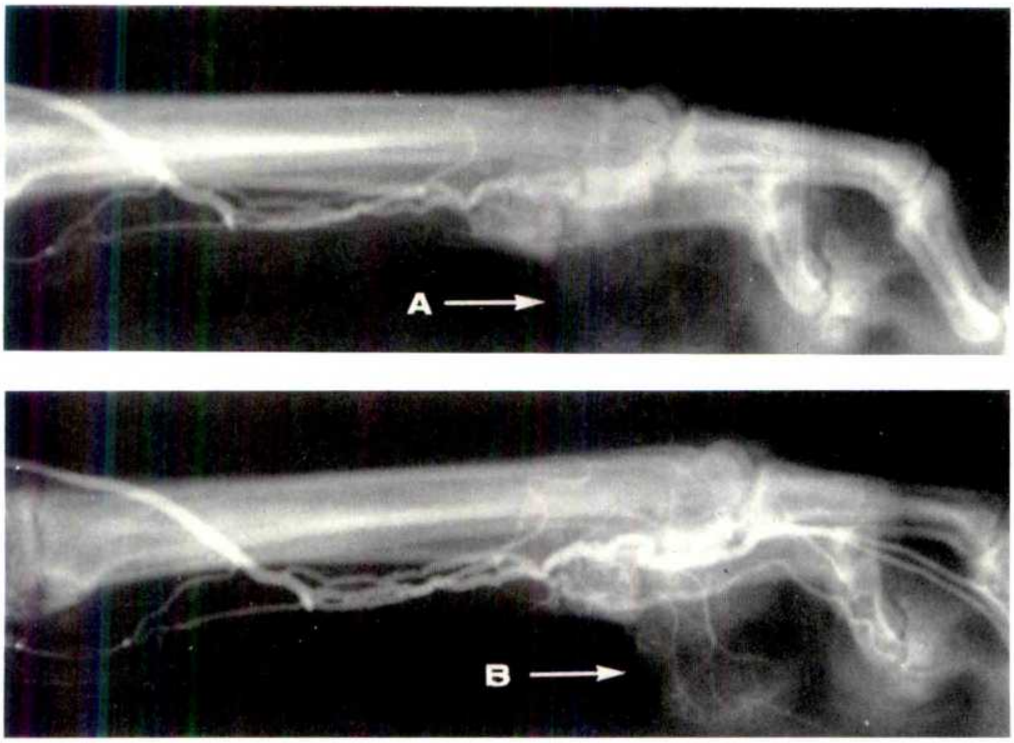

FIG. 1.—Arteriograms of the foot pad of a dog 15 minutes after the injection of 3 ml. S.T.D. Note the blurred appearance of pad A compared with the control B. The major vessels in each case are well filled with contrast medium, with near identical timing following injection.

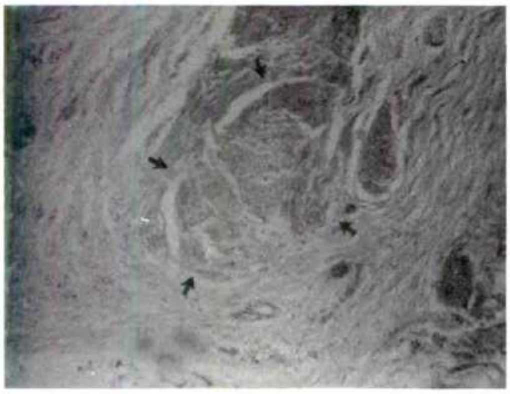

FIG. 2.—Section of the foot pad of a dog 1 week after injection of S.T.D. Necrosis of muscle is visible (arrowed), but there is no change in the vessels.

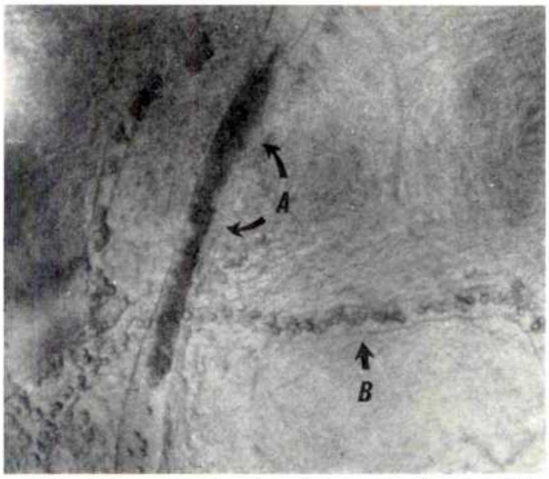

FIG. 3.—Low-power view through the ear chamber of a rabbit during intra-arterial injection of S.T.D. Sludge occupies and occludes the arteriole (A). A normal venule (B) containing blood-cells is seen traversing the field at right-angles.

formation (*Fig.* 3). This thrombus moved slowly down the arteriole into the capillary, where it became impacted. Gradually the whole circulation slowed down with marked stasis in the venules. There was no spasm of the arteriole nor was there any evidence of intimal damage at this stage. An injection of saline moved the sludge up and down the arteriole and capillary. The distal half of the rabbit's ear became blue and cold within an hour of the injection, and subsequently became gangrenous. It was assumed, therefore, that the major effect of the S.T.D. was on the blood-cell mass which it destroyed and converted into an intravascular embolus. It was presumed that secondary thrombosis occurred later owing to stasis and obstruction of the microcirculation and causing gangrene of the ear.

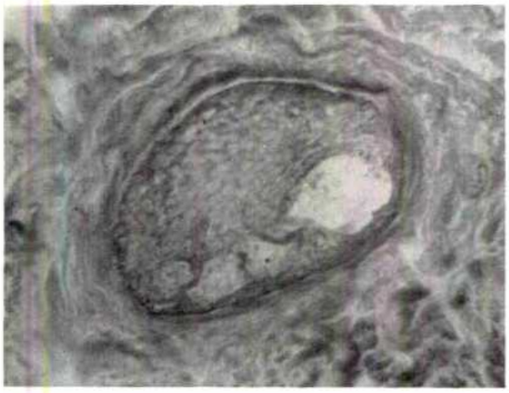

FIG. 4.—Microscopic section of a rabbit's ear 1 hour after an intra-arterial injection of S.T.D. An artery of the ear is blocked by amorphous material or sludge. Note the absence of an inflammatory response in the vessel wall.

Further experiments *in vitro* were performed using S.T.D. and whole normal blood mixed in equal parts. A thick, sticky, homogeneous red lysate was formed which was miscible with water and soluble in fat solvents. All the cellular elements were lysed and fibrin was not formed. On standing for 24 hours the lysate became thicker and more viscid.

The histological details were investigated in 6 New Zealand white rabbits of approximately 3 kg. weight; 0·3 ml. S.T.D. (0·1 ml. per kg.) was injected into the central artery of the rabbit's ear, with a control injection of saline in the opposite ear. If the injection was successful the ear immediately changed in colour and within an hour the distal part of the ear became blue and cold. In 4–5 days gangrenous changes invariably occurred in the distal half of the ear. Two animals were killed, 1 after 1 hour and the other 5 days following injection. Representative histological sections of the ear were made from the site of the injection to the periphery and were stained with haematoxylin and eosin and van Gieson elastin. In the rabbit killed 1 hour after the injection of S.T.D. the main artery and its arterioles were blocked by a yellow amorphous mass of sludge (*Fig.* 4). In the rabbit killed after 5 days the main artery was empty of blood and contained a thin rim of sludge and some proteinaceous material. The smaller branches were blocked completely by the sludge and the surrounding tissues showed coagulation necrosis. The viable tissues outside the affected area showed an acute inflammatory reaction. A section through the main artery proximal to the injection site showed thrombosis without the presence of sludge (*Fig.* 5). There was neither evidence of intimal damage nor thrombosis in the injected vessels distally, even after 5 days, and the perivascular inflammatory reaction that was noted was clearly secondary to the tissue necrosis.

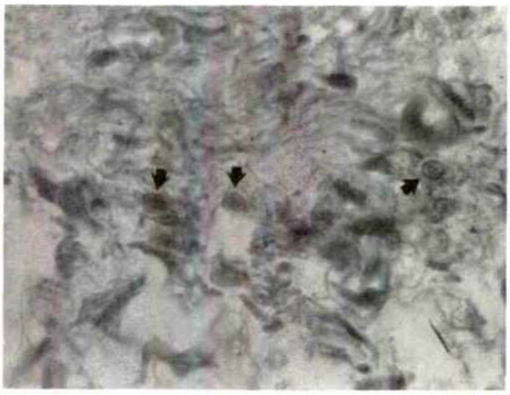

FIG. 5.—Microscopic section of a rabbit's ear 5 days after an intra-arterial injection of S.T.D. This high-power view shows that the small arteries (arrowed) are occluded by sludge. The surrounding collagen shows early necrosis.

DISCUSSION

The results of these experiments indicate that S.T.D., when injected intra-arterially, has little effect on the major vessel and produces no spasm, but is washed into the smaller arteries where it mixes with the blood and denatures it, converting it into a thick lysate or sludge. This sludge or embolus obstructs the microcirculation, causing proximal stagnation, secondary thrombosis, and necrosis. There was no evidence that intimal irritation or damage caused these changes, which appear to be different from the reported effects of S.T.D. on veins, where apparently the intima is denuded immediately with super-added thrombosis (Fegan, 1967).

Many drugs can cause gangrene when injected intra-arterially; besides S.T.D., thiopentone, barbiturate, amphetamine, sodium bromosulphathalein, chlorpromazine, and Ethamolin can all cause similar lesions (Kinmonth and Shepherd, 1959; Engler, Purvis, Kanavage, Ogden, Freeman, and Moretz, 1967). These ischaemic changes are in contrast with the relatively innocuous behaviour of these drugs when injected intravenously. Why the difference? With an intravenous injection, mixing and dilution occur and the material has to pass around the circulation before finally arriving at the distal arterial tree. When injected intra-arterially the irritant material is swept undiluted into the capillaries and arterioles where it exerts its deleterious effects.

How can these effects be prevented? It would seem important to keep to the recommended dosage of 0·5–1 ml. of 3 per cent solution per injection when using S.T.D. for injecting varicose veins, as the effects appear to be dose related. Certainly no more than 8 ml., which is approximately 0·1 ml. per kg. body-weight, should be used at any treatment session. Ethamolin oleate (5 per cent) might perhaps be a more suitable sclerosant, as it appears to cause minimal irritation (Reid and Rothnie, 1968). Special care should be taken when injecting varicose veins near a main artery, particularly in the lower third of the leg where the tibial arteries are relatively superficial and can be entered inadvertently with a needle. Following an intra-arterial injection the patient usually complains immediately of pain in the limb, and within a short time there are obvious colour changes, pallor, and cyanosis. If left untreated the foot can become gangrenous in 3–4 days, with a considerable amount of pain and discomfort to the patient. Heparin should be administered locally and systemically to prevent secondary or spreading thrombosis. Lumbar sympathectomy may help to open up the collateral circulation. The observation that sludge was made to move by forcible injection of saline into the artery of the rabbit's ear suggests that it might be valuable to expose and to cannulate the involved artery in order to dilute and attempt to wash out the sludge with a heparinized saline solution.

Acknowledgements.—We wish to acknowledge the expert assistance of Dr. Sumner Wood, jun., with the experiment which was conducted under his supervision in the Cancer Research Laboratory of the Department of Pathology, The Johns Hopkins Hospital, Baltimore, Maryland. We are grateful to Mr. James Mulvanny, A.I.B.P. (med.), for the photographic illustrations.

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GIANT HYDRONEPHROSIS IN A SOLITARY CROSSED ECTOPIC KIDNEY

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SUMMARY

A case of giant hydronephrosis occurring in a solitary crossed ectopic kidney is presented. This is the seventeenth instance of this renal anomaly, and the first reported in association with a giant hydronephrosis. The diagnosis is discussed, and attention is drawn to the high incidence of genital defects and pathological change associated with solitary ectopic kidneys.

GIANT hydronephrosis has been arbitrarily defined as the presence of more than 1 litre of urine within the collecting system and pelvis of the kidney (Stirling, 1939). A review of the literature by Campbell, Hunsicker, and Marconis (1950) disclosed 100 cases, to which they added a case of their own. Tombari, Power, Harper, and Politano (1968) were able to collect a further 60 cases, and reported the largest hydronephrosis (52 litres) in recent times. However, Glass (1746), a surgeon at Oxford, appears to have documented the most spectacular example, when he described the autopsy findings of a 22-year-old woman, who 'had been remarkable all her life for the preternatural size of her belly'. The circumference of her abdomen was found to be 6 ft. 4 in. (190 cm.), while the distance between the xiphoid cartilage and the os pubis was 4 ft. ½ in. (121 cm.). The autopsy revealed what was clearly a right-sided hydronephrosis, the contents of which were 'found to be not above a pint less than 30 gallons wine measure' (115 litres).

The present case, although not of such extraordinary dimensions, is of interest for the occurrence of a giant hydronephrosis in a solitary crossed ectopic kidney. The subsequent surgical management was complicated further by the posterior rotation of the pelvis.

CASE REPORT

M. F., a 59-year-old man, was admitted with a history of sudden onset of nausea, vomiting, and generalized abdominal pain. He also complained of painless haematuria of 10 days' duration, and thought that his abdominal girth had increased over the past year. A tentative diagnosis of retroperitoneal tumour had been made.

On examination he was found to be pale, sweating, and in severe pain. His temperature was 37·6° C., the pulse-rate was 120 per minute, and the blood-pressure was 140/80 mm. Hg. There was considerable distension of the abdomen by a tense, fluctuant, tender mass. This was central in position, arising out of the pelvis and extending almost to the xiphisternum; it was easily palpable on rectal examination. Bowel-sounds were not audible. There were no obvious abnormalities of the genitalia. Shortly after admission it was evident that the patient was oliguric, catheterization yielding only 100 ml. of blood-stained urine.

Investigations revealed that the haemoglobin was 7·7 g. per cent and the white blood-count was 8700 per c.mm. Examination of the blood-film showed mainly a normochromic anaemia. The blood-urea was 222 mg. per 100 ml., serum sodium 132 mEq. per l., serum potassium 6·2 mEq. per l., and serum bicarbonate 14 mEq. per l. A chest radiograph was normal. A plain radiograph of the abdomen (*Fig.* 1) showed multiple areas of calcification, in particular in the pelvis and medial to the right sacro-iliac joint. An intravenous pyelogram (*Fig.* 2), using 150 ml. of Conray 420, showed opacification of a large mass arising out of the pelvis and reaching up to the level of the second lumbar vertebra.

Following intravenous therapy and resonium enemata the serum potassium level fell to 5·2 mEq. per l., and a cystoscopy was then performed. This revealed that the bladder was indented by an extravesical mass. There was a blood-stained efflux from the left ureteric orifice, while the right ureteric orifice and adjacent ridge were absent. The left ureteric orifice was easily catheterized (*Fig.* 3), and retrograde urography was performed (*Fig.* 4). This showed the left ureter crossing the pelvis to the right side, with a filling defect present in the ureter opposite the right sacro-iliac joint coincidental with the opacity on the plain radiograph. A diagnosis of calculus obstruction of a giant infected hydronephrosis in a solitary crossed ectopic pelvic kidney was made.

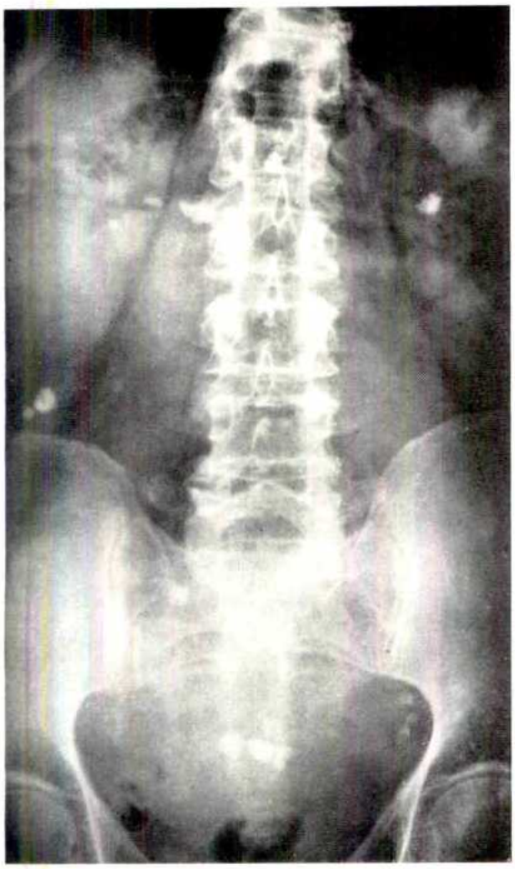

FIG. 1.—Plain radiograph of the abdomen, showing a collection of calculi in the pelvis and a further calculus medial to the right sacro-iliac joint.

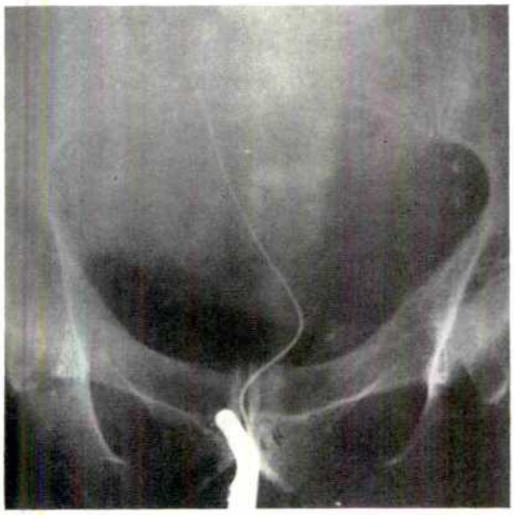

FIG. 3.—Catheter in the left ureter, crossing the pelvis to the right sacro-iliac joint.

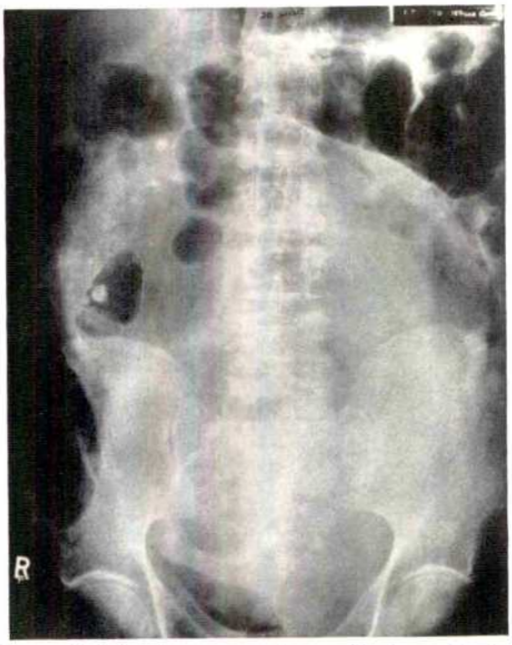

FIG. 2.—High-dose intravenous pyelogram, showing opacification of a large soft-tissue mass, displacing the large bowel.

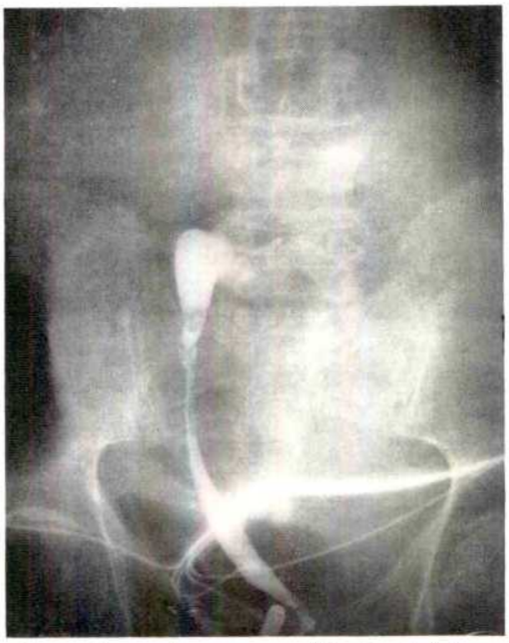

FIG. 4.—Retrograde ureterogram, delineating the left ureter and a filling defect in the pelvi-ureteric junction of the ectopic kidney.

A nephrostomy was performed using a retroperitoneal approach through a low right grid-iron incision, and 4500 ml. of obviously infected urine were drained. Culture yielded a heavy growth of *Escherichia coli*, which was sensitive to ampicillin and cloxacillin, both of which had been administered to the patient preoperatively.

The immediate postoperative course was complicated by a diuretic phase, which required frequent peritoneal dialysis and intravenous fluid replacement over a period of 3 weeks. Six weeks after operation the blood-urea had fallen to 110 mg. per 100 ml., and the creatinine clearance was 9·2 ml. per minute. The patient was discharged for convalescence.

Table I.—DETAILS OF PUBLISHED CASE REPORTS OF CROSSED ECTOPIA OF A SOLITARY KIDNEY

AUTHOR	AGE AND SEX	SIDE OF KIDNEY	NO. OF URETERIC ORIFICES	ABNORMALITIES
Horand (1905)	3½ mth. M.	Left	Two	Patent left ureteric orifice; atrophic left ureter communicating with left vas deferens; absent left seminal vesicle; atrophic right adrenal gland
Lyon-Caen and Marmier (1907)	— —	Left	One, right	—
Day (1924)	32 yr. M.	Left	One, right	Left ectopic testis
Foerster (1934)	— M.	Right	One, left	Undescended testis
Alexander, King, and Fromm (1950)	23 yr. F.	Right	One, left	Anomalies of sacrum, coccyx, and pelvis; hydronephrosis due to vascular band
Blancato (1954)	37 yr. M.	Right	One, left	None
Abeshouse and Bhisitkul (1959)	33 yr. F.	Right	Two	Patent right ureteric orifice; right ureter ending blindly at 4 cm.
Magri (1961)	38 yr. M.	Left	One, right	Absent verumontanum; absent right vas deferens; absent left ejaculatory duct
Purpon (1963)	13 yr. M.	Right	One, left	Pseudohermaphroditism; absent left adrenal gland; short right leg
Irvine and Yaman (1964)	25 yr. F.	Right	One, left	Absent vagina and uterus; atrophic Fallopian tubes; retrocaval ureter
Tabrisky and Bhisitkul (1965)	17 yr. F.	Right	One, left	Absent uterus; vaginal aplasia; anomalous vessels from iliac arteries
Weiss, Maloney, and Beland (1965)	8 mth. F.	Right	One, left	Imperforate anus; anomalies of dorsal spine
Wadskier (1967)	43 yr. M.	Right	One, left	Atrophic left testis and vas deferens; duplication of right thumb; abnormalities of cervical vertebrae
Dworin (1969)	52 yr. M.	Left	One, right	None
Nummi (1969)	41 yr. M.	Right	Two	Patent right ureteric orifice; right ureter ending blindly at iliac crest; left common iliac arterial blood-supply to kidney
Tanenbaum, Silverman, and Weinberg (1970)	7 yr. M.	Right	Two	Patent right ureteric orifice; atrophic right ureter
Present case	59 yr. M.	Right	One, left	Giant hydronephrosis; renal calculi; right common iliac arterial blood-supply to kidney

Two weeks later he was readmitted and laparotomy was performed. This revealed a grossly hydronephrotic solitary kidney lying across the sacrum and extending into the true pelvis and both iliac fossae. The main blood-supply was seen to be derived from the right common iliac artery, and it was clear that the pelvis and ureter lay posterior to the main hydronephrotic mass. Rather than mobilize the kidney and risk compromising the blood-supply, an incision was made in the cortex of the lower pole, and five calculi in the lower calix and a calculus impacted in the pelvi-ureteric junction were removed. The kidney was drained with a nephrostomy tube.

Ten days after operation a nephrostogram demonstrated the greatly distended caliceal system of the kidney, from which a single unobstructed ureter drained into the left side of the bladder. The patient re-established normal micturition following removal of the nephrostomy tube, and at the time of his discharge from hospital, 6 weeks after operation, the urine culture was sterile, the haemoglobin was 10·3 g. per 100 ml., the blood-urea 78 mg. per 100 ml., and the creatinine clearance 11 ml. per minute.

DISCUSSION

Ectopic kidneys have been described in positions from the thorax to the true pelvis. The ectopia may be ipsilateral or contralateral in position. In crossed renal ectopia the anomalous kidney is transposed to the contralateral side with its related ureter crossing the midline to enter the bladder on the correct side. The anomaly is well documented, Abeshouse (1947) in particular reporting a series of 341 cases, and it has been estimated as occurring about once in 2000 autopsies, although Campbell (1970) observed only 4 examples in 51,880 cases. Fusion with the normally situated kidney may or may not occur, non-fusion accounting for 10 per cent of all cases of crossed renal ectopia (Malament and Majnarich, 1960). The varieties of crossed renal ectopia have been classified by Amesur and Singh (1963), crossed fused ectopia with the ectopic kidney in the inferior position being the most common type. Varying degrees of malrotation may occur, with the pelvis tending to overlie the calices, which in turn may point medially.

Crossed ectopia of a solitary kidney is an extremely rare congenital abnormality. The published case reports have been reviewed by Purpon (1963), Dworin (1969), and Tanenbaum, Silverman, and Weinberg (1970). *Table I* represents a continuation of the series with the inclusion of a further example which was reported by Abeshouse and Bhisitkul (1959). The series, including the present report, totals 17 cases, of which 11 are male.

Diagnosis.—The role of radiology, cystoscopy, and ureteric catheterization has been emphasized by Magri (1961). Characteristically, the absence of the ureteric orifice and adjacent trigone on the side of the pyelographically demonstrable kidney is diagnostic of crossed ectopia of a solitary kidney. The position of the anomalous solitary kidney is variable. Although the majority are lumbar in position, Abeshouse and Bhisitkul (1959) and Tabrisky and Bhisitkul (1965) have described examples in which the ectopic kidney was within the confines of the pelvis. In the present case the kidney was probably sacral in position, although the hydronephrosis extended into the pelvis; a further unusual feature was the posterior situation of the pelvis.

Although the ipsilateral ureter is usually absent, it should be observed that there are 4 examples (*Table I*) in which there was a patent ureteric orifice on the same side as the ectopic kidney. In each case the ureter was atrophic and ended blindly, reaching the iliac crest in 1 instance (Nummi, 1969). Clearly, bilateral retrograde urography is indicated in these circumstances in order to clarify the diagnosis.

The recognition of congenital abnormalities of the genital tract may aid or substantiate the diagnosis. The association between anomalies of this system and the probable congenital absence of one kidney is well established, and is reflected in a high incidence of genital abnormalities in conjunction with solitary crossed renal ectopia. Genital defects were present in 6 males and 2 females (*Table I*). Similar findings have been described with the solitary pelvic kidney. Burwell and Kent (1959) reported that 76·9 per cent of females with a solitary pelvic kidney had genital abnormalities with a high incidence of vaginal atresia, while 22·9 per cent of males had associated defects.

Associated Pathology.—Although congenital absence of one kidney is compatible with a normal life-span, the solitary kidney appears to be more prone to disease. Fortune (1927), in an analysis of 422 autopsy cases with solitary kidneys, showed that 22·6 per cent had pathological change of the kidney against the general autopsy average of 15 per cent with renal disease. Campbell (1970) also observed a definitely higher incidence of disease. Furthermore, there is a higher incidence of pathology in the ectopic kidney than in the normally situated organ. In an analysis of 86 cases of solitary ectopic pelvic kidney, Burwell and Kent (1959) disclosed an incidence of 31·4 per cent with pathological change, of which hydronephrosis was a common complication. Abeshouse (1947) found associated renal pathology in 204 of 337 cases of crossed renal ectopia, while Abeshouse and Bhisitkul (1959), in a series of 55 cases of crossed renal ectopia, discovered an associated lesion in 30 (55 per cent). The occurrence of 3 examples of giant hydronephrosis arising in crossed renal ectopia without fusion (Malament and Majnarich, 1960; Pathak, 1965; Hurley, Clery, and Kelly, 1969) is of particular interest in relation to the present case. In each case the crossed ectopia involved the left kidney, which occupied the usual inferior position relative to the right kidney, and stenosis or stricture of the pelvi-ureteric junction was evident as the cause of the hydronephrosis. The present case clearly resembled in position and extent the line drawing of the giant hydronephrosis reported by Hurley and others (1969), except for the higher and posterior situation of the pelvi-ureteric junction in the present example. In addition, a nephrostogram demonstrated an unobstructed ureter, and the hydronephrosis must be attributed to long-standing defective drainage, presenting only when one of the calculi became impacted in the pelvi-ureteric junction.

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INHIBITION OF THE GROWTH OF TUMOUR CELLS IN CULTURE BY NOXYTIOLIN

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SUMMARY

The effect of noxytiolin on the viability of human tumour cells (HeLa) in monolayer culture was determined by vital staining, impairment of plating efficiency, and measurement of concentrations causing inhibition of growth. Concentrations of more than 0·0025 per cent cause significant inhibition of growth. This is much lower than its bacteriostatic concentration, suggesting that its bacteriostatic effect is non-specific.

NOXYTIOLIN (Noxyflex) is a simple compound of low toxicity on systemic administration which has been found to have a wide bacteriostatic effect *in vitro* and some antifungal and protozoal activity (Block, 1967; Horsfield, 1967; Ross, 1967). Its fate *in vivo* is not known nor is its method of action, but it is possible that it acts simply by release of formaldehyde. It has been claimed to be of value in reducing the mortality of faecal peritonitis when instilled into the peritoneum (Browne and Stoller, 1970), and its use as a local adjuvant in the treatment of patients with vesical carcinoma by supervoltage appears, from a controlled trial, to improve prognosis (Garrett, 1969). This study was undertaken to determine the effect of noxytiolin on the viability of human tumour cells in monolayer culture, as there are no existing data of this type to support the claim that noxytiolin has specificity of antibacterial activity.

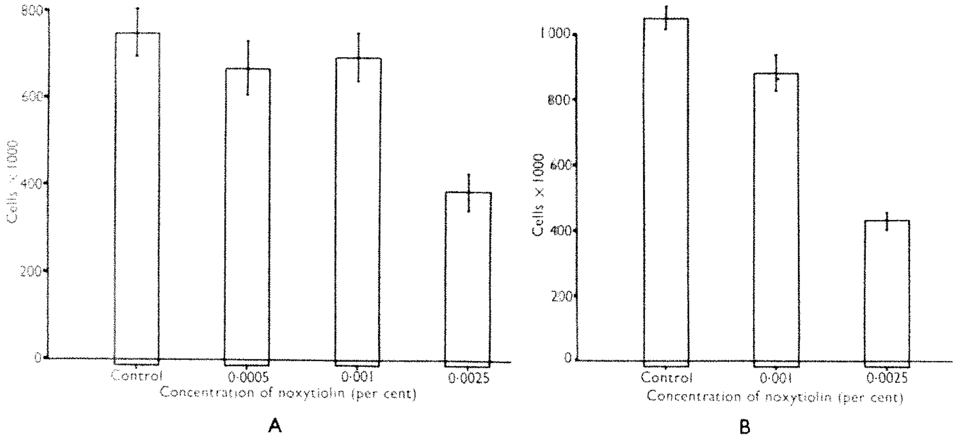

FIG. 1.—Number of cells recovered from groups of ten cultures seeded with 10×10^4 HeLa cells in the presence of varying concentrations of noxytiolin after 48 hours' incubation (mean ± S.E.). Addition of 0·0025 per cent noxytiolin produced significant inhibition of growth.

MATERIALS AND METHODS

The drug was obtained in its pure form and was stored at 5° C. Fresh solutions in Parker's medium 199 were made for each experiment and were sterilized by filtration. The cells used were HeLa (Flow Laboratories) adapted to growth in serial monolayer culture in medium 199 supplemented with 15 per cent foetal calf serum, L-glutamine, penicillin, and streptomycin. The cells were maintained at 37° C. in an atmosphere of air and 5 per cent CO$_2$. In these conditions they have a mean plating efficiency of 75 per cent.

In assessing viability by vital staining, freshly harvested cells were suspended in medium containing varying concentrations of noxytiolin for 4 hours at 37° C. The cells were centrifuged gently and resuspended in equal volumes of medium and 1 per cent trypan blue. After 20 minutes and 4 hours a differential count of the stained and unstained cells was made. In assessing impaired plating efficiency, cells were harvested and several groups of ten cultures were seeded, containing 10×10^4 cells in 4 ml. of medium. Each group contained a different concentration of noxytiolin and one group in each experiment contained no noxytiolin. Hourly observations of the flasks were made for evidence of sheeting of the cells in monolayer culture. In order to assess the growth of the cells, each group was initially fed with normal medium, but after 24 hours, when the cells had entered their exponential growth phase, they were re-fed with medium containing varying concentrations of noxytiolin. Forty-eight hours later the cells were harvested and the number present in each flask was determined using a Model B Coulter counter. Variations in the numbers recovered from each group of flasks reflect variations in growth rate. Control studies were made on the medium containing noxytiolin to ensure that the presence of the drug did not interfere with the counts obtained.

RESULTS

In three experiments exposure for 4 hours to 2 per cent noxytiolin produced significant reduction of viability when measured with trypan blue (viability 44 per cent; control 83 per cent). Exposure to 1 per cent noxytiolin for this period produced no significant decrease in viability.

In four separate experiments, each consisting of four groups of ten cultures, the addition of 0·075 per cent noxytiolin completely prevented sheeting of the cells in monolayer culture.

Seven experiments were performed to measure the growth of HeLa cells in the presence of noxytiolin. Each experiment consisted of five groups of ten cultures containing either no noxytiolin or increasing concentrations of the drug. The results of the two experiments involving critical dose levels are indicated in *Fig.* 1. It can be seen that culture in 0·001 per cent noxytiolin did not significantly affect the growth of HeLa cells, but 0·0025 per cent noxytiolin produced significant inhibition. Greater concentrations produced total inhibition of cell growth.

DISCUSSION

Vital staining is an inaccurate index of cytotoxicity, and the method of assessing cell growth in culture used in this investigation gives an accurate and reproducible index in well-established cell lines such as HeLa (Jamieson, Russin, Benes, DeWitt, and Wallace, 1969). The concentration of noxytiolin producing significant inhibition (0·0025 per cent) is much lower than the effective bacteriostatic concentration of the drug. This study does not, therefore, suggest that this compound has a specific antibacterial effect *in vitro*.

The action and fate of noxytiolin *in vivo* are still unknown but it has been used as a local instillate, in which situation its effects may well be similar to those exhibited *in vitro*. In one series it appeared to offer increased survival when used as a local instillate in cases of advanced bladder tumours, and it is remarkably free of toxic effects (Garrett, 1969, 1970). As it inhibits the growth of tumour cells at very low concentrations it might have a possible value as a local chemotherapeutic agent. It is suggested that this possibility deserves investigation.

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PERIANAL GAS-PRODUCING INFECTION OF NON-CLOSTRIDIAL ORIGIN

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SUMMARY

Five cases of perianal infection caused by non-clostridial gas-producing organisms are reported. Four were males in their sixth decade, 2 of whom were diabetics, and the fifth was a female in her third decade. Two cases died, and the severity of these infections is emphasized. The diagnosis and treatment of non-clostridial gas-producing infections are discussed.

Perianal infection associated with subcutaneous gas is an uncommon alarming condition which immediately raises the possibility of clostridial infection. The purpose of this paper is to draw attention to non-clostridial gas-producing infections so that an early diagnosis may be made, as the treatment often differs from that of clostridial infections which they may closely resemble. Radical surgery may not be warranted, penicillin may not be the antibiotic of choice, gas-gangrene antiserum is contra-indicated, and hyperbaric oxygen is of equivocal value.

CASE REPORTS

Case 1.—A 51-year-old white male was admitted to St. Thomas's Hospital in January, 1969, with a left ischiorectal abscess, symptoms of which had been developing over 10 days. He had had urinary retention for 1 day prior to admission. During the previous 23 years he had suffered frequent attacks of perianal suppuration. Diabetes, which had been diagnosed in 1959, was well controlled with chlorpropamide, and there were no neurological or vascular complications. His course since 1959 had been punctuated with abscesses of the axillae and buttocks, pus from which had grown penicillin-resistant *Staphylococcus aureus*. There was no other past or family history of relevance.

Under general anaesthesia the ischiorectal abscess was drained. A film of pus revealed pus cells, Gram-negative rods, and Gram-positive cocci. Cultures subsequently grew *Escherichia coli*, *Klebsiella aerogenes*, and proteus, all of which were sensitive to ampicillin (*Table I*).

On the third postoperative day the patient was confused, his temperature was 39·4° C., and the leucocyte count 54,000 (neutrophils 85 per cent). His left upper thigh was painful, hot, red, and swollen. Insulin was then given, although his diabetes had been stable and even in the later stage of his illness was fairly well controlled.

Following the commencement of ampicillin the patient's temperature fell, but his condition deteriorated and by the fifth postoperative day he was jaundiced. The left lower limb was now more painful, oedema and cellulitis had extended in the thigh and leg, and a bulla containing black fluid had developed over the medial malleolus. Subcutaneous emphysema was present in the buttock, thigh, and upper leg, and by the next day it had spread to involve most of the limb. Two bullae were now present on the medial aspect of the calf (*Figs.* 1, 2). Clostridial infection

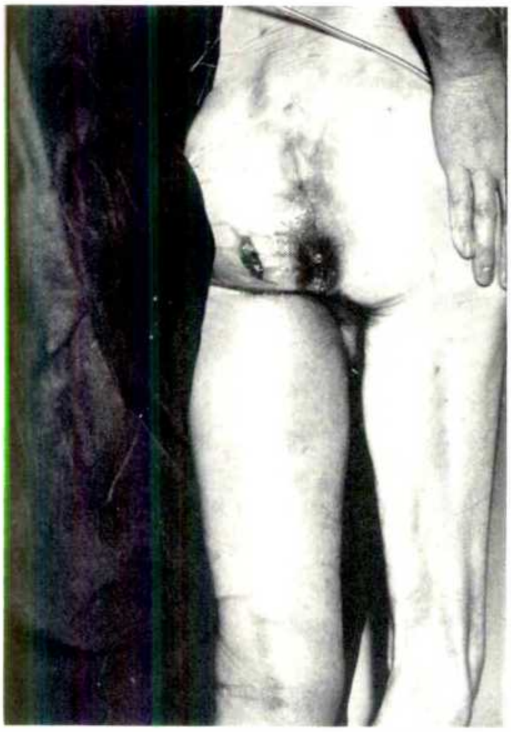

FIG. 1.—*Case* 1. The ischiorectal abscess wound and the swollen left thigh.

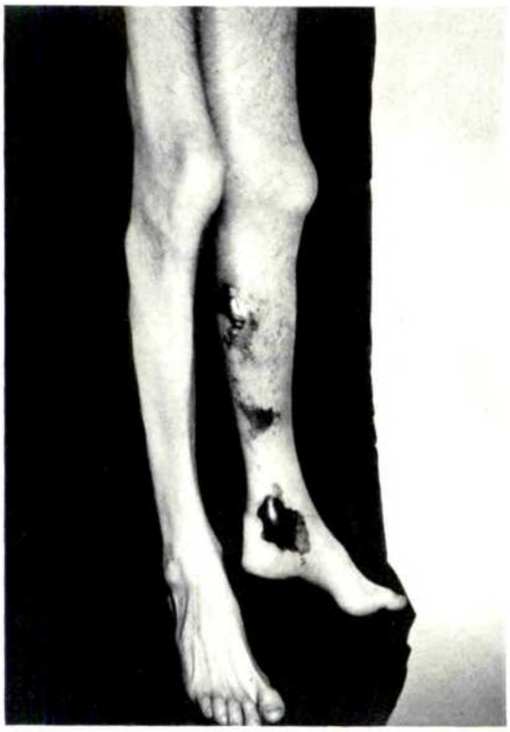

FIG. 2.—*Case* 1. The bullae which were filled with black fluid.

Table I.—THE BACTERIOLOGICAL DATA

CASE	SITE	FILM				CULTURE
		Pus Cells	Gram-negative Rods	Gram-positive Cocci	Gram-positive Rods	
1	Ischiorectal abscess—pus	+	+	+	−	*E. coli* *K. aerogenes* Proteus
	Left lower limb					
	Fluid from bulla	−	+	−	−	Proteus
	Oedematous fluid	−	−	−	−	Proteus
	Subcutaneous tissue	+	+	+	−	*K. aerogenes* Proteus
2	Pelvirectal abscess—pus	+	−	−	−	Coliform organisms Streptococcus
3	Perianal abscess—pus	+	+	+	−	*E. coli* Anaerobic streptococci
4	Penile vesicles—fluid	−	−	−	−	Coliform organisms Anaerobic streptococci
	Perineum—pus	+	+	+	−	Coliform organisms
	Loin abscesses and suprapubic wound—pus	−	+	+	−	Bacteroides
	Scrotum—fluid	+	+	+	−	Anaerobic streptococci
5	Right pelvirectal abscess—pus	+	−	−	−	*E. coli* *C. perfringens*
	Right pelvirectal and left ischiorectal abscess—pus	+	+	+	−	*E. coli* *Ps. pyocyaneus* Anaerobic streptococci
	Left groin—pus	+	+	−	−	*Ps. pyocyaneus*
	Loin abscesses—pus	+	+	−	−	*E. coli* *Ps. pyocyaneus*

was suspected, and under general anaesthesia, multiple long incisions were made in the thigh and leg, extending to the deep fascia and exposing grey muscles. Copious amounts of serosanguineous fluid were drained from the oedematous crepitant tissues, and this fluid together with fluid from the bullae and specimens of subcutaneous tissue were sent for bacteriological examination (*Table I*). No Gram-positive rods were seen in the smear, and it was therefore assumed that the infection was non-clostridial. Septicaemic shock was treated with blood, plasma, dextrose, and saline, and benzyl penicillin was added to the ampicillin.

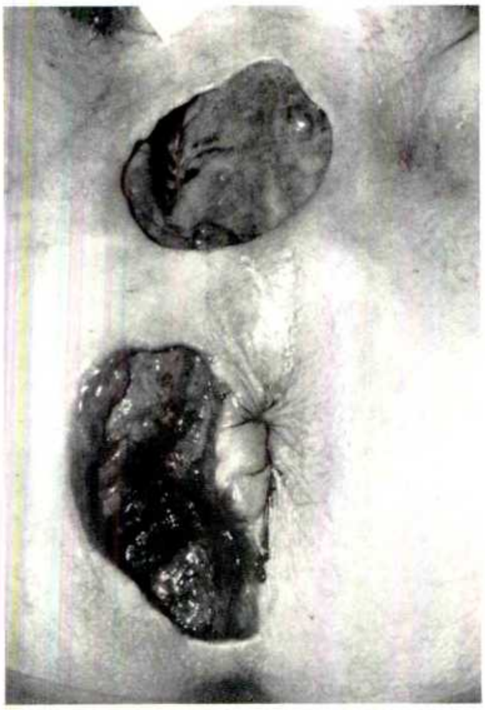

FIG. 3.—*Case* 2. A bridge of skin crosses the perineal wound which anteriorly is very undermined.

The patient lapsed into coma and required intubation. Lumbar puncture was normal. He then rapidly deteriorated: the hepatocellular jaundice deepened, oedema, cellulitis, and crepitus extended to the left flank, and the left lower limb became gangrenous. Four days after his second operation this limb was disarticulated through the hip-joint. There were extensive arterial and venous thromboses in the limb. Postoperatively, a large amount of serosanguineous fluid oozed from the stump, and the patient died the following day.

Post-mortem examination demonstrated a large left ischiorectal abscess, which was excavating behind the ischium but was without communication with the rectum. The amputation wound was infected and the gluteal muscles and surrounding tissues were necrosed.

Case 2.—A 57-year-old white male presented in January, 1968, with a right ischiorectal abscess, symptoms of which had been developing for 2 weeks. Diabetes which had been diagnosed 1 month previously was stable on 10 units of soluble insulin twice daily, and there were no neurological or vascular complications. There was no other personal or family history of relevance.

On examination, cellulitis extended from the right perianal region to the base of the scrotum. Subcutaneous emphysema was present in this area and extended to the right inguinal region. Under general anaesthesia the abscess was laid widely open, and it proved to be a pelvirectal abscess with a fistula into the right lateral wall of the rectum. No Gram-positive rods were seen in pus from the abscess, which subsequently grew coliform organisms and streptococci, both of which were sensitive to ampicillin (*Table I*).

Following transfer to St. Mark's Hospital, the patient's temperature was 40° C., leucocyte count 9100 (neutrophils 61 per cent), and haemoglobin 7·1 g. per cent. The subcutaneous emphysema had extended to the right upper thigh, right iliac fossa and flank, but was not accompanied by oedema or cellulitis in these sites. A large perineal wound extended upwards above the levator ani, posteriorly behind the rectum, and anteriorly under a skin bridge to the base of the scrotum, where the skin was much undermined (*Figs.* 3, 4). The condition of the patient improved with blood transfusion, intravenous fluids, and ampicillin. Six days later sigmoidoscopy under general anaesthesia disclosed the defect in the right lateral wall of the rectum to be about 2·5 cm. in diameter. A sigmoid-loop colostomy was fashioned. Three days after this procedure, chlorpropamide was substituted for insulin, as at no time during the period of admission was the diabetes out of control. The subcutaneous emphysema had by now disappeared. Three weeks later the rectal defect was repaired with catgut sutures, and the perineal wound was laid widely open as it was tending to pocket. The patient was discharged 7 weeks after admission with the wound clean and shallow except for the pararectal extension which was about 8 cm. deep.

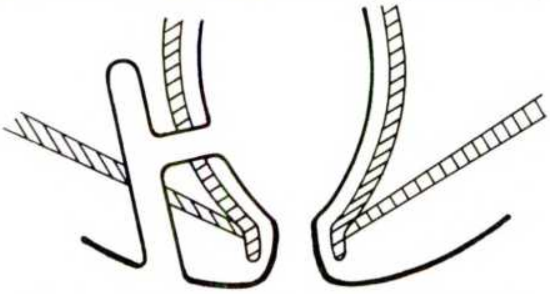

FIG. 4.—*Case* 2. Diagram showing the disposition of the pelvirectal abscess and the fistula into the right lateral wall of the rectum.

Ten months later, i.e., 1 year after presentation, the wound had healed. The colostomy was then closed, and his further course has been uneventful.

Case 3.—A 57-year-old white male presented in June, 1969, with a large anterior perianal abscess, symptoms of which had been present for 2 days. His previous medical history included two myocardial infarctions and a minor stroke. He was taking digoxin, frusemide, Dindevan, and Atromid S. There was no other relevant past or family history.

On examination, the patient's temperature was 38·8° C., and the anterior perineum, including the base of the scrotum, was inflamed. His haemoglobin was 13·5 g. per cent and the prothrombin time was 40 seconds. The abscess was explored under general anaesthesia with penicillin cover. Subcutaneous emphysema was palpated beneath the inflamed area. The abscess was laid widely open, and although the urethra appeared intact there was a large area of perineal necrosis, which was excised (*Fig.* 5). Pus from the abscess contained pus cells, Gram-negative rods, and Gram-positive cocci. It subsequently grew *E. coli* and an anaerobic streptococcus, both of which were sensitive to ampicillin (*Table I*). Because of the extensive tissue necrosis associated with the subcutaneous emphysema the clinical diagnosis was gas gangrene, despite the absence of Gram-positive rods. The patient was immediately transferred to Westminster Hospital where he received 2 hours of hyperbaric oxygen at a pressure of 2 atmospheres.

The abscess cavity bled excessively and the patient's haemoglobin fell to 9 g. per cent. Dindevan was temporarily reversed with Konakion. Blood, plasma, saline, and massive doses of penicillin and ampicillin were given to combat shock. Within a few hours he had recovered sufficiently to tolerate a further 2 hours of hyperbaric oxygen. The following day there was still subcutaneous emphysema of the cellulitic scrotum (*Fig.* 6), but this disappeared over the next 3 days. He rapidly improved, but his further course was complicated by a minor stroke which caused a transient left hemiparesis. At his own request he was discharged 2 weeks after admission and he returned to South Africa where he has been lost to follow-up.

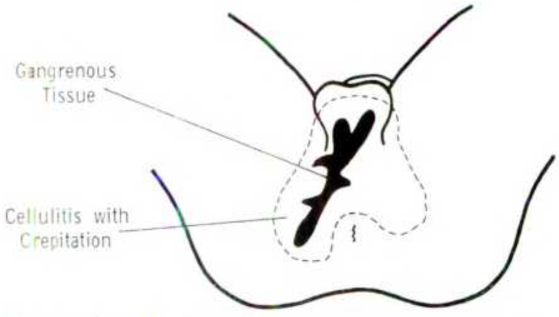

FIG. 5.—*Case* 3. Diagram of the areas of gangrene and cellulitis.

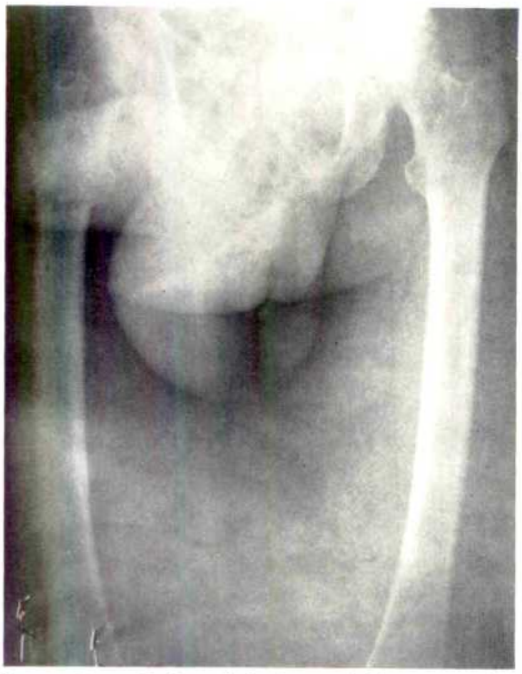

FIG. 7.—*Case* 4. Radiograph showing gas in the scrotum and in the grossly oedematous penis.

Case 4.—A 52-year-old white male was admitted to hospital in November, 1968, with a 1-week history of perianal pain which had become progressively more severe. Three weeks prior to admission he had had an acute anal fissure. There was no other personal or family history of relevance.

On examination, the patient's temperature was 38·8° C., and there were oedema and cellulitis of the perineum and perianal region. He was given intramuscular penicillin, but within 18 hours, oedema and cellulitis had extended to the scrotum. The penis was grossly swollen, with ecchymoses and vesicles, and crepitus was palpated in the shaft. No pus cells or Gram-positive rods were seen in the offensive, amber-coloured fluid which was aspirated from the penile vesicles, but coliform organisms and an anaerobic streptococcus were later grown (*Table I*). Ampicillin and kanamycin were given in addition to the penicillin. The presumptive diagnosis was gas gangrene and the patient was transferred to Whipps Cross Hospital.

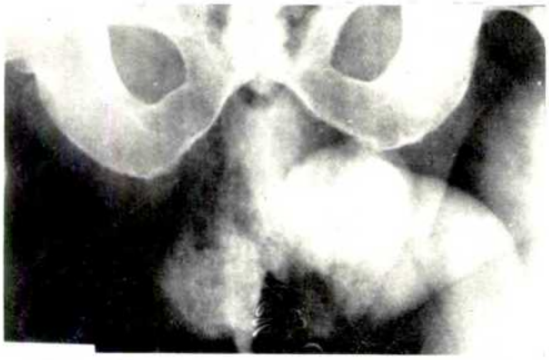

FIG. 6.—*Case* 3. Radiograph depicting gas in the scrotum.

On admission, his leucocyte count was 9000 (neutrophils 64 per cent) and the haemoglobin was 14·4 g. per cent. Oedema, cellulitis, and crepitus were present in the perineum, scrotum, and penis (*Fig.* 7). On the dorsum of the shaft of the penis there was a pregangrenous area of skin. The suprapubic region was tender, inflamed, and indurated, but crepitus was not elicited. The patient improved during the day of admission following the administration of cephaloridine and two treatments of hyperbaric oxygen. On the next day he received one treatment with hyperbaric oxygen, and following this, incisions were made under general anaesthesia in the gluteal regions, the perineum, and the penis to evacuate gas and watery pus, which subsequently grew coliform organisms, bacteroides, and an anaerobic streptococcus (*Table I*). Although there had been no difficulty in micturition, a suprapubic catheter was inserted as a precautionary measure. The patient received hyperbaric oxygen on the 4 subsequent days, during which time his general condition improved, although abscesses had now formed in both loins. On the fifth day after admission both loin abscesses were drained, the suprapubic wound was laid more widely open, and necrotic skin was removed from the dorsum of the shaft of the penis. Hyperbaric oxygen and antibiotics were stopped after 3 more days of treatment, but within 2 days the penis became infected and hyperbaric oxygen was given daily for the following 9 days. The suprapubic catheter was then removed. The glans button-holed through the skin defect in the dorsum of the penis, but this rapidly epithelized.

Nine weeks after presentation all wounds had healed and the patient was discharged home. His further course has been uneventful.

Case 5.—A 21-year-old white female was admitted to hospital in August, 1970, with a right ischiorectal abscess, symptoms of which had been present for 2 weeks and which had discharged spontaneously 1 week prior to admission. Apart from a doubtful allergy to penicillin there was no past or family history of relevance.

On examination, the patient's temperature was 38·8° C., the leucocyte count was 21,000 (neutrophils 89 per cent), and haemoglobin was 12·5 g. per cent. The perineum was inflamed, and the right ischiorectal abscess was discharging thick pus. No Gram-positive rods were seen in the pus, which later grew *E. coli* and *Clostridium perfringens* (*Table I*). The patient was given Septrin, but 3 days later abscesses appeared in the left ischiorectal fossa, the left groin, and the lower abdominal wall. Cellulitis and oedema, which had been limited to the gluteal regions and the perineum, had now spread to the lower abdomen, the left groin, and both upper thighs. Crepitus was present in these inflamed oedematous areas (*Fig.* 8). Clostridial infection was suspected and polyvalent gas-gangrene antiserum administered, but this provoked a widespread urticarial reaction.

Under general anaesthesia both ischiorectal fossae were laid widely open, and on the right side the abscess proved to be pelvirectal. No Gram-positive rods were seen in the thick pus from these abscesses, and *E. coli*, *Pseudomonas pyocyaneus*, and an anaerobic streptococcus were later grown (*Table I*). An incision in the left inguinal region allowed drainage of thick pus and gas from this region and also from the lower abdominal wall. No Gram-positive rods were seen in the pus from this area and the only organism which was cultured was *Ps. pyocyaneus* (*Table I*). Despite intensive treatment, including blood transfusion, cephaloridine, and tetracycline, the patient's condition deteriorated, and 2 days after the drainage procedures she was transferred to Whipps Cross Hospital.

On admission, the patient was critically ill with a temperature of 39·7° C. and a leucocyte count of 25,600 (neutrophils 84 per cent). Hyperbaric oxygen was given on the day of admission and on the 4 succeeding days. She continued to deteriorate, and on the fifth day, abscesses of both loins were drained under general anaesthesia. The abscess in the left loin extended inferiorly to the left iliac fossa, superiorly under the diaphragm, posteriorly to the vertebral bodies, and anteriorly to within 5 cm. of the midline, and sloughing in this area resulted in a large defect. No Gram-positive rods were seen in the pus from these abscesses and subsequent growth revealed *E. coli* and *Ps. pyocyaneus* (*Table I*). Hyperbaric oxygen was given over the next 3 days and she then gradually improved. One month after admission to Whipps Cross Hospital all wounds were clean and the left loin defect was skin-grafted. However, on the next day the patient's temperature rose to 40·5° C., and 5 days later she died suddenly. Postmortem examination demonstrated an empyema and extensive pulmonary suppuration.

DISCUSSION

The causes of tissue gas may be physical, chemical, or infective. Physical causes include skin penetration and perforation of an air-containing cavity. Chemicals which generate gas on contact with body tissues include hydrogen peroxide, benzine, and certain magnesium compounds. Organisms causing gas-producing infections may be classified as follows:—

1. Clostridial.
2. Non-clostridial.
    - *a.* Aerobic.
        - i. *E. coli* and *K. aerogenes.*
        - ii. Haemolytic streptococcus.
    - *b.* Anaerobic.
        - (i) Streptococcus.
        - (ii) Bacteroides.

1. Clostridial Infections.—Although usually associated with trauma, especially involving lacerated or crushed muscle, clostridial infections of the perianal region may follow anal fistula and perianal or ischiorectal abscesses (Berkow and Tolk, 1923; Campbell, 1929; Thomas, 1946; Sterling, Ong, Klaus, and Goldsmith, 1954; Boskovic, 1962; Ahmed, 1965; Colwill and Maudsley, 1968; Duff, McLean, and MacLean, 1970).

The diagnosis of clostridial infections is essentially clinical, although occasionally there may be difficulty in making an early diagnosis as the distinguishing features (*Table II*) may not be present in the earlier stages. MacLennan (1962) emphasizes that the most important features of clostridial myonecrosis are local pain and swelling, severe toxaemia, muscle necrosis, and jaundice with haemoglobinuria and haemoglobinaemia. If there is any doubt about whether a lesion is gas gangrene, then it is almost certainly not.

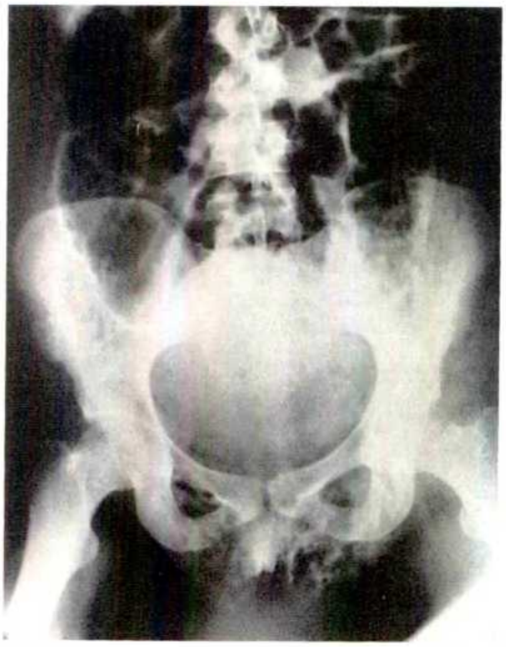

FIG. 8.—*Case* 5. Radiograph in which gas is seen in the perineum and in the lower abdominal wall.

Surgery in clostridial cellulitis is usually limited to the provision of adequate drainage, whereas in myonecrosis all infected tissue must be excised. Penicillin is the antibiotic usually given. It has been claimed that with hyperbaric oxygen treatment, early and radical operations, apart from relieving incisions, are rendered unnecessary (Colwill and Maudsley, 1968), and that gas-gangrene antiserum is of no additional value (Van Zyl, 1967).

2. Non-clostridial Infections.—Chiari (1893) was the first to describe a non-clostridial gas-forming infection. This was due to a colon bacillus and occurred in the gangrenous lower limb of a diabetic patient. Most of the recorded cases of non-clostridial gas-producing infections have occurred in diabetics who had neurological or vascular complications of their diabetes, which was usually out of control (Spring and Kahn, 1951; Wills and Reece, 1960). The 2 diabetics reported in the present series were both well controlled prior to their infection, and even during their illness the diabetes was easily managed. Neither had neurological nor vascular complications of the diabetes, and the extensive thrombosis in *Case* 1 followed the infection. Nearly all the reported cases have originated in the lower limbs, and only 2 cases have followed perianal infection. Terrel (1940) recorded a case of non-clostridial crepitant cellulitis which originated from an anal fistula, and Altemeier and Culbertson (1948) noted a similar infection which originated from a perirectal abscess.

Non-clostridial gas-forming infections are not uncommon in war-time (MacLennan, 1962) and, as in peace-time, the most frequent organisms isolated have been the coliforms.

Table II.—CLINICAL FEATURES OF THE COMMON AEROGENIC INFECTIONS*

CRITERION	CLOSTRIDIAL CELLULITIS	CLOSTRIDIAL MYONECROSIS	STREPTOCOCCAL MYOSITIS	COLIFORM INFECTION
Onset	Gradual	Acute	Insidious	Gradual
Pain	Absent	Severe; first symptom	Usually severe	Variable; often first symptom
Swelling	Slight	Marked	Marked	Marked
Skin reaction	Little change	Marked; tense, bronzed, or erythematous	Marked; often coppery tinge	Marked; erythema
Muscles	No change	Marked change	Oedema initially	Variable
Gas	Abundant	Rarely pronounced except terminally	Slight	Abundant
Exudate	Serous	Serous	Seropurulent	Purulent
Smell	Foul	Sweet	Sour	Foul

* Modified from MacLennan (1962).

a. Aerobic Infections.—

i. E. coli *and* K. aerogenes: The frequency of infection with these organisms has increased since the introduction of antibiotics (Altemeier, 1966). Diabetics with ischaemic or gangrenous extremities are particularly prone to gas-producing infection with these organisms (Chiari, 1893; Hitschmann and Lindenthal, 1899; Warren, 1938; Gillies, 1941; Spring and Kahn, 1951; Wills and Reece, 1960). Reasons for this include: excessive amounts of tissue carbohydrate which may enhance gas production by *E. coli*; decreased body resistance to infection because of neurological and vascular lesions; and ischaemia may also be a contributory factor in that any gas produced may not be absorbed. Infections with these organisms usually involve subcutaneous or epifascial tissue, but may involve muscle and thus simulate clostridial myonecrosis. The first symptom is usually pain which is less severe than in clostridial myonecrosis and precedes swelling or erythema by 1–3 days (Altemeier and Culbertson, 1948). The absence of pain in the 4 cases of aerobic cellulitis reported by Wills and Reece (1960), all of which were fatal, was ascribed to neurological complications of diabetes. Within 24 hours the temperature is raised to about 38·3–40° C. The pulse and respiratory rates are also raised, although less than with clostridial infection. Necrosis and crepitation occur within 2–5 days of onset, gas being maximal in the fascial layers. With increased swelling there is increased pain and tenderness. The tempo is slower than with clostridial lesions and toxicity is therefore of later onset. Dysuria and urinary retention are common with perineal infections (Altemeier and Culbertson, 1948).

Microscopical examination of the exudate reveals pus cells and a number of different organisms. Muscle biopsy exhibits an oedematous, contractile muscle of normal colour.

The condition is usually not correctly diagnosed till a late stage is reached, and the uncertainty as to the best method of treatment and, in particular, the choice of antibiotic is complicated by the uncertainty of the causative organism, as the infection is usually polymicrobic.

Both *E. coli* and *K. aerogenes* are normal inhabitants of the gastro-intestinal tract, the various members of which exhibit marked synergistic activity (Altemeier, 1941, 1942). *K. aerogenes* is, however, the more resistant organism. The gas produced by both these organisms consists of carbon dioxide and hydrogen, which *E. coli* produces in equal volumes, whereas with *K. aerogenes* the ratio is 2 : 1 (Harden, 1901, 1905; Harden and Walpole, 1906).

ii. *Haemolytic streptococcus*: This organism may produce an epifascial, spreading gangrene in which thrombosis of the skin vessels is prominent. It occurs particularly in the extremities, the perineum, and the face. Pain and swelling are prominent at the wound site, and later cellulitis and bullae appear. The temperature and the pulse are elevated, and in the later stages the patient is toxic. Only rarely is crepitation present.

b. Anaerobic Infections—

i. *Streptococcus*: Although sporadically reported (Bingold, 1914; Marwedel and Wehrsig, 1915; Bérard, Lumière, and Donet, 1918; Bell and Gaebe, 1926; Meleney, 1936) the rare condition of streptococcal myonecrosis was first studied by MacLennan (1943a, b). Superficially, it may resemble clostridial myonecrosis. Pain, however, is of late onset, although it then rapidly becomes severe and may produce a toxic type of reaction. According to MacLennan (1962) there is usually no systemic reaction, but Slack, Hanson, and Chew (1969) observed that their patients were flushed, sweating, had temperatures of 38·8° C. or more, and were critically ill within 24 hours of onset. Cutaneous erythema is more pronounced than with clostridial myonecrosis, and gas, which is invariably present although rarely pronounced, is not as extensive as in clostridial myonecrosis. Oedema, which is moist rather than gelatinous, progresses diffusely and is not very haemorrhagic unless haemolytic streptococci are involved. Large quantities of seropurulent fluid with a peculiar sour odour are discharged from the wound. The muscles which at first are pale and soft are later more haemorrhagic than in clostridial myonecrosis. They then become bright red and later dark purple, and eventually become gangrenous. Microscopical examination of the exudate and the muscle smear is important and is of great help in differentiating the condition from clostridial myonecrosis. Mixed infections are rare and the characteristic picture is of pus cells and long chains of streptococci, which are smaller than aerobic streptococci.

Although still not fully classified (Topley and Wilson, 1964) the anaerobic streptococci have been subdivided on their growth characteristics into nine groups (Thomas and Hare, 1954). They are obligate anaerobes and are encountered in the normal female genital tract, mucosae, and skin, and they have been isolated from brain abscesses, wounds, and muscle. In fluid culture, abundant gas is produced, provided that sulphur is present. The commonest potential pathogen, *Streptococcus putridus*, is the only well-documented member and has been recognized for over 60 years (Schottmüller, 1910).

ii. *Bacteroides*: These have only very rarely been incriminated in crepitant infections involving subcutaneous and retroperitoneal tissues and muscle (Altemeier, 1966), and they are always part of a mixed flora. The spread is local and slow. Thrombosis of the skin vessels is prominent, the tissues appearing brown or black (Altemeier and Culbertson, 1948) and foul-smelling pus being produced. They are normal inhabitants of the respiratory, gastro-intestinal, and genital tracts. Being strict anaerobes, usually Gram-negative, very pleomorphic, and non-spore-bearing, they are difficult to culture and are avirulent for animals, as are the anaerobic streptococci (Altemeier, 1940).

THE DIAGNOSIS OF NON-CLOSTRIDIAL GAS-PRODUCING INFECTIONS

Clinically, the presence of gas in infected tissues may be denoted by swelling, bubbling from a wound, and most commonly by crepitation, although this sign will not be elicited in a subfascial structure unless the fascia has disintegrated. With auscultation, Hunnicutt (1965) diagnosed crepitus earlier than by palpation, and he also detected the presence of gas 2–5 cm. beyond the extent which was delineated radiologically.

When confronted with a gas-producing infection it is important to distinguish between clostridial and non-clostridial infection, because the treatment of these conditions differs. Differentiation is primarily on clinical grounds (*Table II*), but help may be gained from bacteriological and radiological examinations.

Clostridial infections are characterized by extensive tissue necrosis without significant suppuration, and microscopical examination of any discharge reveals Gram-positive, square-ended rods, numerous red blood-cells, and usually no pus cells, although if these are present they are very few and degenerate. The necrosis resulting from non-clostridial infections is usually less extensive, and the discharge, which is purulent, does not contain Gram-positive, square-ended rods, but there are numerous pus cells. Aerobic and anaerobic cultures should be set up. Both clostridial and non-clostridial discharges usually contain a variety of organisms, and members of one group may be present as contaminants in infection caused by an organism or organisms of the other group and thereby perhaps cause confusion as to the true nature of the infection. The stormy clot test (Altemeier, 1944) which was designed to be specific for *Clostridium perfringens* (*welchii*) is also positive for *Clostridium septicum* and *E. coli* and is therefore of no help in differentiating between clostridial and non-clostridial infections. Because the isolation of a particular organism does not prove that it is the culprit the diagnosis must be based on the clinical picture.

Radiologically, tissue gas presents as translucent bubbles, pockets, or linear streaks and is best demonstrated by lateral views with the suspected area uppermost. In cases of clostridial myonecrosis, gas is seen within muscle bundles as multilinear streaks, whereas in clostridial cellulitis and non-clostridial infections the gas is never intramuscular. Multilinear streaks similar to those seen in clostridial myonecrosis may be seen in the elderly as a result of increased fat deposition and also following buttock injury in obese people (Kemp, 1945).

In the 5 cases of non-clostridial gas-producing infection reported here the initial lesions were a perianal abscess (*Case* 3), anal fissure (*Case* 4), ischiorectal abscess (*Case* 1), and pelvirectal abscesses (*Cases* 2 and 5), symptoms of which had been present for between 2 days and 2 weeks. There was a 23-year history of perianal infection in *Case* 1. Two cases were well-controlled diabetics (*Cases* 1 and 2) without neurological or vascular complications, and during their illness they presented little problem as regards the management of the diabetes. All the patients were very ill, with temperatures of 38·8° C. or more and with leucocyte counts varying from 9000 to 54,000. The infections were purulent and were accompanied by varying amounts of tissue necrosis. Subcutaneous gas was clinically prominent, and radiologically there was no evidence of intramuscular gas. Gram-positive rods were not seen in any of the smears. In *Case* 5, *C. perfringens* (*welchii*) was cultured from the thick pus from a pelvirectal abscess, but on retrospect this must have been a contaminant. No clostridia were cultured from the other cases. In order of frequency the non-clostridial gas-producing organisms cultured were coliforms, anaerobic streptococci, bacteroides, and a haemolytic streptococcus. These organisms were sensitive to ampicillin, except the bacteroides, which was sensitive to tetracycline.

THE TREATMENT OF NON-CLOSTRIDIAL GAS-PRODUCING INFECTIONS

Treatment may be considered under the headings of surgery, antibiotics, antiserum, and hyperbaric oxygen. The administration of intravenous fluids, blood transfusion, renal dialysis, and other measures will depend on individual circumstances.

Surgery.—In the absence of peripheral arterial disease, surgery can usually be limited to decompression, evacuation of pus, and excision of necrotic material. If infection occurs in an ischaemic limb this may well require amputation, as in *Case* 1. In cases of clostridial myonecrosis involving the perineum there is often a reluctance to remove all of the infected tissue because of the subsequent functional disabilities, and this most probably accounts for the high mortality-rate of these cases (MacLennan, 1962). In non-clostridial infections the approach may be more conservative.

Antibiotics.—The most commonly used antibiotic in these infections has been penicillin. In the present series all non-clostridial organisms, except the tetracycline-sensitive bacteroides, were sensitive to ampicillin. This drug was used alone (*Case* 2), with penicillin (*Cases* 1 and 3), and with penicillin and kanamycin (*Case* 4). The fifth case was treated with Septrin, cephaloridine, and tetracycline. Slack and others (1969) found no response to intramuscular penicillin or ampicillin and recommended cephaloridine. Guidance will, however, be obtained from sensitivity tests.

Gas-gangrene Antiserum.—There is no indication for its use in non-clostridial infections, and even in cases of doubtful clostridial infection its administration is to be condemned, as hypersensitivity reactions are common (Rifkind, 1963). Polyvalent gas-gangrene antiserum provoked a widespread urticarial reaction in *Case* 5.

Hyperbaric Oxygen.—Hyperbaric oxygen at 2 atmospheres is toxic for aerobes and anaerobes *in vitro* and *in vivo*, and bacteria differ in their susceptibility (McAllister, Stark, Norman, and Ross, 1964; Ross and McAllister, 1964). Although of value in clostridial lesions, Slack and others (1969) observed that it was less effective in non-clostridial infections. They noted that if there was no clinical improvement after 3 hours of treatment a crepitant infection was unlikely to be clostridial. Until there are further reports of the use of hyperbaric oxygen in the treatment of non-clostridial infections its value must remain in doubt.

Non-clostridial gas-producing infections, although uncommon, must be differentiated from clostridial infections, and early and adequate treatment instituted. Despite intensive treatment, 2 of the 5 cases reported here died from overwhelming infection (*Cases* 1 and 5), and the experience with these 5 cases suggests that these infections warrant a reputation as sinister as that of clostridial infections.

Acknowledgements.—I am grateful to Mr. H. E. Lockhart-Mummery and Professor H. Ellis for their comments. My thanks for permission to publish cases who were admitted under their care are due to Mr. H. E. Lockhart-Mummery (*Cases* 1 and 2), Mr. F. A. d'Abreu (*Case* 3), and Dr. W. K. Slack (*Cases* 4 and 5). The illustrations were prepared by the Departments of Medical Photography at St. Thomas's Hospital (*Figs.* 1, 2), St. Mark's Hospital (*Fig.* 3), and Westminster Hospital (*Figs.* 4, 5, 6, 7, 8).

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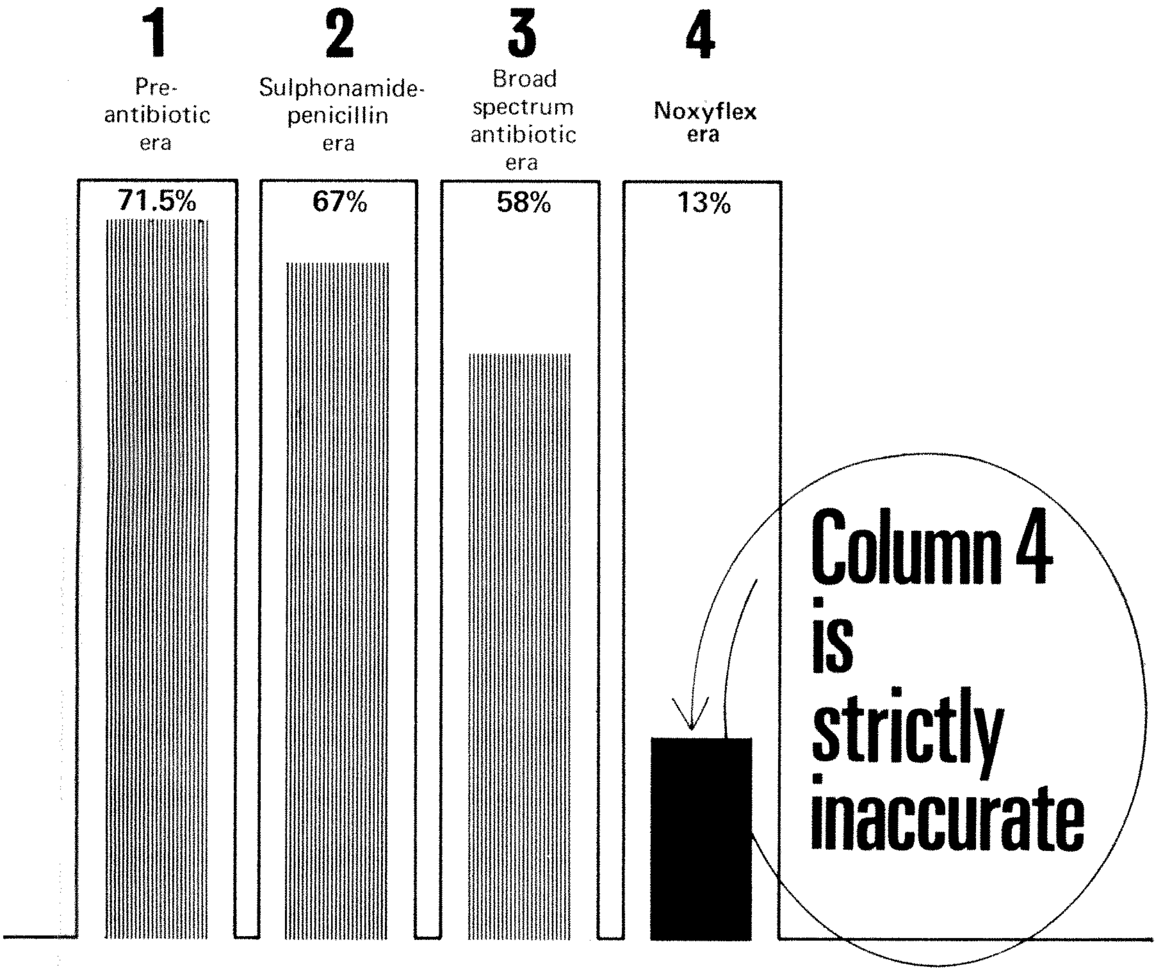
The graph below compares mortality rates due to faecal peritonitis, era by era.
It is not pedantically accurate because its sources differ. But the point is fairly made.



Column 4 is strictly inaccurate

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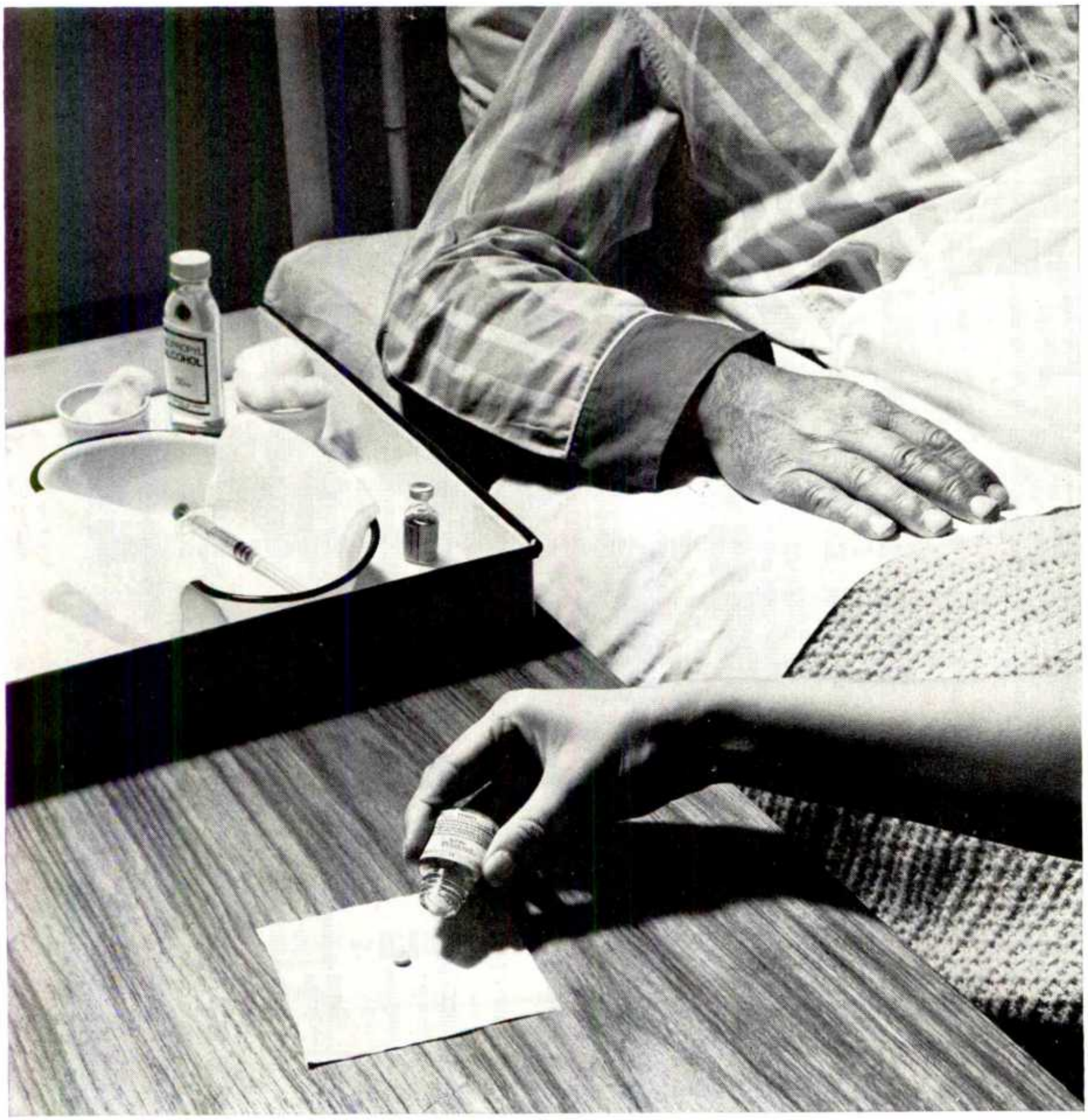

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PRIMARY SKIN-GRAFTING IN THE TREATMENT OF CHRONIC OSTEOMYELITIS

BY A. NAYLOR AND D. J. CROCKETT

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SUMMARY

Attention is called to the value of primary split-thickness skin-grafting, as opposed to secondary grafting, used in conjunction with radical excision of avascular, sclerotic bone in the treatment of chronic osteomyelitis.

Nine cases treated by this method are described. These have remained healed following this procedure after periods of recurrent infection and disability varying from 28 to 2 years, 6 patients having recurrent osteomyelitis for over 10 years before operation. Five cases have remained healed for periods varying from 3 to 5 years following operation, the more recent remaining cases being asymptomatic for 1½–3 years subsequently.

THERE is general agreement that the radical treatment of chronic osteomyelitis requires excision of all avascular bone and fibrous tissues, but there are varying views concerning the method of subsequent closure. Whilst closure may be obtained in many cases by direct suture, such a method involves the risk of leaving undrained pockets and cavities with subsequent sinus formation and recurrent infection. This is particularly prone to occur in the tibia, where obliteration of the cavity by a pedicled muscle-graft may not be possible. Whilst split-skin closure of the cavity has been advocated it is infrequently practised, and adherents of this method (Lord, 1902; Kelly, Rosarty, and Murray, 1945; Knight and Wood, 1945; Evans and Davies, 1969) describe a two-stage procedure of bone excision with secondary skin-grafting 4–7 days later, after the formation of a layer of granulations over the bony walls of the cavity. It is the aim of this paper, by a study of 9 cases who were treated by a one-stage, immediate, primary skin-grafting procedure, to show that the two-stage, delayed, secondary grafting procedure is unnecessary, subjecting the patient to an additional procedure and being liable to hide an inadequate excision of avascular bone. The primary grafting, one-stage procedure is considered to be preferable.

MATERIAL

Over a period of 6 years 9 cases of chronic osteomyelitis have been treated by a one-stage procedure of excision of all avascular infected bone and immediate closure with split skin-grafts.

TECHNIQUE

Radiological examination of the affected part, using different penetrations, projections, and tomography, will help to delineate the probable extent of the excision of bone required, but it is no substitute for direct vision at the time of operation.

Bacteriological examination of any discharge is made and appropriate chemotherapy is instituted some days prior to operation. If no sinus is present, reference to the bacteriological state at previous examinations when a sinus was discharging will assist a decision regarding appropriate chemotherapy, but where such information is not available, ampicillin or tetracycline is administered.

At operation a tourniquet is used in the immediate gross excision of scar tissue and sclerotic bone. It is then removed to allow further excision of any dense or evident avascular bone to be completed. The walls and floor of the cavity should then consist of healthy bleeding bone, and their contours are shaped to form a shelving cavity with no residual irregularities or pockets. Bleeding is arrested with packs and by elevation of the limb throughout the operation. A generous area of free-hand skin-graft of intermediate thickness is prepared. A completely successful take of a graft depends on achieving intimate contact with every contour of the cavity; tenting across the depths will lead to failure in that area. Therefore, separate sheets of graft are sutured to the two margins of the defect and draped into the cavity so that one overlays the other. The cavity is packed very firmly with acriflavine emulsion wool, the two sheets of graft sliding over each other so as to adapt to every detail of the walls and floor. The procedure is completed with a pressure dressing and the patient is nursed with the leg elevated. The wound is examined 7 days later when the sutures are removed and the overlapping skin-graft is cut away. Any small areas which have not taken indicate underlying dead bone which must be further excised and skin-grafted. As a corollary to this, successful take of grafts is certain proof that the underlying bone is living.

A Blue-line bandage is worn when the patient is allowed up and is retained for 3 months. The skin-graft increases in thickness from about 0·5 mm. at the time of application to nearly 3 mm. and it attains considerable stability.

CASE REPORTS

Case 1.—S. C., aged 50 years. In 1954 this patient had fallen down a ship's hold, sustaining a compound fracture of the right femur. A Steinmann's pin had been used to treat the fracture and the pin track had subsequently become infected. Since that time the patient had had recurrent episodes of discharge and pain at the site of insertion of the Steinmann pin.

The patient was admitted to hospital on 6 Aug., 1965, with a discharging ulcer on the medial aspect of the upper end of the tibia. A radiograph of this area showed a chronic bone abscess with ring sequestra (*Fig.* 1). Bacteriological examination showed the infecting organisms to be staphylococcus, which was sensitive to cloxacillin and Ceporin, and resistant to penicillin, tetracycline, and erythromycin, and proteus, which was sensitive to cloxacillin, Kanomycin, and Ceporin.

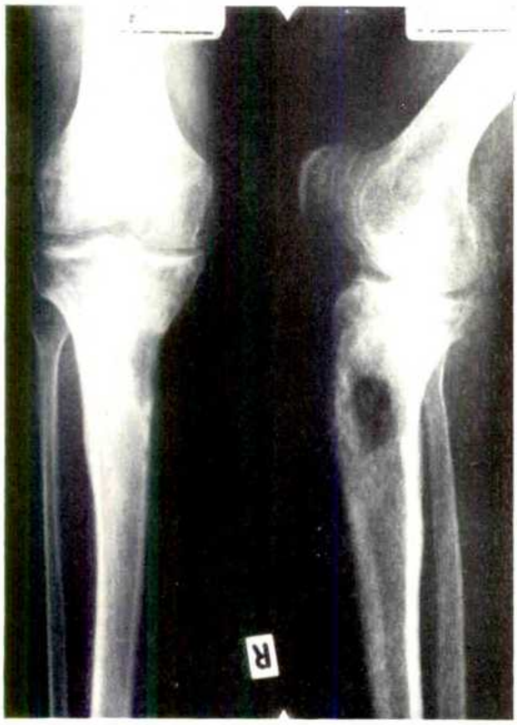

FIG. 1.—*Case* 1. Radiographs showing chronic bone abscess.

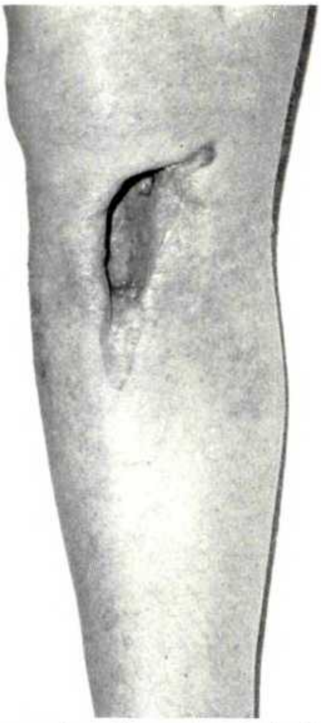

FIG. 2.—*Case* 1. Bone cavity surfaced with split grafts.

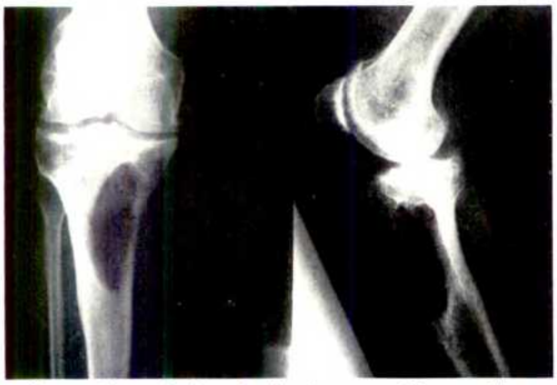

FIG. 3.—*Case* 1. Radiographs showing extent of bone excision.

On 16 Aug. the sinus was excised together with sequestra and sclerotic bone. The wound was revised. Old scar-tissue granulations were excised and a split graft was placed on to exposed cancellous bone, resulting in an 85 per cent take.

There was still some discharge persisting on 16 Sept., and therefore resaucerization of the cavity with further split grafts was carried out.

On 21 Oct. some areas of dead bone were removed by curetting with a Volkmann's spoon and the cavity was regrafted to give 100 per cent cover.

On 12 March, 1966, radiographs showed osteo-arthritic changes in the knee. No sequestra were present. The patient was able to start light work, and on 6 May he returned to work as a heavy labourer, the graft having healed satisfactorily.

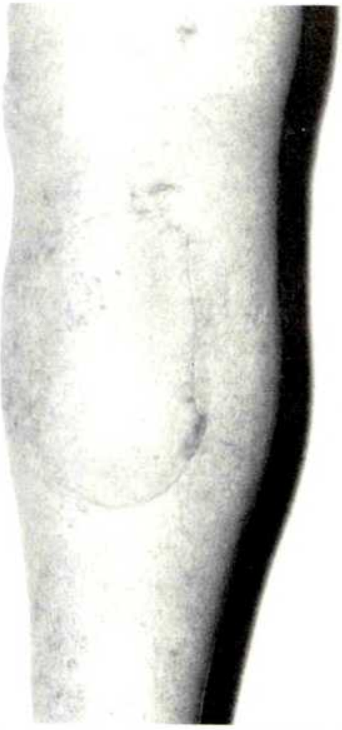

FIG. 4.—*Case* 1. Split grafts replaced with full-thickness, tube-pedicle graft.

On 14 Nov. one area in the upper part of the cavity, 1 cm. in diameter, reopened. A small area of dead bone was present (*Fig.* 2). On 6 Dec. curettage was performed and a split graft, 1 cm. in diameter, was applied. A tube pedicle was later raised from the abdomen, was transferred via the left wrist, and was inserted with fat to fill the cavity after the lining had been excised. The graft had healed by 13 Dec., and to date (August, 1971) remains satisfactory (*Figs.* 3, 4).

COMMENT.—This case demonstrates the value of the split-graft technique in revealing remaining areas

Table I.—SUMMARY OF CASE RECORDS

CASE NO.	AGE (years) AND SEX	HISTORY	DURATION OF INFECTION (years)	INFECTING ORGANISMS AND SENSITIVITY*	ANTIBIOTICS USED	RADIOGRAPHIC APPEARANCES	PERCENTAGE INITIAL TAKE OF GRAFT	RESULT
1. S. C.	50 M.	Open fracture of right femur in 1954. Treated by traction with Steinman's pin in upper third of tibia. Recurrent discharge and pain from pin-track	11	*Staph. aureus* R. Penicillin Tetracycline S. Cloxacillin Proteus S. Cloxacillin	Cloxacillin	Chronic bone abscess with ring sequestrum	85	Remains healed 5 years after operative treatment. No symptoms
2. E. C.	61 M.	Brodie's abscess in upper third of tibia excised in 1954. Closure by suture. Recurrent flares of infection	11	*Staph. aureus* R. Penicillin Ampicillin S. Tetracycline Erythromycin Cloxacillin	Cloxacillin	Sclerotic osteitis of upper third of tibia	80	Remains healed 4 years after treatment. No symptoms
3. T. A.	56 M.	Gunshot wound with open fracture of tibia in 1944. Recurrent infection. Excision and bone-chip grafting in 1957 failed to heal	23	*Staph. aureus* R. Penicillin S. Ampicillin Proteus S. Ampicillin Penicillin	Ampicillin	Sclerotic osteitis of upper third of tibia	90	Remains healed 3 years after treatment. Deep-vein thrombosis followed cross-leg reconstruction
4. T. D.	20 M.	Tibia kicked by horse in 1962. Recurrent osteomyelitis with discharging sinuses	6	*Staph. aureus* S. Penicillin Ampicillin Streptococcus R. Cloxacillin Penicillin S. Ampicillin	Ampicillin	Sclerotic osteitis of upper third of tibia	100	Remains healed and free of symptoms 3 years after treatment
5. S.M.	43 M.	Osteomyelitis in lower third of tibia at age of 15. Pain and pyrexia for 1 month	28	*Staph. aureus* S. Cloxacillin R. Penicillin	Cloxacillin	Ankylosis of ankle. Osteitis with abscess cavity of lower third of tibia	95	Remains healed and free of symptoms 2 years after treatment
6. G. P.	34 M.	Open comminuted fracture of upper tibia in 1960. Recurrent infection and sinus formation	9	*B. pyocyaneus* S. Colomycin	Colomycin	Sclerotic osteitis of upper tibia	95	Small sequestrum extruded 1 year after treatment. Remained healed since
7. V. B.	17 F.	Recurrent osteomyelitis of tibia since age of 6	11	*Staph. aureus* S. Penicillin	Penicillin	Sclerotic osteitis of midshaft of tibia	100	Remains healed
8. J. G.	27 M.	Open fracture of left tibia after parachute jump in Spanish Army in 1968. Treated by intramedullary nail. Infected. Recurrent sinus formation	2	No growth on culture	Cloxacillin	Sclerotic osteitis with sequestra in middle third of tibia	50; 50 per cent lost because of haematoma; 100 per cent take on regrafting	Remains healed
9. S. C.	12 M.	Sickle-cell anaemia. Recurrent sinus from bilateral tibial osteomyelitis for 4 years. Stiff left hip and knee	4	Haemolytic streptococcus S. Cloxacillin Ceporin R. Penicillin Ampicillin *Staph. aureus* R. Ampicillin S. Cloxacillin	Cloxacillin	Diaphysis of each tibia with extensive chronic osteitis	Right leg: all grafts lost due to infection; regraft 1 week later; 95 per cent take. Left leg: 100 per cent take	Remains healed 4½ years after treatment

* R = Resistant, S = Sensitive

of dead bone. With other methods of closure these would have led to more extensive chronic infection.

Case 2.—E. C., aged 61 years. In 1954 this patient had had a Brodie's abscess with sequestrum in the upper one-third of the tibia. The cavity had been drained, curetted, and filled with bone chips. The wound had healed approximately 2 months later. Subsequently the patient had had recurrent flares of infection, the infecting organism being *Staphylococcus aureus*, which was sensitive to tetracycline, erythromycin, and cloxacillin, but resistant to penicillin and ampicillin.

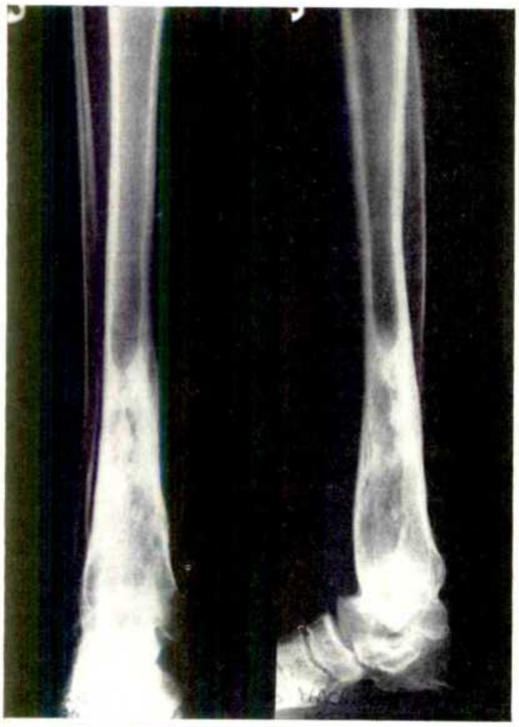

FIG. 5.—*Case* 5. Radiographs of tibia, showing ankylosed ankle, abscess cavities, and sclerotic bone.

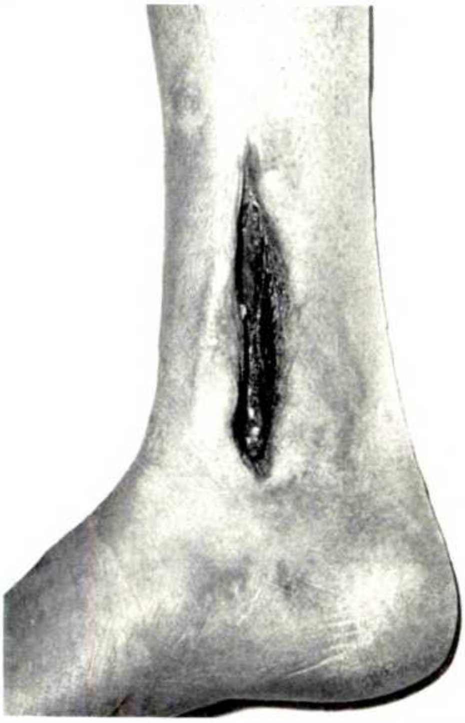

FIG. 6.—*Case* 5. Stable, healed, primary, split-skin grafts line the cavity remaining after excision.

At the present admission in February, 1967, skin, scar tissue, and sclerotic bone were excised and split grafts were applied. On 3 March, 1967, an 80 per cent take of the graft was noted, and excision of a small fragment of necrotic bone was carried out. Following this procedure the grafts took satisfactorily (23 March). On 13 April a further small fragment was removed and a small graft was applied.

The graft remains dry and soundly healed in August, 1971.

Case 3.—T. A., aged 56 years. This patient had sustained a gunshot wound in his left leg with a compound fracture of the midshaft of the left tibia in 1944. The scar tissue had been excised and the wound had been closed by secondary suture in July, 1948. On 14 Aug., 1957, he had been to hospital with a Brodie abscess. The abscess with the sclerotic bone had been excised, and the cavity had been packed with iliac chips. The wound had been closed, and had healed satisfactorily, although recurrent infection in July, 1959, had required drainage of a localized abscess. In 1964 an adherent scar had been excised and resurfaced by split grafts to the periosteum. The patient has had recurrent flares since then, the last being in early 1967, when it was evident that sclerotic avascular bone was still present.

The old scar was excised on 19 Sept., 1967. The infecting organisms were found to be proteus, which was sensitive to ampicillin but resistant to penicillin, and *Staph. aureus*, which was sensitive to both ampicillin and penicillin. All the sclerotic bone was excised over a wide area until healthy bleeding bone was exposed. Split grafts from the right thigh were used to cover the left tibia, and the graft healed satisfactorily. In view of the patient's type of work, further protection by full-thickness skin cover was thought to be advisable. This was carried out in several stages.

On 5 Oct. a first-stage cross-leg flap was raised, and on 19 Oct. the cross-leg flap was elevated and sutured over the tibia after excision of the split-skin grafts, which had taken fully. The flaps were separated and reinserted on 1 Nov. The patient was discharged on 2 Dec., and he returned to work on 20 Feb., 1968. The graft remained soundly healed in August, 1971.

COMMENT.—Initial inadequate excision of infected and sclerotic bone and direct suture over the cavity resulted in further scarring and recurrent episodes of infection. Primary grafting at that time would have revealed areas of necrotic bone still to be present. A more radical excision and primary skin-grafting should have been undertaken in 1957. The bone chips could then have been inserted at the time of a cross-leg-graft reconstruction if necessary.

Case 4.—T. D., aged 20 years. This patient had been kicked by a horse 6 years previously and had since had recurrent osteomyelitis of tibia. On examination on 4 Jan., 1968, there was an adherent scar in the upper part of the left tibia with a discharging sinus, 2·5 × 1·8 cm. The infecting organisms were *Staph. aureus*, which was sensitive to penicillin, and streptococcus, which was sensitive to ampicillin but resistant to cloxacillin, penicillin, and tetracycline. A radiograph showed old osteitis at the upper end of the left tibia.

On 19 Jan. the scar, the sclerotic tissue, and the sclerotic bone were excised. The cavity was saucerized and split grafts were applied, with 100 per cent take. A cross-leg flap was raised. On 1 March, 1968, the cross-leg flap was raised and was inserted into the graft area after excision of the split grafts.

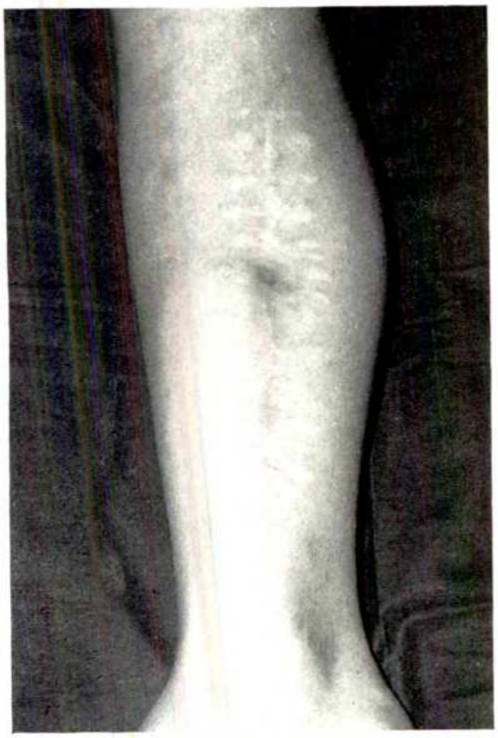

FIG. 7.—*Case* 7. Unstable scar and sinus overlying sclerosed infected bone.

The patient resumed working on 11 June, and the graft remains satisfactory to date (August, 1971).

Case 5.—S. M., aged 43 years. The patient presented on 12 Feb., 1969, with a 2-week history of pain in the right ankle. The ankle was ankylosed, the patient having had osteomyelitis at 15 years of age. Radiographs showed complete obliteration of the ankle-joint (*Fig.* 5), and there were abscess formation and sclerosed bone in the lower third of the tibia. The infecting organism was *Staph. aureus*, which was sensitive to cloxacillin, streptomycin, and erythromycin, but resistant to penicillin and tetracycline.

Sequestrectomy and saucerization were carried out on 14 March. Pus under tension was evacuated, and a primary split graft was applied. On 21 March a good take of 95 per cent was recorded. On 27 March a small strip of graft in the base, 1·8 cm. wide, had not taken. Furacin and a compression bandage were applied, and on 17 April the graft appeared to be healed (*Fig.* 6). The patient returned to work on 9 Sept. and the leg has remained satisfactory.

COMMENT.—Primary grafting succeeded in the presence of an infection where pus was under tension.

Case 6.—G. P., aged 34 years. This patient had sustained a compound comminuted fracture of the upper end of the left tibia and fibula on 7 Feb., 1960. The fracture had been treated by wound excision and plaster immobilization, the leg remaining in plaster until 7 Oct. when the fracture had been clinically firm.

On 26 Jan., 1961, the patient had had manipulation of the knee to improve knee movements. He had been seen again in 1961 with some discomfort at the fracture site, and again in May, 1964, with a recurrent discharging sinus over the upper end of the tibia in the original wound. No localized sequestra had been seen but sclerotic bone had been evident. Local dressings had been applied, antibiotics had been given, and the sinus had healed.

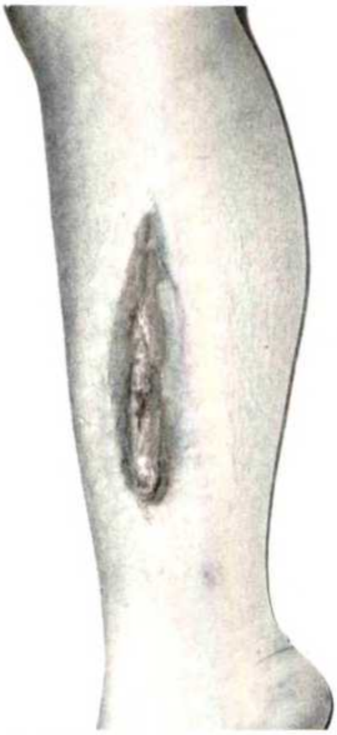

FIG. 8.—*Case* 7. Stable skin cover after excision of necrotic and sclerotic bone.

The patient presented on 17 July, 1969, with recurrent pain in the left knee and the sinus had reopened. On 31 Oct., 1969, the infecting organism was shown to be *Bacillus pyocyaneus*, which was sensitive to colomycin.

On 17 Oct. the scarred area was excised. The necrotic bone was cut away, but there was a ring of dense bone at the fracture site and it could not all be removed without weakening the tibia. A primary skin-graft was applied and it took satisfactorily (95 per cent). One small area in the upper angle of the wound, less than 0·6 cm. in diameter, has discharged a little intermittently since.

On 30 June, 1970, radiographs revealed a very small sequestrum to be present which was coincident with the area which had not healed. The sequestrum was removed and a small split-skin graft was applied. The wound has remained healed since.

COMMENT.—This case illustrates the limitations of the method of primary skin-grafting, i.e., it must be possible to remove all the necrotic bone without disturbing the structural stability of the affected bone.

Case 7.—V. B., aged 17 years. This patient had had recurrent osteomyelitis of the right tibia since initial treatment as a child at the age of 6. The primary infection had been *Staph. aureus*, which had been sensitive to penicillin.

Examination on 13 Feb., 1970, revealed a broad, ugly, unstable scar over the lower half of the tibia. A radiograph showed some sclerosis of the midshaft of the

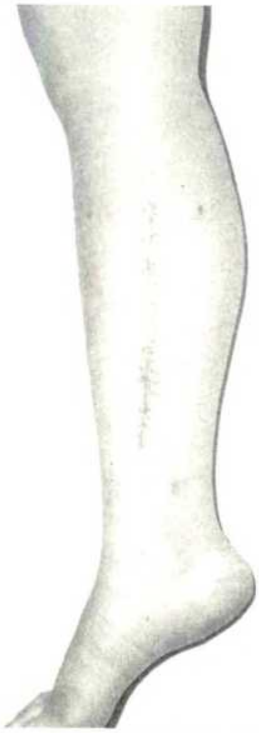

FIG. 9.—*Case* 7. Full-thickness skin cover after excision of split-skin grafts.

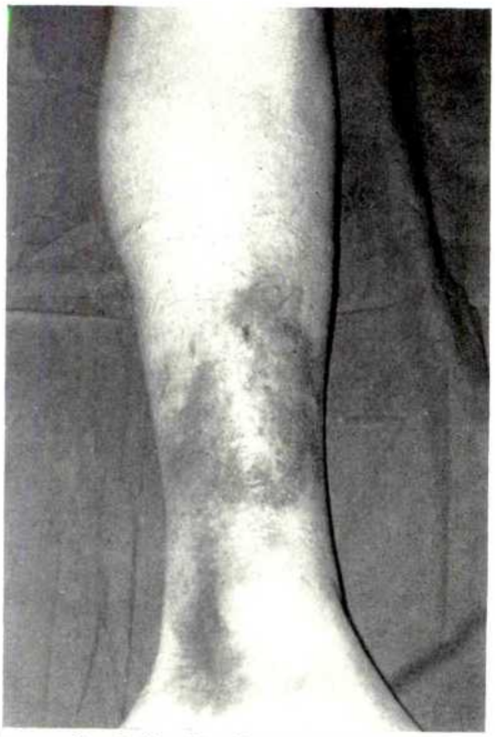

FIG. 10.—*Case* 8. Unstable adherent scar and sinus overlying necrotic bone.

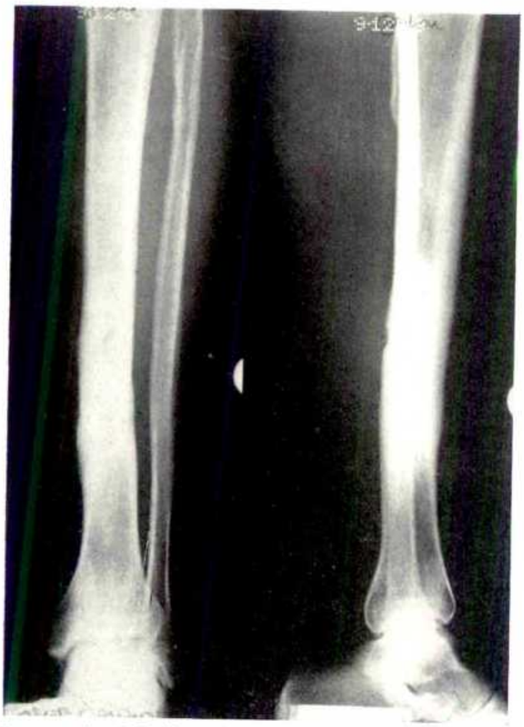

FIG. 11.—*Case* 8. Radiograph showing dense sclerotic bone with a small sequestrum separating posteriorly.

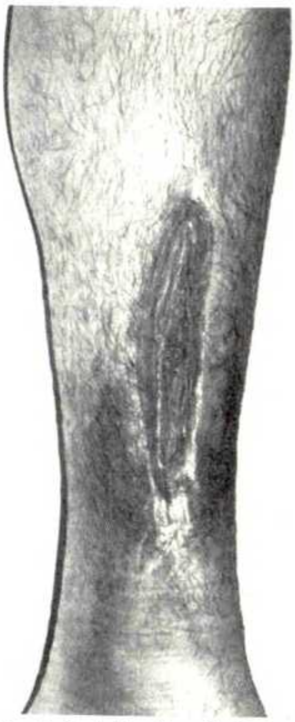

FIG. 12.—*Case* 8. Cavity lined by split-thickness grafts.

tibia (*Fig.* 7). The old scars were excised, and a large area of thick sclerotic bone was removed from the mid-shaft of the tibia until healthy bone was exposed. Very small sequestra were present in the granulation tissue. The infecting organisms were *Staph. aureus* and *Staph. albus*, which were sensitive to penicillin. A primary split-skin graft from the same thigh was applied, and it took satisfactorily (100 per cent). A sound, stable split-skin cover was noted on 13 April (*Fig.* 8). In June the graft was replaced with full-thickness skin by local resuture in order to produce a cosmetically acceptable scar. The split grafts were excised and local resuture was performed in September. The area remains healed at the present time (*Fig.* 9).

Case 8.—J. G., aged 27 years. This patient had sustained a compound fracture of the left tibia when he had been a parachutist in the Spanish Army in 1968. The wound had been excised and 5 days after the injury he had had an intramedullary nail inserted into the tibia. Four weeks later this had to be removed because of infection. Another plaster had been applied and the wound had gradually healed. The patient had had a further operation in Sept, 1969, in Spain for a sinus.

On examination on 9 Dec., 1969, a small discharging sinus 7·5 cm. above the ankle in the midst of a large area of excoriated skin was present. Clinical alinement of the tibia was good. A radiograph showed a united fracture of the tibia with some sclerosis at the fracture site. A small cavity and sequestrum were visible (*Figs.* 10, 11).

The patient was admitted to Woodlands Orthopaedic Hospital on 13 Feb., 1970. At operation an incision was made along the original scar, including the sinus in the incision. The bone was very sclerotic and was marble hard. The bone was saucerized using a gouge and chisel. There was a small amount of pus deep in the cavity, from where the small sequestrum was removed. The sinus track was dissected out and removed. An inlay skin-graft was taken from the same thigh and was inserted into the cavity.

A 50 per cent take of the graft was noted on 9 March. There was loss of graft from the lateral side and the floor of the cavity owing to a haematoma. The necrotic graft was removed on 10 March and the defect was covered by new grafts from the left thigh. On 19 March the dressing was removed in the operating theatre under general anaesthetic. One hundred per cent take of the graft was noted (*Fig.* 12).

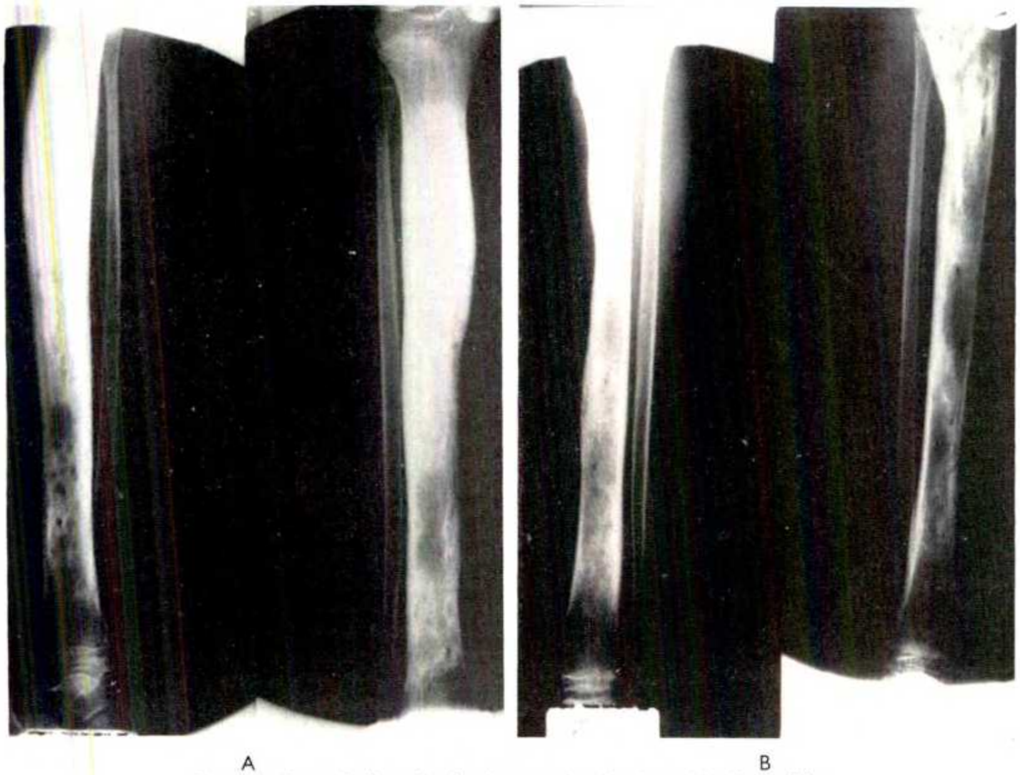

FIG. 13.—*Case* 9. Radiographs showing extensive chronic osteitis of both tibiae.

When the donor area had healed, the patient was allowed up, with a Blue-line bandage on the leg. He was discharged from hospital on 29 March.

At review on 27 Oct., 1971, the graft had healed soundly, and the patient was able to work.

COMMENT.—Inadequate haemostasis produced a partial take of the primary grafts. Regrafting of the unhealed area, after removal by curettage of any granulations, produced 100 per cent take.

Case 9.—S. C., aged 12 years. This patient had had recurrent osteomyelitis of both tibiae for 4 years. The left knee and hip had been stiff for at least 2 years.

On examination, in November, 1966, there were multiple scars and sinuses over both tibiae, chiefly on the subcutaneous surface from the knee to the ankle, and healed scars over the lower end of the left femur. Left knee movement was 180–160°, while the right knee movement was full. Full ankle movements of both legs were present. There was left hip flexion to 90°, and rotation to half range. Radiographs showed chronic osteomyelitis with multiple dense areas extending throughout the whole of the diaphyses of each tibia. The left hip showed evidence of avascular necrosis in the epiphysis of the head of the left femur (*Fig.* 13). Blood examination showed a negative test for 'sickling'. In Singer's test less than 2 per cent of the haemoglobin resisted alkali denaturation. Electrophoresis of the haemoglobin at *p*H 8·9 revealed a single haemoglobin band of similar mobility to that of haemoglobin C. Red-cell morphology was strongly suggestive of haemoglobinopathy. The haemoglobin was 69 per cent, W.B.C. 10,000, polymorphs 5300, lymphocytes 4000, and eosinophils 300. A study of the red-cell morphology revealed anisocytosis, target cells + + +, polychromasia + +, hypochromia + +, and 3 per cent reticulocytes.

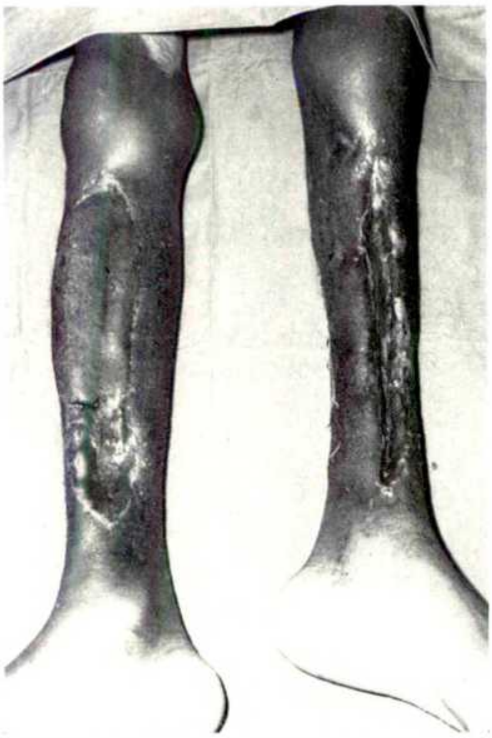

FIG. 14.—*Case* 9. One-hundred per cent split-skin cover of both legs. The upper half of the right leg has been replaced by a full-thickness cross-leg flap.

A swab taken from the wounds cultured *Staph. aureus*, which was coagulase positive and resistant to penicillin and ampicillin but sensitive to cloxacillin, Ceporin, erythromycin, and Tetracycline, and haemolytic streptococcus, group A, which was sensitive to penicillin, ampicillin, cloxacillin, and erythromycin.

Cloxacillin was begun 2 days prior to operation on 10 Dec., 1966. The diaphysis of the right tibia was guttered from end to end. Split-skin grafts were sutured into the cavity. Two pints of blood were transfused during the operation, which was performed without a tourniquet. Removal of the dressings of the right leg on 15 Dec. revealed total failure of the grafts. A further swab confirmed that haemolytic streptococci were still present. The wound was packed. On 5 Jan., 1967, excision of the sclerotic bone and guttering of the left leg was performed. Split grafts were applied. Granulations were stripped from the wound of the right leg and the area was regrafted. On 12 Jan. the right leg had 100 per cent take and the left leg had a 95 per cent take of the grafts (*Fig.* 14). On 26 Jan. a long abdominal tube pedicle graft, 21·8 × 7·5 cm., was raised. A cross-leg flap of the left leg was also raised, and a Thiersch graft was used to cover this. A series of procedures were undertaken in order to transfer these tubes to cover the defects in both the legs. By 12 June all the flaps and both the thighs had healed with full-thickness skin cover (*Fig.* 15). The patient was then allowed to take his full weight on both legs. Both tibiae have remained healed and free from symptoms since.

COMMENT.—The initial operative procedure was undertaken too soon before control of the streptococcal infection by antibiotic therapy. When the infection had been controlled, primary grafting direct to the bone succeeded.

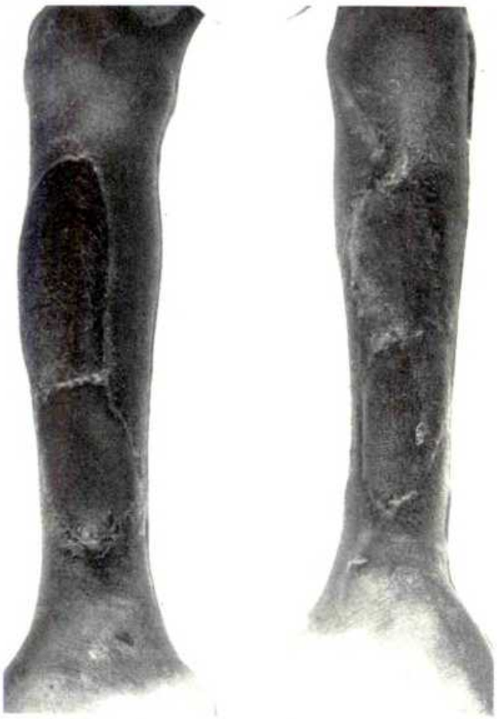

FIG. 15.—*Case* 9. Complete full-thickness skin cover obtained.

DISCUSSION

Chronic osteomyelitis is synonymous with the persistence of infected, avascular bone accompanied by soft-tissue fibrosis and, in many cases, by dense, adherent, superficial scarring, and is characterized by acute phases of pyrexia, pain, loss of function, and often recurrent sinus formation.

Whilst rest and antibiotic therapy may produce subsidence of such an acute episode, frequent recurrences require a more radical procedure. A radical excision of all avascular bone, scar tissue, and unstable skin is essential and is common practice, but there is still some variation in the subsequent methods of closure and repair. After radical excision a cavity is left which must be obliterated if a haematoma is not to ensue with resulting recurrence of infection and scarring, and yet direct suture and closure without obliteration are often practised with |subsequent failure to eradicate the infection. Obliteration by granulation and epithelization under a plaster cast by the Winnett Orr method often results in prolonged hospitalization, chronic sinuses, and unstable, adherent, ugly scars. The cavity in many cases can be obliterated by the use of a pedicled muscle-flap which because of its vascularity is highly resistant to infection, and adequate skin closure without tension may then be possible. There are many situations, however, for example, the tibia and lower end of the femur, where such an obliteration is difficult or impossible and where an adequate skin closure cannot be made by simple suture. These cavities can be very satisfactorily closed with adequate skin cover by means of a primary, inlay, split-skin graft, as shown by Robertson and Barron (1946), yet the treatment of chronic osteomyelitis by such a method has failed to receive the general adoption its effectiveness indicates. Where skin-grafting has been advocated (Lord, 1902; Armstrong and Jarmon, 1936; Kelly and others, 1945; Knight and Wood, 1945; Kelly, 1946; Evans and Davies, 1969), grafting as a secondary procedure 4–7 days after excision and saucerization is the recommended procedure. Primary grafting at the time of saucerization as a one-stage procedure is preferable, with one contra-indication, to a secondary-grafting procedure, and it has been the aim of this paper to recall and to stress the advantages of this method. Secondary grafting has been recommended by other authors because it was thought that a layer of granulations on the floor and walls of the cavity was essential for skin-grafts to take on cortical bone, or that grafts would not take in the presence of infection. This belief is erroneous. A split graft will take on cortical or cancellous bone, provided that the bone is adequately vascularized. Where small areas of the skin-graft do not take, it is therefore evident that the saucerization procedure has been inadequate and that sclerotic bone has been left in the walls of the cavity on which the grafts will not survive. Such areas can then be locally excised and small grafts can be applied to complete the closure, or they may close by direct epithelization. With the exception of infection with haemolytic streptococcus, the split graft will take in the presence of infection. The presence of haemolytic streptococcus at the time of operation is the one contra-indication to the use of primary grafting.

A further advantage of the primary one-stage procedure is that the risk of development of secondary infection after the saucerization procedure, which is liable to occur in a two-stage procedure, is considerably reduced. The split grafts remain quite stable and they thicken to 3 mm. Survival of the grafts indicates that the radical excision of avascular infected bone has been complete, thus eliminating any further risk of recurrence of the infection. If there is a risk of further local trauma a full-thickness skin replacement may be undertaken later, either by local direct suture or by rotation of local flaps or by cross-leg-flap or tube-pedicle procedures.

The method is equally applicable to the treatment of open, infected fractures, particularly when union is delayed.

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HYPERKALAEMIA FOLLOWING TEMPORARY OCCLUSION OF THE PORTAL VEIN AND HEPATIC ARTERY

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SUMMARY

Temporary occlusion of the hepatic artery and the portal vein during operations on the liver has been considered a safe procedure provided that the period of ischaemia is not extended beyond 20–30 minutes. Measurement of serum potassium in the portal and systemic circulation of dogs which were subjected to 20 minutes' hepatic ischaemia reveals a transient hyperkalaemia of sufficient degree to cause cardiotoxicity. It is concluded that even this short period of inflow occlusion to the liver is inadvisable.

Haemorrhage is a hazard that complicates liver surgery (Stone and Saypol, 1952; Madding and Kennedy, 1965). A variety of surgical techniques have been described that minimize such bleeding (Wangensteen, 1945; Nakayama, 1957; Balasegaram, 1968), including temporary occlusion of the portal vein and the hepatic artery to arrest blood-flow through the liver while resection is being performed. This method was described by Duchinova in 1926 and by Wangensteen in 1951, and was subsequently recommended by Brunschwig (1955) and by Madding and Kennedy (1965).

Patients have been subjected to hepatic circulatory arrest for 30–45 minutes at normal body temperature without apparent harm (Brunschwig, 1955; Anastasia, Williams, and Byrne, 1967), but by no means all patients have survived this operative procedure

(Wangensteen, 1951), and there has been considerable speculation concerning the maximum time that the blood-supply to the liver may be safely interrupted.

Raffucci and Wangensteen (1951) found that 20 minutes was the maximum period of continuous occlusion of the hepatic artery and portal vein that was tolerated by normal dogs without showing evidence of hepatic necrosis. This was confirmed by Goodall, Hyndman, and Gurd (1957). Longer periods of ischaemia are usually fatal (Bernhard, McMurrey, and Curtis, 1955) but are tolerated if a portacaval shunt (Jolly and Foster, 1963) or hypothermia (Bernhard, Cahill, and Curtis, 1957) is employed.

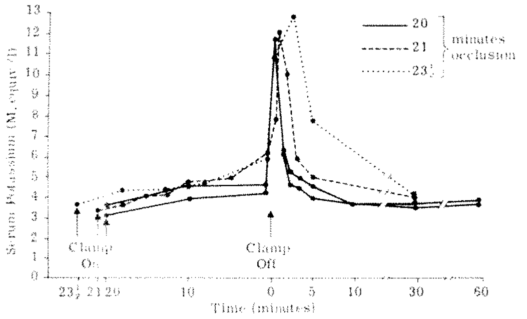

FIG. 1.—Serum potassium levels in the pulmonary artery before, during, and following arrest of the hepatic circulation for 20, 21 and 23½ minutes.

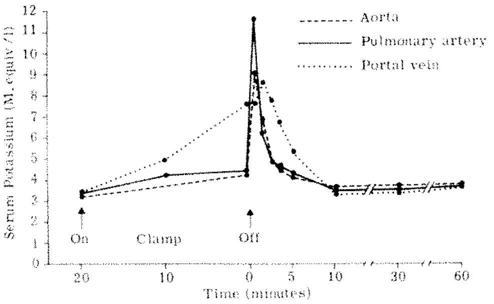

FIG. 3.—Serum potassium levels in the pulmonary artery, the portal vein, and the aorta before, during, and following 20 minutes' hepatic circulatory occlusion.

The mortality and morbidity resulting from longer periods of hepatic inflow arrest have been variously ascribed to hypovolaemic shock (Elman and Cole, 1934; Brunschwig, 1955), release of a vasodepressor material (Shorr, Zweifach, and Furghott, 1945; Buckberg, Hiromichi, Joseph, Tocornal, Fonkalsrud, and Longmire, 1968), acidosis (Barnett, Turner, and Walker, 1958), and anaerobic bacteriaemia (Markowitz, Rappaport, and Scott, 1949; Battersby, Balderson, Winch, and Burnett, 1971).

Hyperkalaemia has been noted with interest by several observers but has been discounted as a cause of death (Backlund, Stevens, Hamit, and Jordan, 1965; Stewart, Potter, Hubbard, and Anderson, 1953). These authors agree that the serum potassium level in the hepatic veins rises progressively while the hepatic circulation is arrested for periods longer than 20 minutes, but it falls promptly to normal when the circulation is restored. Jolly and Foster (1963), and Bengmark, Hafström, Hultin, Jagenburg, and Vosmik (1969), however, observed a rise in serum potassium when the circulation was restored following 2 hours' liver ischaemia. This could be dangerous, for circulatory hyperkalaemia is cardiotoxic causing a variety of arrhythmias (Blake, 1839; Ewy, Karliner, and Bedyner, 1971) and cardiac arrest (Ringer, 1883), and could account for some of the morbidity or mortality of temporary arrest of the hepatic circulation.

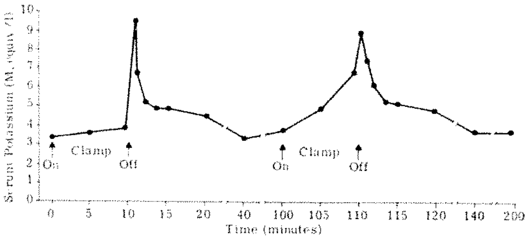

FIG. 2.—Serum potassium levels in the pulmonary artery before, during, and following two 10-minute periods of hepatic circulatory arrest.

Ischaemic liver cells are known to release large amounts of intracellular potassium (Flink, Hastings, and Lowry, 1950; Abouna, Skillen, Hull, Hodson, and Kirkley, 1969). If the amount of potassium is sufficient to allow detection in the hepatic veins and the suprahepatic vena cava while the hepatic bloodflow is at a standstill, it is to be expected that the accumulated potassium would be flushed out of the liver on restoration of the circulation and would cause an increase rather than a decrease of serum potassium levels in the hepatic veins and the systemic circulation. A simple experiment has been undertaken to investigate this hypothesis, and the results are reported here.

MATERIALS AND METHODS

Five dogs weighing 14–16 kg. were anaesthetized with intravenous Nembutal and the pulmonary artery and descending aorta were catheterized via the femoral vein and artery respectively. Upper midline laparotomy was performed and the main portal vein was cannulated via the splenic vein. These catheters enabled constant recording of pressure and intermittent sampling of blood for serum potassium estimation from the portal vein, pulmonary artery, and aorta. Blood was sampled from the pulmonary artery rather than from the suprahepatic vena cava because samples from the pulmonary artery would indicate the true potassium concentration of the mixed venous blood returning to the heart. An electrocardiogram using standard limb leads was monitored.

The blood-supply to the liver was then interrupted by means of a clamp applied across the hepatoduodenal ligament to occlude the portal vein and hepatic artery as they entered the porta hepatis. In 4 dogs hepatic circulatory arrest was maintained for 20 minutes, this being the accepted maximum 'safe period' for normothermic ischaemia of the liver in dogs. The fifth dog was subjected to two 10-minute periods of hepatic ischaemia which were separated by a recovery period of 90 minutes.

Blood samples were collected before, during, and immediately following the period of hepatic circulatory arrest. The animals were sacrificed at the conclusion of the experiment.

RESULTS

Serum Potassium.—*Fig.* 1 shows the serum potassium levels of blood in the pulmonary artery before, during, and following hepatic circulatory arrest. The period of hepatic ischaema in 4 dogs was 20, 20, 21, and 23½ minutes respectively.

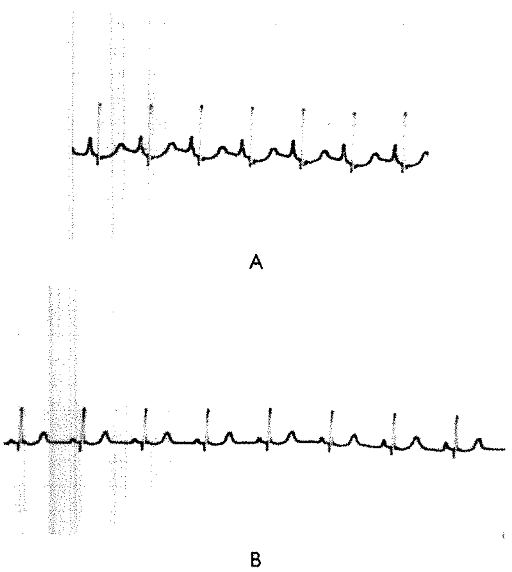

FIG. 4.—The electrocardiogram (lead II) (A) before and (B) 30 seconds following 10 minutes' hepatic circulatory arrest.

There was a small rise in serum potassium during the period of hepatic ischaemia, from 3·4 to 5·2 mEq. per l. On restoring the circulation there was a very rapid rise to high peak levels (10·8–12·7 mEq. per l.) within ½–2½ minutes. These were not maintained, however, and fell to normal limits within 5–10 minutes, remaining so for 1 hour. From this three factors emerge:—

1. The circulating serum potassium rose rapidly to cardiotoxic levels immediately following 20 minutes' stasis of the hepatic circulation.
2. This hyperkalaemia was transient and would have been missed if sampling were delayed by 5 minutes.
3. Hyperkalaemia was more marked and of longer duration following the longer period of hepatic ischaemia.

Fig. 2 shows the potassium levels (pulmonary artery) for two 10-minute periods of ischaemia which were separated by a 90-minute period for recovery. Severe but transient hyperkalaemia is again demonstrated and, in addition, there is a more marked rise during rather than following the second period of ischaemia. This suggests two further factors:—

1. Ten minutes' arrest of the liver circulation, i.e., half of the recommended 'safe period', produced hyperkalaemia of a potentially dangerous degree.
2. One and a half hours was insufficient for full recovery of the liver, the latter releasing almost twice the quantity of potassium during the second ischaemic phase.

Fig. 3 compares the serum potassium levels in the portal vein, the pulmonary artery, and the aorta of the 2 dogs which were subjected to identical 20-minute periods of hepatic stasis. Potassium increase in the portal vein was considerable while the blood-flow was occluded, but that in the systemic circulation was negligible. On releasing the clamp there was no immediate potassium increase in the portal vein at ½ minute, as was seen in the pulmonary artery, but

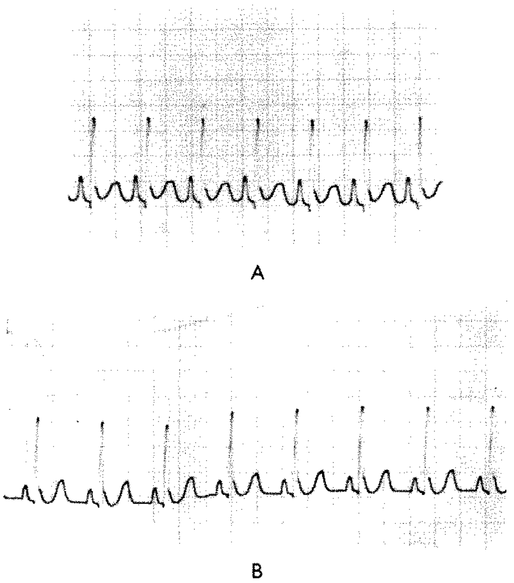

FIG. 5.—The electrocardiogram (lead II) (A) before and (B) 1 minute following 20 minutes' hepatic circulatory arrest.

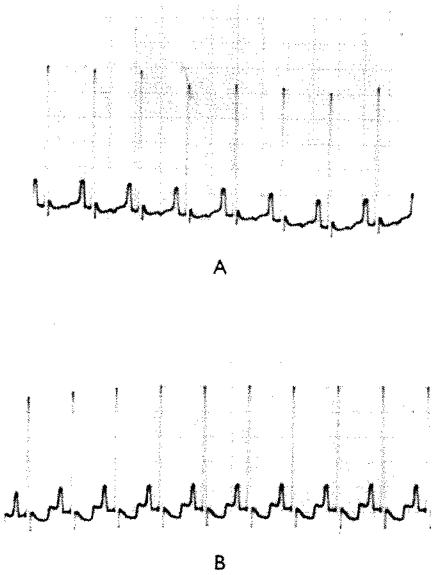

FIG. 6.—The electrocardiogram (lead II) (A) before and (B) 5 minutes following 21 minutes' hepatic circulatory arrest.

a peak followed at 1½ minutes. This sequence of events suggests that the secondary peak in the portal vein was a reflection of the systemic hyperkalaemia which was delayed by the normal circulation time from the heart to the liver. Of greater importance is the contribution of the portal venous potassium accumulation during stasis to the systemic hyperkalaemia.

Pressure in the portal vein rose from 1–8 mm. Hg to 46–95 mm. Hg when it was occluded. The intestines became congested, and 2 of the 4 dogs developed extensive petechial haemorrhages in the mesentery and small bowel. Blood samples from the portal vein during this period (and from the pulmonary artery on release of the clamps) showed variable degrees of haemolysis. (The haemolysis was of no significance to the potassium estimation because the potassium content of red cells in the dog is negligible (Stewart and others, 1953).) Jolly and Foster (1963) and Grana, Saldana, Donnellan, and Swenson (1968) have shown that intestinal congestion may be avoided by a portacaval shunt, but this does not diminish the potassium concentration in the hepatic veins. Flink and others (1950) showed, in addition to the release of potassium by ischaemic liver cells, the immediate uptake of potassium by the same cells when they were reoxygenated. Thus, it is unlikely that the portal hyperkalaemia contributes significantly to that of the systemic circulation which has been described.

The peak potassium level which was measured in the abdominal aorta was lower than that in the pulmonary artery. This was to be expected as a result of dilution during pulmonary circulation, the potassium concentration of the blood perfusing the coronary vessels lying between the two levels.

Electrocardiographic Changes.—Complete electrocardiogram (E.C.G.) records (*Figs.* 4, 5, 6) were available in 3 of the 5 experiments, each of them showing features of hyperkalaemia: reduced P wave, tented T wave, increased Q–T interval, and loss of U wave (*Fig.* 4), and diminished P wave, 'tented' T wave, and S–T depression (*Fig.* 6). These changes developed a few seconds after restoring the hepatic circulation and persisted for approximately 10 minutes. It should be noted that the changes in *Fig.* 4 occurred after only 10 minutes' ischaemia.

Tanturi, Mejia, Canepa, and Gomez (1960) investigated the electrocardiographic changes resulting from the temporary occlusion of the portal vein of the dog, and they reported marked signs of cardiac ischaemia but failed to mention any signs of hyperkalaemia. In the experiments reported here some cardiac ischaemic changes were seen while the hepatic circulation was arrested, but the E.C.G. reverted to normal on restoring the blood-flow and then developed the signs of raised potassium a few seconds later.

CONCLUSION

It is clear that temporary occlusion of the hepatic artery and portal vein in the dog causes transient but severe hyperkalaemia of a sufficient degree to cause cardiotoxicity, even when the duration of circulatory arrest is only 10 minutes. It has not been possible to undertake similar measurements on patients who have been subjected to this operative procedure, but it would be reasonable to expect a similar effect.

Thus, the suggestion of Anastasia and others (1967) that the currently accepted limits of hepatic ischaemia be extended cannot be endorsed. Rather, an alternative method of haemorrhage control should be sought.

Acknowledgements.—I am grateful to Lord Brock, Director of the Department of Surgical Sciences, Royal College of Surgeons of England, for providing the facilities for this investigation. I would also like to thank Miss M. Jacques and Mr. J. Manders for their technical assistance, the staff of the Clinical Pathology Department, Royal Marsden Hospital, for performing the potassium estimations, and Mr. D. M. Wallace, Consultant Surgeon, Royal Marsden Hospital, for his encouragement.

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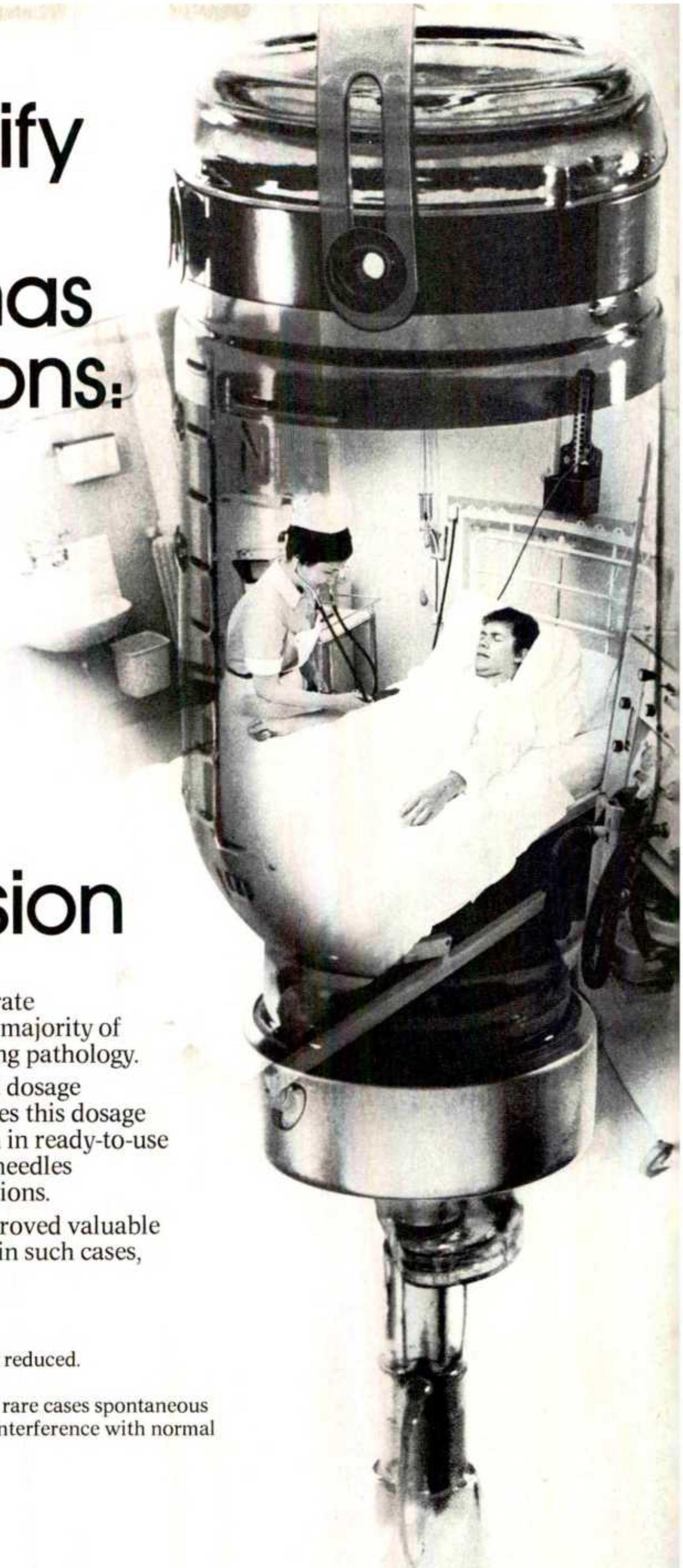

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OMENTAL REINFORCEMENT OF INTESTINAL ANASTOMOSES

AN EXPERIMENTAL STUDY IN THE RABBIT

By D. C. CARTER, D. H. R. JENKINS,* and H. N. WHITFIELD†
DEPARTMENT OF CLINICAL SURGERY, UNIVERSITY OF EDINBURGH

SUMMARY

1. A series of end-to-end everting colonic anastomoses were performed in 95 rabbits in order to assess the value of omental reinforcement. The animals were divided into three groups: (*a*) control animals, (*b*) animals with anastomoses reinforced by a free omental graft, and (*c*) animals with anastomoses reinforced by an omental pedicle.

2. Reinforcement with a free omental graft carried a prohibitive increase in mortality. The use of an omental pedicle appeared to strengthen the anastomosis against forced disruption in the immediate postoperative period but it did not improve the survival rates and it may carry long-term dangers. The explanation for these findings is discussed.

3. It is our view that there is no place for omental reinforcement in colonic surgery.

THE natural protective powers of the omentum are well recognized. As Freeman (1916) observed: 'a well known function of the omentum is its almost intelligent ability to seek out and attach itself to raw or inflamed surfaces, wrapping itself around them in such a way as to afford a maximum of protection'. The artificial use of the omentum in the deliberate reinforcement of end-to-end intestinal anastomoses was first advocated by Tietze (1876), and the majority of subsequent reports have favoured the use of free or pedicled omental grafts in hazardous areas of gastro-intestinal surgery (Senn, 1888; Scudder, 1908; Sweet, Chaney, and Wilson, 1915; Finton and Peet, 1919; Bothe, 1929; Devine, 1946; Chester, Bell, and McCorkle, 1949). Nevertheless, sporadic reports have appeared which conflict with this majority view. Springer (1906) could find no special advantages in the use of free omental grafts to reinforce small intestinal anastomoses in the dog and could envisage no indications for their use in practical surgery. Wilkie (1911) was unfavourably impressed by the propensity of free grafts to form extensive adhesions, while Lexer (1924) concluded from extensive clinical and experimental observations that necrosis of the transplanted tissue was inevitable and that free transplantation of the peritoneum should not be performed either within or outside the peritoneal cavity. On the other hand, Pettet, Judd, and Woolner (1956) considered that free grafts will usually survive and provide some reinforcement of an anastomosis, although they agreed that their use within the peritoneal cavity was limited by dense adhesion formation. Kleinsasser, Cramer, and Warshaw (1950) found no particular advantage in omental reinforcement of end-to-end anastomoses in the oesophagus of the dog, while Goldsmith, Andrew, and Randall (1968) found omental pedicles to be of value in this experimental situation and worthy of further clinical trial.

While there may be little ground for concern as to the security of end-to-end anastomoses in viable small intestine in human surgery, the same cannot be said to apply to large-bowel anastomoses. Goligher, Graham, and de Dombal (1970) and Goligher, Morris, McAdam, de Dombal, and Johnston (1970) have drawn attention to the frequency with which leakage may occur in the latter situation, in some cases with fatal results and at least a significant increase in morbidity.

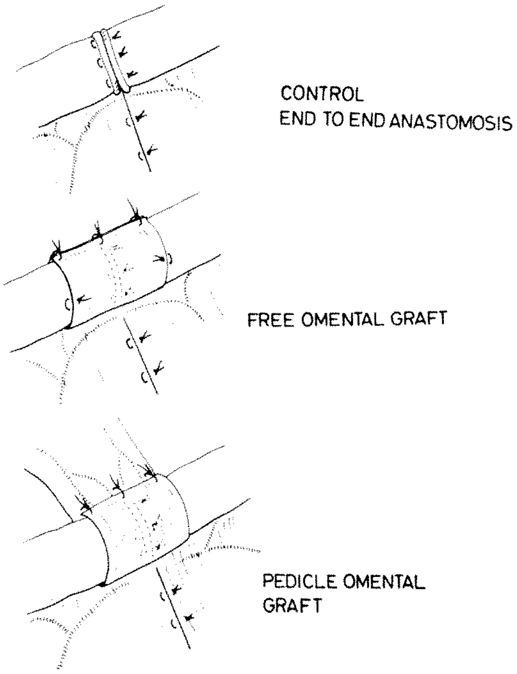

FIG. 1.—Technique of anastomosis and omental reinforcement.

It is valuable, therefore, to re-examine the whole problem of free and pedical omental grafts in an animal model where leakage from a colonic anastomosis might be anticipated, and in this way to determine the relative value of the techniques and their possible role in human surgery.

MATERIALS AND METHODS

Experiments were performed on a total of 95 rabbits of the New Zealand white strain. The animals were not starved prior to operation and no attempts were made to sterilize the bowel lumen or to achieve purgation of the intestinal contents. Anaesthesia was induced by intravenous Nembutal (24 mg. per kg. body-weight) and was maintained by nitrous oxide (1·5 litres per minute), halothane (0·5 per cent), and oxygen (0·75 litre per minute), using an open circuit.

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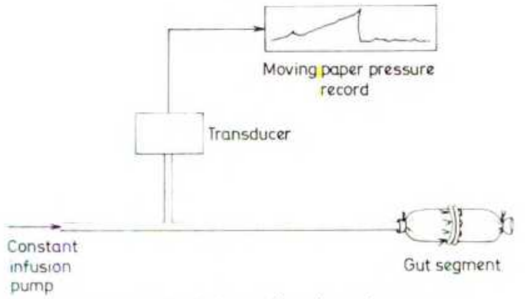

FIG. 2.—Method of recording disruption pressure.

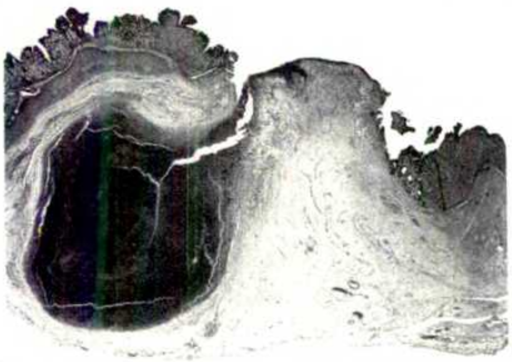

FIG. 4.—Peri-anastomotic abscess as seen at 7 days (free-graft group). H. and E. (× 5·7.)

The abdomen was opened through a longitudinal midline incision and the ascending colon was identified. The marginal artery was ligated at two points, 1 cm. apart, on either side of the proposed line of anastomosis, and the bowel was then divided transversely between occlusion clamps. An end-to-end everting anastomosis was performed using interrupted sutures of 00000 silk (*Fig.* 1). The occlusion clamps were removed and any gross defects in intestinal continuity were closed by additional sutures. No drains were led down to the anastomosis and no topical or systemic antibiotics were used.

The animals were then allocated to one of three groups in a sequential manner:—

Control Group (26 Rabbits).—On satisfactory completion of the anastomosis the mesenteric defect was closed with interrupted 00000 silk sutures and the abdomen was closed with a double layer of 000 continuous chromic catgut.

Free Omental Graft Group (41 Rabbits).—Prior to closure of the mesenteric defect a strip of the free border of the greater omentum was removed between haemostats and was applied around the anastomosis (*Fig.* 1). Adherence between the omentum and the intestinal serosa was reinforced by interrupted sutures at the proximal and distal margins of the graft, care being taken not to enter the bowel lumen while placing these additional sutures. Closure was then instituted as in the control group.

Omental Pedicle Graft Group (28 Rabbits).—The anastomosis was reinforced in this group of animals by wrapping the free border of the greater omentum around the anastomosis, as shown in *Fig.* 1, without interruption of the omental blood-supply. Closure was carried out as in the control group.

ASSESSMENT OF RESULTS

Histological Assessment.—One animal in each group was sacrificed at 6 hours, and 1, 3, 7, 14, and 21 days after completion of the anastomosis, solely for histological assessment with light microscopy using standard histological techniques.

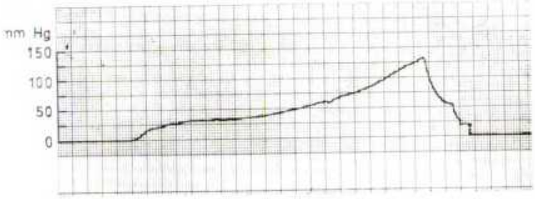

FIG. 3.—Typical disruption tracing.

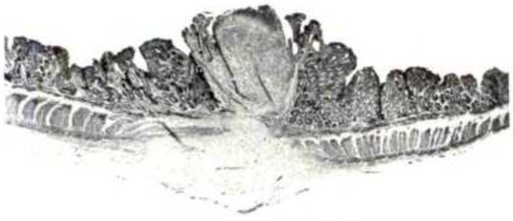

FIG. 5.—Restoration of mural continuity by fibrous tissue as seen at 21 days (pedicle-graft group). H. and E. (× 10.)

Pressure Studies.—Three animals in each group were sacrificed at 1, 3, 7, 14, 21, and 28 days after completion of the anastomosis. A standard 10-cm. length of bowel including the anastomosis was removed, surrounding adhesions being preserved by an *en bloc* removal of neighbouring adherent structures where necessary. The distal end of the colon was sealed by a ligature and an open-tipped catheter was tied into the proximal end. The catheter was connected to a Harvard constant-infusion pump (Model 901, infusion rate 3·82 ml. per minute), and by an open three-way connexion to a Sanborn Differential Pressure Transducer No. 267BC (*Fig.* 2). Disruption of the anastomosis resulted in visible leakage of the contents of the intestine and was reflected by a sudden fall in pressure in the transducer and its associated pen recorder (*Fig.* 3). The mean bursting pressure for the three values recorded on each day within the three groups was then calculated.

Deaths.—The success or failure of omental reinforcement was judged ultimately by the number of deaths occurring within each experimental programme. To provide the necessary number of animals for pressure and histological studies, additional experiments were performed in each group to replace animals dying before the appointed day of sacrifice.

RESULTS

Histological Assessment.—The potential gap between the everted ends of anastomoses in the control animals was plugged by fibrinous exudate within 6 hours of operation, and by 24 hours the sealing thrombus became covered by a layer of cells of serosal appearance. The characteristic changes of acute inflammation were observed in all animals. Although both the free and pedicle grafts remained viable in the material examined, partial degeneration of the graft with destruction of the omental fat invariably occurred around the anastomosis. This increased the inflammatory reaction and delayed the rate of subsequent organization in the reinforced groups. Occasional giant cells were seen in later sections from all groups but only in the vicinity of suture material.

Table I.—ANASTOMOTIC DISRUPTION PRESSURES (mm. Hg)

TYPE OF ANASTOMOSIS	NO. OF DAYS FROM OPERATION					
	1	3	7	14	21	28
Control	2 22 28	1 25 10	12 13 20	92 103 168	135 185 226	186 212 226
Free omental graft	32 48 58	30 45 95	90 96 114	155 195 215	159 185 252	150 200 220
Omental pedicle graft	42 96 102	85 114 125	68 130 156	85 140 160	125 161 200	120 148 200

Table II.—NUMBER OF DEATHS

SURVIVAL	CONTROL	FREE OMENTAL GRAFT	OMENTAL PEDICLE GRAFT	TOTAL
Deaths	2	17	4	23
Survivors to day of sacrifice	24	24	24	72
Total	26	41	28	95

Table III.—TIMING OF DEATHS

TYPE OF ANASTOMOSIS	POSTOPERATIVE DAY OF DEATH	TOTAL NO. OF DEATHS
Control	5, 8	2
Free omental graft	2, 3, 3, 3, 5, 5, 6, 7, 7, 7, 8, 9, 10, 10, 11, 26, 27	17
Omental pedicle graft	5, 5, 6, 12	4
All methods	—	23

Peri-anastomotic abscesses were noted in all three groups (*Fig.* 4) but were more extensive in the presence of an omental barrier. Exuberant granulation tissue was a constant feature of the organization process, and new vessel formation was not noticeably increased in animals with reinforcement by an omental pedicle. The resulting fibrous tissue bridge had restored the continuity of submucosa and muscle layers by the third week (*Fig.* 5), although regeneration of the muscle layers was not detected in the material examined. The mucosa showed an initial contraction from the suture-line in all the animals, and although reconstitution of the mucosal lining became evident the process was far from complete in all the sections taken within 21 days of operation.

Pressure Studies.—The results are set out in *Table I* and are shown diagrammatically in *Fig.* 6, where each point represents the mean of three bursting-pressure readings. The control anastomoses were slow to gain strength and on day 7 were significantly weaker than anastomoses reinforced by either free omental grafts ($t = 11{\cdot}13$, $n = 4$, $P < 0{\cdot}01$) or omental pedicles ($t = 3{\cdot}928$, $n = 4$, $P < 0{\cdot}05$). Thereafter, the bursting pressures approximate in all three groups, and the apparent superiority of the free-graft technique at 14 days is not statistically significant (free versus control group: $t = 2{\cdot}278$, $n = 4$, $P > 0{\cdot}05$; free versus pedicle group: $t = 2{\cdot}103$, $n = 4$, $P > 0{\cdot}10$).

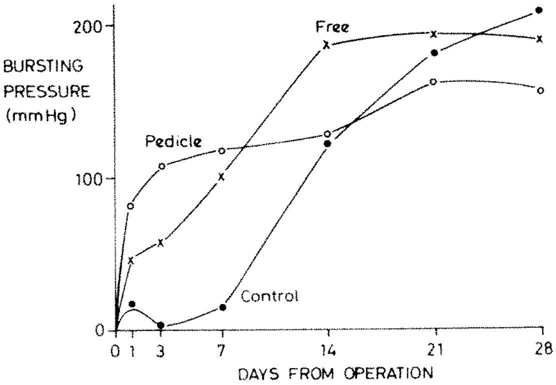

FIG. 6.—Mean anastomotic disruption pressures.

Deaths.—In order to obtain the 24 animals required for histological and pressure studies on the predetermined postoperative days a total of 26 animals had to be used in the control group. Similarly, 41 animals were needed in the free omental graft group, and 28 in the omental pedicle group (*Table II*). The number of deaths occurring in the free omental graft animals before the appointed day of sacrifice is significantly greater ($\chi^2 = 8{\cdot}93$, $P < 0{\cdot}01$) than the number of deaths in the control group. *Table III* shows the number of days elapsing between operation and the number of deaths in all three groups. In all the animals anastomotic leakage appeared to make a major contribution to death. Adhesion formation was difficult to assess at autopsy but was noticeably lacking in the immediate postoperative period in the free omental graft group. Of the 2 animals dying on the twenty-sixth and twenty-seventh postoperative days within this group, both showed extensive adhesion formation, and in 1 animal this had resulted in intestinal obstruction.

DISCUSSION

Despite an initial impression favouring the use of everting intestinal anastomoses (Getzen, 1966; Getzen, Roe, and Holloway, 1966; Healey, McBride, and Gallagher, 1967) the weight of surgical opinion has remained in favour of conventional inverting techniques. The recent publication from Goligher, Morris, and others (1970) has reinforced the conclusions reached in later animal experiments (Hargreaves and Keddie, 1968; Gill, Fraser, Carter, and

Hill, 1969; Garner, Hargreaves, and Keddie, 1969; McAdams, Meikle, and Medina, 1969; Rusca, Bornside, and Cohn, 1969) and leaves little doubt that everted anastomoses carry a higher risk of morbidity and even mortality from anastomotic leakage. For this reason a single-layer everting anastomosis was adopted in the present experiment and the possibility of leakage was increased further by the deliberate avoidance of bowel preparation in any form.

The most striking feature of the present experiment is the high mortality observed in the free omental graft group, despite an increased resistance to forced disruption in the immediate postoperative period in those animals surviving to the specified day of sacrifice. Contrary to the conclusions of Lexer (1924), we would agree with Bothe (1929) and Pettet and others (1956) that death of the transplanted tissue is not inevitable and at least part of the graft remains viable. However, survival is invariably offset by an intense inflammatory reaction and necrosis. Thus, while an omental graft might confer an added mechanical protection against forced disruption of the suture-line, it is unlikely that the graft, itself partially degenerate, could mount an effective biological response to major anastomotic leakage, should this occur.

In a series of animal experiments Laufman and Method (1948) reported that the absorbable materials, geletin sponge and oxidized cellulose, were deleterious to survival when applied around colonic anastomoses and suggested that the materials acted as an isolated bacteriological culture medium. Similarly, Trowbridge and Howes (1967) found that urethane-foam-reinforced anastomoses in the dog colon withstood lower disruption pressures than controls, unless the material was impregnated with neomycin. Canalis and Ravitch (1968) have shown conclusively that wrapping an everted intestinal anastomosis with an inert material such as polyethylene film or Silastic is almost invariably followed by anastomotic leakage, which leads on to abscess formation, generalized peritonitis, and death of the animal. Mellish, Ty, and Keller (1968) found that an inert silicone rubber membrane produced little or no adhesive reaction when applied around unopened bowel in the rat. When the membrane was sutured around an everting small-bowel anastomosis all 20 animals died from generalized peritonitis, the anastomoses failing to heal and there being no adhesion formation. Even in a similar group of membrane-wrapped inverting anastomoses the technique carried a prohibitive mortality, 8 out 19 animals succumbing to generalized peritonitis. All of these experiments indicate that any method of preventing adhesion formation by separating the anastomosis from the peritoneal cavity results in a serious impairment of the normal healing process and a definite increase in anastomotic breakdown and generalized peritonitis.

Although the degree of adhesion formation is difficult to quantify, it is our impression that in the immediate postoperative period a free omental graft behaves to some extent as an inert membrane, in that the biological defences contained in peritoneal adhesions may be denied adequate early access to the immediate suture-line. Thus, in the presence of significant anastomotic leakage a major infection could develop behind the omental barrier, protected from the natural defence mechanisms until established and in many cases overwhelming. The eventual destruction of the omental graft would release large quantities of contaminated material into the peritoneal cavity. Even if the animal survives the postoperative period, the presence of extensive adhesions within the peritoneal cavity could now only be detrimental to long-term survival. This sequence of events would explain the observations of Wilkie (1911) and Pettet and others (1956) on the long-term dangers of adhesion formation in association with free omental graft reinforcement of intestinal anastomoses.

In our experience the marginal strengthening of colonic anastomoses attributable to free omental grafts in surviving animals is far outweighed by the attendant mortality and potential long-term dangers of extensive adhesion formation.

The use of an omental pedicle appears much less dangerous in the present experiment and also results in an increased resistance to forced disruption in the immediate postoperative period (*Fig.* 6). While persistent viability of the pedicle seems assured, the attractive theoretical advantage of an immediate increase in blood-supply to the area of the suture-line was not apparent in our survival figures. As shown in *Table II*, the omental pedicle group of animals ultimately fared no better than the control animals in this respect. In the absence of any striking effects on survival, the omental pedicle does not appear to be a useful adjunct to routine colon surgery and could conceivably predispose to intestinal obstruction.

While the present experiment might be criticized in its failure to examine the problems arising from omental reinforcement of anastomoses performed in the conventional inverting manner, it seems unlikely that the events following leakage from an inverted anastomosis would differ markedly from those reported here. It is probable that free omental grafts would again fail in exactly the group of patients that they are designed to protect, namely, patients with significant anastomotic leakage. Again the experiment might be criticized in its failure to investigate the problems of distal colonic surgery. While this may justify a further experimental series, it seems certain that if omental grafting fails to improve the results of right-sided colonic surgery, its effects on more distal colonic anastomoses will be even more disastrous. We believe that the natural protective powers of the omentum are best left undisturbed by operative interference and that omental reinforcement is unjustified in any area of colonic surgery at the present time.

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THE ROUTINE USE OF ULTRASOUND FOR THE DIAGNOSIS OF POSTOPERATIVE DEEP-VEIN THROMBOSIS IN A DISTRICT GENERAL HOSPITAL

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SUMMARY

The results of 6 months' experience in routine screening for deep-vein thrombosis in all postoperative patients in a district general hospital are presented. Clinical methods and ultrasound diagnosis are compared. Ultrasound was found to be easy and safe to use and to be more accurate than clinical methods. A case is made for the use of ultrasound as a routine method of screening postoperative patients for deep-vein thrombosis.

The diagnosis of postoperative deep-vein thrombosis is a problem that continues to tax all those involved in the care of surgical patients. In 1951 McLachlin and Patterson reviewed venous thrombosis and pulmonary embolism. They stated: 'A clinical test which may help in the detection of thrombi in this area is urgently needed.' Twenty years later the need is still as urgent, and up until now has not been fully met.

There is almost universal agreement that the classic clinical signs of an elevated temperature on the tenth postoperative day, pain in the calf, calf tenderness, ankle oedema, and a positive Homan's sign can no longer be regarded as diagnostic, and often the first sign of deep-vein thrombosis is pulmonary embolism.

Routine use of ultrasound offers a convenient and accurate method of diagnosing deep-vein thrombosis. Using this technique, it was decided to examine daily all postoperative cases in a district general hospital with two aims:—

1. To ascertain the incidence of deep-vein thrombosis.
2. To see if it was feasible in terms of time and workload to examine routinely all patients in this way.

MATERIALS AND METHODS

The machine used was a Sonicaid D.205 (*Fig.* 1). This has the advantage of simplicity of operation, as well as being portable, inexpensive, and totally safe to the patient. The machine consists of a transmitter operated at 2 MHz, a receiver, an audio-amplifier, and a loudspeaker contained in a case approximately 30 × 20 × 7·5 cm. and weighing 9–13·5 kg. which can easily be carried from bed to bed. A transducer containing two ceramic crystals, one of which emits ultrasound and the other acting as a receiver, is connected to the case by a detachable lead. Usually the examiner listens for a 'whooshing' sound, although, if desired, permanent recordings can be obtained by connecting a lead from a pen-recorder to the transmitter, or, alternatively, if he does not wish the patient to hear the sound, the examiner can listen through a set of headphones.

The femoral artery is first located with the transducer by the characteristic pulsatile sound of major arterial flow, and the transducer is moved medially over the femoral vein, the calf is squeezed, and venous flow is detected by the presence of a roar. This is the so-called 'augmentation' or 'A-wave', described by Sigel, Popky, Wagner, Boland, Mapp, and Feigl (1968a). Similar observations can be made with the transducer over the inferior vena cava, the iliac veins, the femoral vein in the adductor canal, or the popliteal vein, thus localizing the site of any obstruction. Obstruction is indicated by the absence of a sound, although with practice one could recognize diminished sound compared with the other leg or with what is recognized as normal values. For the purposes of this study, thrombosis was only diagnosed by the absence of sound.

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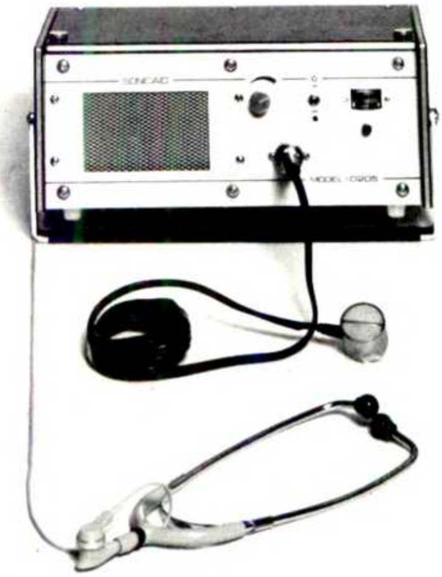

FIG. 1.—The ultrasound apparatus which was used, with probe and headphones.

Table I.—THE DIAGNOSIS OF DEEP-VEIN THROMBOSIS BY CLINICAL AND ULTRASOUND METHODS IN 322 LEGS

CLINICAL DIAGNOSIS	ULTRASOUND DIAGNOSIS		
	Normal	Positive	Total
Normal	299	9	308
Positive	7	7	14
Total	306	16	322

RESULTS

Over a 6-month period, 322 legs were examined. Only those patients undergoing surgery were included in the study. Patients who spent less than 48 hours in hospital for minor surgical procedures were excluded.

It takes only 2–3 minutes to examine patients who are sitting in bed, and this can readily be fitted into the daily round. With practice in this technique it was found that the patients in a ward with 20 beds could be examined in 30–40 minutes, and the procedure did not interfere with ward routine or add much to workload.

Table I shows that of 14 legs thought to have thrombosis on clinical grounds, only 50 per cent were confirmed by ultrasound, but a further 9 legs thought to be clinically negative were positive on ultrasound. Thus, the overall incidence of deep-vein thrombosis on routine screening of all postoperative patients was 5·19 per cent.

There were 4 patients in the series who had pulmonary emboli confirmed by clinical examination, chest radiographs, and electrocardiograms. *Table II* indicates that all of these patients were shown to have had a deep-vein thrombosis by ultrasound, whereas 2 were thought to have been negative on clinical grounds.

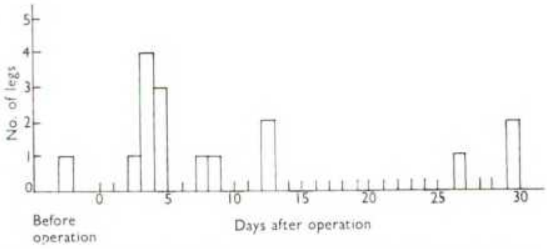

FIG. 2.—The stage at which ultrasound shows deep-vein thrombosis to be present.

Table II.—THE CORRELATION BETWEEN ULTRASOUND AND CLINICAL DIAGNOSIS IN PATIENTS DEVELOPING PULMONARY EMBOLISM

CLINICAL DIAGNOSIS	ULTRASOUND DIAGNOSIS	NO. OF PATIENTS
Positive	Negative	None
Positive	Positive	2
Negative	Positive	2

Fig. 2 shows that 50 per cent of the patients who developed deep-vein thrombosis did so on or before the fourth postoperative day. It is significant that 50 per cent of the patients who had a pulmonary embolus were in this group.

There were 4 deaths in the series, 2 from pulmonary embolism, both of whom had deep-vein thrombosis diagnosed by ultrasound. The presence of deep-vein thrombosis was confirmed at post-mortem examination in both cases. One other death was due to carcinomatosis and the fourth to a myocardial infarct. The cause of death was confirmed by post-mortem examination and neither was shown to have had deep-vein thrombosis either by ultrasound or at post-mortem examination.

DISCUSSION

It is agreed that deep-vein thrombosis presents a considerable problem in diagnosis by clinical methods. The correlation between an operative procedure and pulmonary embolism is well documented. Morrell and Dunnill (1968) reviewed the post-mortem incidence of pulmonary embolism and found that 63 per cent of postoperative deaths had had a recent pulmonary embolus compared with 45 per cent of other deaths. In their series the majority of post-operative pulmonary emboli occurred in the first week.

Deep tenderness was advocated by Murley (1950) as the most constant indication of a deep-vein thrombosis. Lowenburg (1954) stated that a sphygmomanometer cuff could be inflated to a pressure of 250 mm. Hg before discomfort was noted in a normal individual, whereas in one with deep-vein thrombosis discomfort would be experienced at 150 mm. Hg or less. However, Makin (1968) concluded that Lowenburg's test was of no value in the prediction of the likelihood of deep-vein thrombosis, or in the early diagnosis of the condition, as the response was too variable.

Phlebography (Kakkar and Flanc, 1968) and isotopic studies (Flanc, Kakkar, and Clarke, 1968; Atkins and Hawkins, 1968) have been advocated as the methods for routine screening for postoperative deep-vein thrombosis. Both methods involve the use of sophisticated and expensive equipment and require highly skilled technical staff and time. They, therefore, have certain disadvantages for routine use in a busy district general hospital.

Strandness, Schultz, Sumner, and Rushmer (1967) suggested the use of ultrasound for the diagnosis of venous disease, an idea which was expanded by Sigel and others (1968a, b) in America, and by Evans and Cockett (1969) in this country.

These two papers showed ultrasound diagnosis to be far superior to clinical diagnosis of deep-vein thrombosis, and Sigel and others (1968b) confirmed their findings by phlebography, post-mortem examination, or operation. In those with proved thrombosis, ultrasound was 86 per cent accurate compared with a clinical accuracy of 57 per cent. They also found that where clinical diagnosis and ultrasound diagnosis were at variance, ultrasound was accurate in 84 per cent of cases compared with 16 per cent for clinical diagnosis.

Evans and Cockett (1969) compared ultrasound and clinical diagnosis with phlebography or isotopic studies. Of 19 legs thought clinically to have deep-vein thrombosis, 8 were positive by ultrasound compared with 10 positive by radiographic or isotopic studies. In 19 clinically normal legs, 2 were positive by ultrasound compared with 3 positive by radiographic or isotopic methods. Similar results were obtained by Evans (1970) in a series in which there were no false-positives, and he advocated ultrasound as the routine method for screening those at risk of deep-vein thrombosis.

In the present series only half of the patients who were thought to have deep-vein thrombosis on clinical grounds were shown to have a positive deep-vein thrombosis by ultrasound. More significantly, however, over 50 per cent of those who were shown to have a deep-vein thrombosis by ultrasound were judged clinically to be negative. The overall incidence of deep-vein thrombosis on routine screening was found to be 5·19 per cent. These results correlate closely with previously reported series.

It is again emphasized that deep-vein thrombosis occurs much earlier than the classic tenth postoperative day. Of those who had a positive deep-vein thrombosis, 50 per cent were positive on or before the fourth postoperative day. It is this group that is largely clinically negative and it is in this group that half of those who developed pulmonary embolism are found.

The routine use of ultrasound causes the minimum of inconvenience to the patient, and there are no contra-indications to its use to exclude deep-vein thrombosis in even seriously ill patients. The technique described takes little time to learn and the interpretation of results is simple, the presence of a venous roar or A-wave when the calf is squeezed signifying normal flow and the absence of sound indicating a thrombus. To examine postoperative patients takes little more time than would normally be spent in assessing such patients each day, and can readily be fitted into the daily routine.

Thus, after 20 years it would seem that the answer to McLachlin's plea for a simple clinical test to help in the detection of deep-vein thrombosis has been found in ultrasonics. Certainly it is time that this procedure became part of the routine management of all postoperative patients.

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EXTRAHEPATIC BILIARY DRAINAGE IN EXPERIMENTAL LIVER INJURY

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SUMMARY

A case has been made by many authors for the routine drainage of the biliary tract in patients with liver injuries, and this case is summarized. To test the logic of such treatment the outcome of a standard lethal injury in dogs was studied and was found not to be influenced by drainage of the common bile-duct. Survival was improved by excision of the damaged tissue. The experimental evidence does not support the practice of routine drainage of the extrahepatic biliary tract.

LIVER necrosis, subphrenic abscess, and bile fistula cause morbidity and mortality after liver injuries. Merendino, Dillard, and Cammock (1963) suggested that routine decompression of the extrahepatic biliary tree might lessen complications by decreasing the leakage of bile through the damaged liver tissue. This idea gained rapid and wide acceptance, especially in the United States, so that drainage of the common bile-duct or gall-bladder became regarded as an important part of the treatment of liver injuries (Byrne, 1964; Longmire, 1965; Madding and Kennedy, 1965; Williams and Byrne, 1966; Mays, 1971). A summary of the arguments for and against extrahepatic biliary drainage has been given by Lucas (1970). Perry and La Favre (1964) extended this concept when they suggested that extrahepatic biliary drainage might remove the need for other external drainage. Experimental support for this idea followed when Lane, Johnson, and Walker (1967) and Wasowski (1968) reported that extrahepatic biliary drainage improved the results in their experimental preparations. Lane and others (1967) suggested that tube drainage of the common bile-duct in dogs produced a significant improvement in survival over control animals.

It remains to be shown that extrahepatic biliary drainage confers any advantage over, or in addition to, formal excision of a liver injury. The latter is soundly based on established surgical principles and is more frequently possible because of adequate resuscitation and an understanding of liver surgery. This paper compares drainage and excision.

MATERIALS AND METHODS

Adult mongrel dogs, weighing 10–15 kg., were used. General anaesthesia was induced by an intravenous injection of 5 per cent thiopentone sodium and was maintained with nitrous oxide and oxygen through an endotracheal tube. Cannulae were inserted into the femoral artery and femoral vein—one for pressure measurement and the other to permit bleeding and reinfusion. The method of study employed the standard injury described by Lane and others (1967), in which a rat-trap is allowed to spring closed across the chosen lobe of the liver. In their hands (Lane and others, 1967) the injury was always lethal, but our preliminary experiments with this model resulted in the death of only 4 of 18 dogs. A combination of liver injury and bleeding was then used (a pattern that incidentally more closely resembles that of human liver injury) which without treatment was lethal.

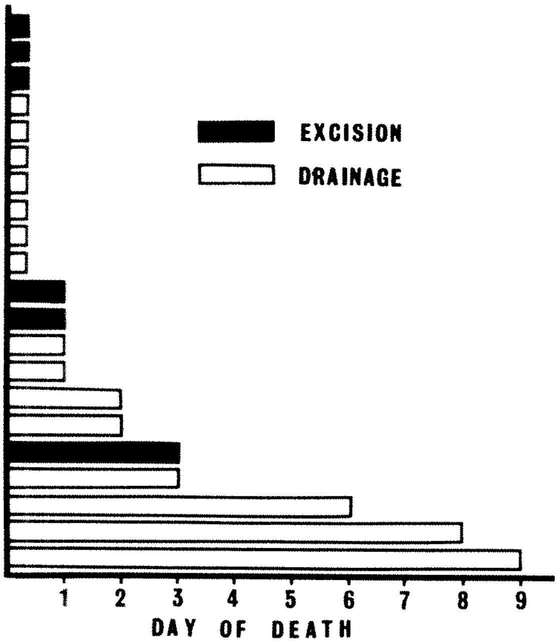

FIG. 1.—Day of death of animals, showing method of treatment. The uppermost 10 animals all died within 8 hours of operation.

Through an upper midline incision the left lateral lobe of the liver was delivered into the wound, was placed on the base of a fully opened rat-trap, and was submitted to six blows. The effect of the injury was to leave the lobe of the liver hanging by a few strands of tissue which contained blood-vessels. Bleeding was profuse initially, but soon stopped. Directly after injury, blood was run from the femoral vein cannula at a rate of 50 ml. per minute (Ehrlich, Kramer, and Watkins, 1969) until the systolic blood-pressure fell to a level of 73 ± 25·5 mm. Hg. After 1 hour an equal volume of Hartmann's solution was reinfused and the animal was randomly allocated for treatment either by drainage of the common bile-duct or by excision of the damaged tissue.

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In those animals which were treated by drainage a Portex nylon cannula (external diameter, 2·75 mm.) was placed in the supraduodenal part of the common bile-duct. Damaged tissue was excised after clamping and ligating those structures which remained in the line of the liver wound. Good haemostasis was secured in this way. The laparotomy wound was closed and the animal was allowed to recover. Antibiotics were not given. Animals alive after 10 days were classed as survivors.

RESULTS

The outcome of these experiments is shown in *Table I*. There is a significant ($P < 0{\cdot}05$) difference between the animals which were treated by excision and those which were treated by drainage when the results are analysed using Fisher's test (Langley, 1970).

Table I.—RESULTS OF TREATMENT

TREATMENT	NO. OF ANIMALS TREATED	NO. OF ANIMALS SURVIVING
Excision	13	7
Drainage	16	1

Table II.—COMPARISON OF THE EFFECTS OF BLEEDING

TREATMENT	INITIAL BLOOD-PRESSURE (mm. Hg systolic)	BLOOD-PRESSURE AFTER BLEEDING (mm. Hg systolic)	RATIO
Excision	172 ± 25·7	78 ± 25·6	2·49 ± 0·98
Drainage	175 ± 33·4	68 ± 23·9	2·89 ± 0·79
	t	0·97	1·19
	P	$0{\cdot}40 > P > 0{\cdot}30$	$0{\cdot}30 > P > 0{\cdot}20$

Because the only objective measurement of the severity of the injury was the level to which the blood-pressure fell, this decrease has been compared between the two groups both directly and by expressing the ratio of the initial systolic blood-pressure to the systolic blood-pressure after bleeding. Student's t-test was applied to these figures and the results confirm that the groups were similarly treated (*Table II*).

The time of death of the animals is shown in *Fig.* 1, which indicates that only 1 death in an animal which was treated by excision occurred later than 24 hours after operation. In contrast, 5 deaths in the group which was treated by drainage occurred in the period from 24 hours to 9 days following operation.

We consider that these results confirm the hypothesis that drainage would not be preferable to excision as a method of treatment for liver injury.

DISCUSSION

As a treatment option in this model, excision is clearly superior to drainage, converting a lethal injury into one which has about an equal chance of death. Excision is particularly effective in preventing deaths which occur later than 24 hours after operation. This conclusion differs from that of Lane and others (1967) and Wasowski (1968). The results of Lucas, Lenaghan, and Walt (1969), although they could not be statistically analysed, support our findings; the injury that they inflicted on their animals was not lethal, but extrahepatic biliary drainage did not influence the mortality or the rate of abscess formation. However, their most important observation was that extrahepatic biliary drainage did not produce a significant fall in the extrahepatic pressure, even when the common bile-duct had been ligated. Thus, it seems unlikely on theoretical grounds that drainage will have anything to offer, a conclusion borne out by the present results.

The results described do not show whether drainage could better the outcome after excision. However, in view of the failure of drainage to reduce intrahepatic biliary pressure and the preliminary results of these two treatment options in man (Lucas and Walt, 1970), it seems unlikely that synergism would occur.

We conclude that drainage of the common bile-duct as part of the standard treatment for liver injuries is not justified.

Acknowledgement.—I am indebted to Professor Hugh Dudley for his advice and encouragement during this study.

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A TECHNIQUE FOR DETECTING REJECTION EPISODES IN HUMAN TRANSPLANT RECIPIENTS USING RADIOACTIVE FIBRINOGEN*

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SUMMARY

Radioactive ^{125}I-labelled human fibrinogen was given to 32 patients who had received renal transplants. In each case radioactivity was measured over the transplant and expressed as a percentage of the value recorded over the heart. Recipients that were experiencing rejection episodes had higher levels of radioactivity over their transplants when compared with patients who were free of rejection at the time. It is suggested that this technique could be of value in the diagnosis of rejection episodes, particularly in those recipients who remain oliguric after transplantation.

It is well recognized that fibrinogen is deposited as fibrin in the vessels of kidney transplants that are undergoing rejection. Such deposits have been found in sections taken from rejected kidney transplants (Porter, 1967; Dammin, 1968; Lindquist, Guttman, and Merrill, 1968; McKenzie and Whittington, 1968; Busch, Braun, Carpenter, Corson, Galvanek, Reynolds, Merrill, and Dammin, 1969), and fibrin degradation products have been detected in the urine of transplanted patients at times of rejection (Braun and Merrill, 1968; Antoine, Neveu, and Ward, 1969; Colman, Braun, Busch, Dammin, and Merrill, 1969; Carlsson, Hedner, Nilsson, Berkentz, and Ljungqvist, 1970; Clarkson, Morton, and Cash, 1970).

The use of ^{125}I-fibrinogen has become popular recently as a method of detecting deep-vein thrombosis in the lower limbs, and the labelled product is now freely available. In a previous report (Salaman, 1970) experiments were described in which ^{125}I-fibrinogen was given to a small group of patients with renal transplants in order to determine whether the labelled fibrin would be concentrated in the kidney at times of rejection. It was found by external scintillation counting that radioactive fibrin was indeed retained by renal transplants that were undergoing rejection, and it was suggested that this finding might be of use as a test for rejection. A larger group of patients has now been studied and the results obtained are presented here.

MATERIALS AND METHODS

Thirty-two renal transplant recipients were studied on one or more occasions after transplantation and all had consented to receiving radioactive material. Two kidneys had been obtained from living related donors and the remaining 30 were from cadavers. Details of the techniques that were used have already been published (Salaman, 1970). For each test 90–130 μc. ^{125}I-labelled human fibrinogen were injected intravenously, and counts were recorded 6 hours later and then daily from over the patient's heart, renal transplant, bladder, contralateral iliac fossa, and liver. Uptake of radioactive iodine by the thyroid was blocked by administering 50 mg. of potassium iodide daily for 2 weeks, commencing on the first day of the test. Surface radioactivity was measured in the early experiments with a semi-portable detector linked to a linear amplifier and scaler, but in later experiments a small transistorized rate-meter (Pitman Model 235) was used. On each day of the test the counts registered over the transplant were expressed as a percentage of the counts recorded over the heart. A value greater than 120 per cent was regarded as evidence that radioactive fibrin had been deposited within the kidney.

Of the 32 patients studied, 5 were investigated on two occasions and 1 was tested three times. The results will be considered in four groups.

The tests in group 1 were performed on recipients with well-functioning transplants showing no evidence of rejection. In group 2 the tests were conducted in recipients who had had good renal function previously, but who were showing signs of rejection at the time that the test was performed. These rejection episodes were diagnosed from a renal biopsy result or from an observed deterioration in renal function in the absence of any other cause. In groups 3 and 4 the tests were undertaken in recently transplanted patients who were oliguric as a result of ischaemic tubular necrosis. It could be shown from renal biopsy and other evidence that the recipients in group 3 were free of rejection, whereas those in group 4 were experiencing a rejection episode during this early postoperative period.

RESULTS

The injection of ^{125}I-fibrinogen was uncomplicated and no patient became jaundiced. Radioactivity levels in the body declined rapidly after the injection owing to the short biological half-life (±3 days) of the labelled fibrinogen (*Fig.* 1). As a result, scintillation counting became difficult and somewhat inaccurate when continued for more than 5 days, and only those readings obtained within this period have been evaluated. The highest level of 'percentage radioactivity' that was recorded for each renal transplant during this interval is that given in *Tables I–IV*.

Group 1: Functioning Transplants with No Rejection.—The results of the nine tests that were performed in this group of patients are given in *Table I*. In 5 cases the transplant radioactivity remained below that of the heart throughout the period of testing (maximum transplant radioactivity

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* Based on a paper read to the Surgical Research Society at Cambridge on 3 July, 1970.

< 100 per cent). The readings that were obtained for *Case* 5 are shown in *Fig.* 1. In 2 patients the transplant radioactivity exceeded marginally that of the heart, and maximum values of 108 per cent were obtained. In the 2 remaining patients much higher values were found (140 and 290 per cent), although neither was thought to be undergoing rejection. Both patients had developed painful swellings in the region of their transplants at the time that the tests were performed, and it was thought likely that in each case these high readings were caused by a haematoma that had formed around the transplant. One transplant (*Case* 8) was explored subsequently and a haematoma was found.

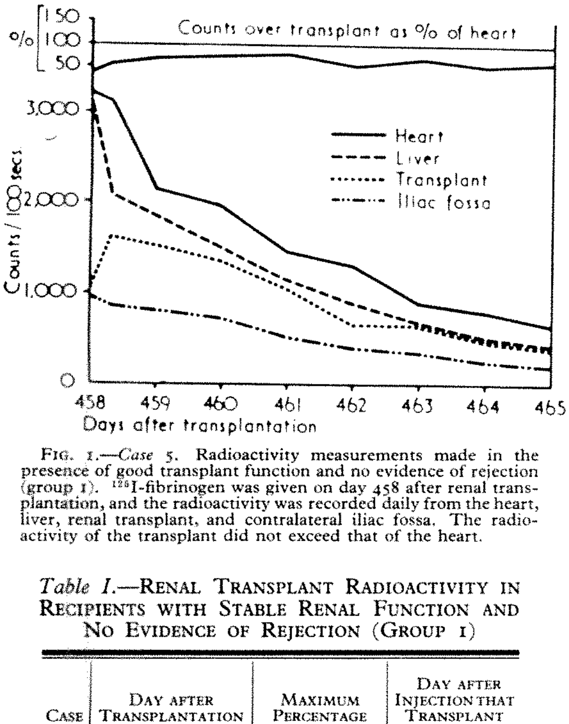

FIG. 1.—*Case* 5. Radioactivity measurements made in the presence of good transplant function and no evidence of rejection (group 1). ^{125}I-fibrinogen was given on day 458 after renal transplantation, and the radioactivity was recorded daily from the heart, liver, renal transplant, and contralateral iliac fossa. The radioactivity of the transplant did not exceed that of the heart.

Table I.—RENAL TRANSPLANT RADIOACTIVITY IN RECIPIENTS WITH STABLE RENAL FUNCTION AND NO EVIDENCE OF REJECTION (GROUP 1)

CASE NO.	DAY AFTER TRANSPLANTATION ON WHICH TESTS BEGAN	MAXIMUM PERCENTAGE RADIOACTIVITY OF TRANSPLANT	DAY AFTER INJECTION THAT TRANSPLANT RADIOACTIVITY EXCEEDED 120 PER CENT
1	22	108	—
2	449	99	—
3	239	99	—
4	207	96	—
5	458	74	—
6	209	97	—
7	301	108	—
8	9	140*	3
9	9	290*	2

* Patients with wound haematomata (*see* text).

Group 2: Functioning Transplants with Rejection.—The tests in this group were conducted in 11 patients who were suspected of having rejection at the time. In 7 patients there was a rapid rise in the percentage radioactivity of the transplant, and values greater than 120 per cent were recorded within 48 hours of the injection (*Table II*). These patients were given antirejection therapy, and renal function recovered in 4. Three patients failed to respond and a rejected kidney was removed a few weeks later from 2 of them. A typical result (*Case* 10) is shown in *Fig.* 2.

The 4 other patients in this group showed little or no rise in renal transplant radioactivity. One of these was receiving anticoagulant drugs at the time of the rejection episode, and the 3 others were experiencing a much more gradual deterioration in renal function that had progressed despite treatment with prednisone, antilymphocyte globulin, and graft irradiation. Histological changes in these kidneys were those of an obliterative vascular rejection in 2 and recurrent nephritis in the third.

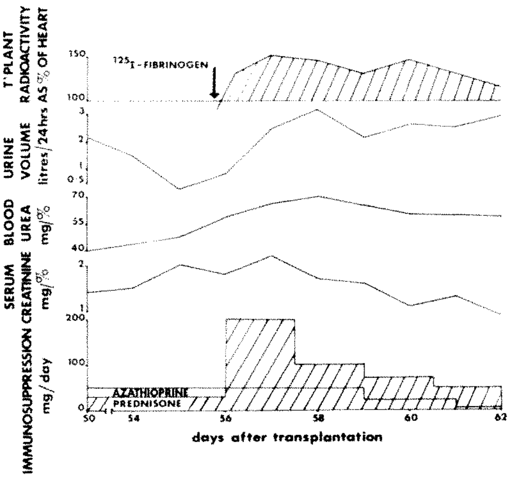

FIG. 2.—*Case* 10. Transplant radioactivity measured during an episode of acute rejection (group 2). Renal function started to deteriorate on the fifty-fifth day after transplantation and ^{125}I-fibrinogen was given on the following day. A rapid rise was observed in the percentage radioactivity of the transplant, which reached a maximum of 150 per cent in 24 hours. The rejection episode was treated successfully.

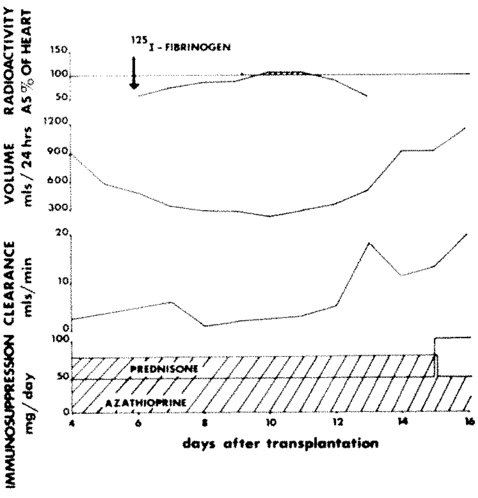

FIG. 3.—*Case* 21. Transplant radioactivity measured at a time of ischaemic tubular necrosis (group 3). Urine volume fell below 500 ml. per 24 hours on the fifth day. ^{125}I-fibrinogen was given on the sixth day, and very little concentration of radioactivity took place in the renal transplant. Renal function started to recover on the thirteenth day and no antirejection treatment was given.

Group 3: Oliguric Transplants with No Rejection.—Ten patients were examined in this group. All were oliguric as a result of ischaemic tubular necrosis, and ^{125}I-fibrinogen was given in most instances when oliguria had persisted for more than 1 week. Rejection could be discounted in 4 cases from evidence obtained by renal biopsy, and was considered to have been unlikely in the remainder when renal function returned without recourse to antirejection therapy.

Table II.—RENAL TRANSPLANT RADIOACTIVITY IN RECIPIENTS WITH REJECTION WHO HAD HAD GOOD RENAL FUNCTION PREVIOUSLY (GROUP 2)

CASE NO.	TYPE OF REJECTION	DAY AFTER TRANSPLANTATION ON WHICH TEST BEGAN	MAXIMUM PERCENTAGE RADIOACTIVITY OF TRANSPLANT	DAY AFTER INJECTION THAT TRANSPLANT RADIOACTIVITY EXCEEDED 120 PER CENT	OUTCOME AFTER ANTI-REJECTION TREATMENT
1	Acute	31	247	1	Recovered
10	Acute	56	150	1	Recovered
11	Acute	177	130	2	Recovered
12	Acute	48	142	1	Recovered
13	Acute	38	250	2	Rejected; kidney removed
14	Acute	24	150	2	Rejected
15	Acute	4	200	2	Rejected; kidney removed
16	Acute	41	110	—	Rejected; kidney removed
17	Chronic	580	80	—	Died
18	Recurrent nephritis	278	120	—	Kidney removed
5	Chronic	640	77	—	Died

Table III.—RENAL TRANSPLANT RADIOACTIVITY IN RECIPIENTS WITH ACUTE TUBULAR NECROSIS (A.T.N.) BUT NO EVIDENCE OF REJECTION (GROUP 3)

CASE NO.	DAY AFTER TRANSPLANTATION ON WHICH TEST BEGAN	MAXIMUM PERCENTAGE RADIOACTIVITY OF TRANSPLANT	DAY AFTER INJECTION THAT TRANSPLANT RADIOACTIVITY EXCEEDED 120 PER CENT	BIOPSY REPORT*	DAY OF ONSET OF DIURESIS
12	6 22	96 109	—	A.T.N. (9 and 22)	26
14	10	110	—	—	14
19	9	87	—	—	15
20	2	120	—	—	8
21	6	105	—	—	16
22	8	110	—	—	11
23	21	63	—	A.T.N. (23)	Died on day 30; kidney did not function
24	4	100	—	A.T.N. (8)	21
25	8	95	—	—	14
26	7	130	3	A.T.N. (13)	15

* Day after transplantation on which the biopsy was performed is indicated in parentheses.

Table IV.—RENAL TRANSPLANT RADIOACTIVITY IN PATIENTS WITH A COMBINATION OF ACUTE TUBULAR NECROSIS AND REJECTION (GROUP 4)

CASE NO.	DAY AFTER TRANSPLANTATION ON WHICH TEST BEGAN	MAXIMUM PERCENTAGE RADIOACTIVITY OF TRANSPLANT	DAY OF TEST THAT TRANSPLANT RADIOACTIVITY EXCEEDED 120 PER CENT	REPORT ON BIOPSY OR NEPHRECTOMY SPECIMEN*	OUTCOME AFTER ANTIREJECTION TREATMENT
10	6	270	2	—	Recovered
13	10	140	2	—	Recovered
27	17	144	2	Rejection + A.T.N. (19)	Recovered
28	7	135	5	Rejection (30)	Rejected; kidney removed
29	14	140	3	Rejection (23)	Died
30	5	165	4	Rejection + A.T.N. (12)	Rejected; kidney removed
31	4	180	1	Rejection + A.T.N. (9)	Recovered
32	6	150	5	Rejection (13)	Rejected; kidney removed

* Day after transplantation on which histology was obtained is indicated in parentheses.

The results obtained in this group are given in *Table III*. The levels of radioactivity recorded from the transplants were a little higher than those in group 1, but only 1 recipient had a level that exceeded 120 per cent. The results obtained for *Case* 21 are shown in *Fig*. 3 and are typical for the group.

Group 4: Oliguric Transplants with Rejection.—The eight recipients in this group were tested when they were oliguric as a result of ischaemic tubular necrosis. In addition, rejection was suspected and was confirmed by histological examination of renal biopsies in 3 cases and by examination of the excised renal transplant in 3 others. In the remaining 2 recipients histological evidence was lacking and rejection was inferred from the fact that renal function improved within 24 hours of administering a booster dose of corticosteroids. After injection of ^{125}I-fibrinogen all 8 patients exhibited a progressive rise in the percentage radioactivity of their transplants to reach maximum levels of 135–270 per cent (*Table IV*). Detailed results obtained for *Case* 30 are shown in *Fig*. 4. This patient received a cadaveric renal transplant with a warm ischaemic time of 75 minutes. The kidney failed to excrete any urine initially and on the fifth day ^{125}I-fibrinogen was given. A slow but progressive rise was observed in the percentage transplant radioactivity, which reached a value of 165 per cent after 5 days. A biopsy was performed 2 days later which showed the features of advanced rejection (*Fig*. 5). Because of severe herpes simplex infection of the patient's face it was considered unwise to give large doses of immunosuppressive drugs, and instead the transplant was allowed to be rejected completely.

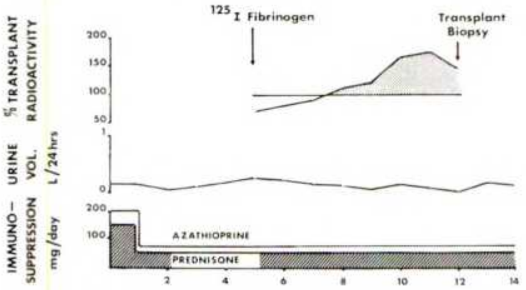

FIG. 4.—*Case* 30. Transplant radioactivity in a case of ischaemic tubular necrosis combined with rejection (group 4). A progressive rise was observed in the percentage radioactivity of the transplant.

In 1 patient (*Case* 28) a rise in transplant radioactivity occurred comparatively late after injection of the isotope, and the significance of this rise was not appreciated until rejection had become irreversible. ^{125}I-fibrinogen had been administered on the seventh day when the transplant was still oliguric as a result of ischaemic tubular necrosis. Although renal function soon showed signs of recovery the percentage transplant radioactivity began to increase steadily (*Fig*. 6). This was not recognized as an early indication of rejection until 1 week later when renal function fell once more. Antirejection treatment was instituted but this was not successful in restoring function, and soon afterwards the rejected kidney was removed.

All the patients in this group were treated for rejection once the diagnosis had been made, and the eventual outcome is recorded in *Table IV*.

DISCUSSION

The results obtained for the recipients in group 1 have shown that well-functioning kidney transplants do not take up radioactive fibrinogen from the circulation to any great extent. The 2 patients who had raised levels of transplant radioactivity were thought to have perinephric haematomata, for both had developed tender swellings beneath their operative incisions without any accompanying fall in renal function. Such a haematoma would 'trap' labelled fibrin in the vicinity of the kidney and would maintain the radioactivity at a high level whilst that in the blood would continue to fall. The resulting effect would be an apparent increase in the percentage radioactivity of the transplant.

During episodes of acute rejection the uptake of labelled fibrinogen by the renal transplant was increased, and this accords with the findings of others who noted fibrin deposits in histological preparations of rejected renal transplants (Lindquist and others, 1968). There was 1 patient (*Case* 16), however, who underwent an acute rejection episode without displaying any increase in the level of transplant radioactivity. This patient had been receiving an anticoagulant drug (warfarin, 4 mg. per day), which might have been a factor in producing this false-negative result, since warfarin is known to have an inhibitory effect on fibrin deposition in renal allografts which are undergoing rejection (Kincaid-Smith, 1970). Low levels of radioactivity were also found over the transplants of 3 recipients with chronic rejection or recurrent nephritis. It is known that in these conditions fibrin deposition does not occur to

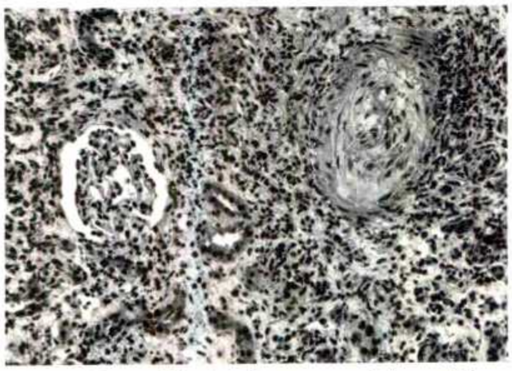

FIG. 5.—*Case* 30. Histological appearance of the renal biopsy. There is a heavy infiltration of mononuclear cells and destruction of tubules. An interlobular arteriole shows marked intimal thickening with virtual obliteration of its lumen.

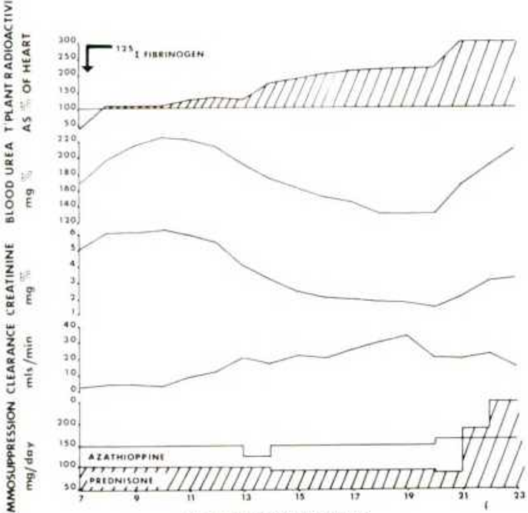

FIG. 6.—*Case* 28. Transplant radioactivity measured in a recipient who underwent rejection following an episode of ischaemic tubular necrosis (group 4). A rise in transplant radioactivity was apparent a week before rejection brought about a fall in renal function.

any great extent (McKenzie and Whittington, 1968; Kincaid-Smith, 1970), and it is quite possible that such small deposits of fibrin may not be detected by this technique.

The period of oliguria which frequently follows cadaveric renal transplantation is a difficult time for the clinician, as rejection is not easy to detect and kidneys may be lost as a consequence. The test described above has been of value in this situation (groups 3 and 4), and the false-positive rate has been acceptably low (1 case). There were no false-negative results, and the raised levels of transplant radioactivity that were observed were related to rejection episodes and were frequently the first indication that such episodes were taking place.

Not infrequently we have observed oliguria in the second week of transplantation after an initial period of renal function. An example is shown in *Fig.* 3. Our previous practice has been to treat all such cases as rejection, but by using ^{125}I-fibrinogen we have now found it possible to differentiate rejection from 'delayed' tubular necrosis and in this way avoid prescribing large, potentially harmful doses of drugs to patients who do not require them.

The ^{125}I-labelled fibrinogen test would appear to be devoid of complications and the results of this trial suggest that it could become a useful tool in the management of renal transplant recipients.

Acknowledgements.—I would like to thank Professor J. P. Blandy and Mr. D. L. Crosby for permission to report patients under their care.

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ABDOMINAL WOUND INFECTIONS AND PLASTIC WOUND GUARDS

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SUMMARY

A study is reported of the influence of plastic wound protectors on the incidence of wound infection in patients having abdominal operations involving the opening of the alimentary tract or biliary system.

Of 167 patients, 84 were randomly allocated to a group in which Vi-Drape wound protectors were used during the operation. In the whole series there was a low incidence of wound infection (12 per cent), but no difference was found between those who had plastic wound protectors and those who did not.

INFECTION in surgical wounds often results from organisms contaminating the wound at the time of operation. These organisms can come from the members of the surgical team, from the operating-room atmosphere, from the patient's skin, or from the organisms in the patient's alimentary tract. The high incidence of wound infection after abdominal surgery, and in particular after operations on the large bowel, suggests that contamination with organisms from the alimentary tract plays an important part. For this reason it would seem wise to protect the wound edges in order to minimize the risk of contamination. Protection with permeable wound guards is likely to be ineffective as these merely act as wicks, dipping into the wound and ensuring prolonged contact between the wound and the organisms. An impervious type of wound guard theoretically offers the greatest chance of protecting the wound edges, and it also has the theoretical advantage of preventing desiccation of the wound edge during the operation and reducing the physical trauma of damage to the wound edge by instruments and handling. The theoretical disadvantage is that infected intraperitoneal fluid may track up around the outside of the plastic drape by capillary action and so contaminate the wound, and also that organisms from the patient's own skin may similarly track along to the wound edge.

Impervious self-retaining wound liners have been produced in convenient sterile packs for use during laparotomy, and there have been enthusiastic reports about their efficacy in reducing the rate of wound infection (Harrower, 1968; Ellis, Manz, Carlson, Humphrey, and Nicoloff, 1969). Other reports, however, have failed to demonstrate any significant reduction in abdominal wound infection when these impervious drapes have been used. The present report is of a prospective controlled trial designed to investigate the effects of the use of plastic wound drapes on the incidence of abdominal wound infection.

MATERIALS AND METHODS

The impervious wound drapes used were Vi-Drape (Parke-Davis). These are transparent plastic sheets having a central hole of 18, 23, or 28 cm. diameter, around which is fixed a semi-rigid circular collar. This collar can be squeezed flat so that the central hole in the drape is introduced into the abdominal wound. When released the collar springs back to a circle beneath the abdominal wall, holding the plastic sheet in close proximity to the wound edge.

Patients were chosen for the trial who were to have a midline or paramedian laparotomy associated with the opening of some part of the bowel or biliary tract. These patients were considered to have a high risk

Table I.—Example of a Form which was used to record Data in the Trial

A Trial to Evaluate the Efficacy of Vi-Drape Abdominal Wound Protectors in preventing Wound Infection

VI-DRAPE to be used YES ☐ NO ☐

Patient's Number in Trial ☐

Name:—	Age ☐ yr. Sex	1 = Male 2 = Female	Date of operation ☐☐☐ Day Mth. Yr.

Diagnosis:—	Operation:—	Operative findings:—

	Date From	Date To	Antibiotic	Dose	Reason
Antibiotics given pre- or post-operatively					

- -

Surgeon: Please also complete the following particulars, then detach at above dotted line and send this part of the form to Bacteriology Department.

This patient is included in the Vi-Drape trial — Patient's number in trial ☐

Name:—	Ward:—	Hospital number:—	Date of operation ☐☐☐ Day Mth. Yr.

Bacteriologist: The following to be completed by Dr. Brown and the form then sent to Mr. Alexander Williams' research office in Withering House.

State of wound at 3 days, date ☐☐☐ Day Mth. Yr.	0 = No infection 1 = Mild infection 2 = Moderate infection 3 = Severe infection	Culture, if taken:—
State of wound at 7 days, date ☐☐☐ Day Mth. Yr.	0 = No infection 1 = Mild infection 2 = Moderate infection 3 = Severe infection	Culture, if taken:—

Bacteriologist's comments:—

of wound contamination with intestinal organisms. The patients were all operated on by one of two surgical firms. Once the suitability for inclusion in the trial of a particular patient had been established the book of record forms (*Table I*) was consulted in order to place the patient in either the trial group, using Vi-Drape abdominal wound protectors, or the control group, using either no wound protection or standard permeable cloth wound guards. After consulting the record book, one half of a form was completed, giving the date, the patient's name, number, and ward, and the type of operation performed, but not indicating the type of wound protection used. This half of the form was detached and sent to the bacteriology department. On the other half of the form the same particulars were indicated, plus a record of the pre- and postoperative antibiotic régime, the operative diagnosis, and a note if there was any particular wound contamination. Apart from the use or non-use of the Vi-Drape abdominal wound protector, there was no other variation from the usual operative routine. Wound lavage, drainage, or local antibiotic application was used according to the judgement of the particular surgeon. Although the surgeon obviously knew which type of wound protection he had used, there was no conscious differentiation in the technique of wound closure or in the treatment of the wound.

The bacteriologist, who was informed of the entry of the patient into the trial by the receipt of the appropriate half of the form, visited the patient in the ward and inspected the wound on two separate occasions after the operation, classifying the wound as showing either no infection, mild wound infection (erythema), moderate wound infection (exudate), or severe wound infection (pus). If he considered the wound to be infected, swabs were taken for culture. The bacteriologist inspecting the wound did not know in which treatment group the patient had been included. For the first 96 patients in the trial the inspection by the bacteriologist was on the third and the seventh postoperative days. It became clear, however, that there was never any indication of infection on the third day even in those patients who later showed infection. The protocol was then altered to allow inspection on the seventh and tenth days. In those patients discharged before the tenth day it was considered that there was no infection if the wound had been normal on the seventh day and if no subsequent wound infection was reported by the patient when he returned to follow-up.

The allocation to either the trial or the control group was by random selection, and was designed to allow equality in numbers after each group of 10 cases.

Completed records were received from 170 patients, 3 of whom had died within 24 hours of operation and were therefore excluded from the analysis. Eighty-four patients were in the Vi-Drape group and 83 in the control. Seventy-five were male and 92 female, the sexes being divided equally between the two groups. The ages of the patients ranged from 16 to 92 years, the median being in the range 51–60 for both groups. There were, however, slightly more older patients in the Vi-Drape group. Of the 44 patients aged over 60, 27 (61 per cent) were in the Vi-Drape group.

The site of operation is shown in *Table II*. The operations on the stomach and duodenum were usually for peptic ulcer, there being 30 vagotomies and pyloroplasties for duodenal ulcer and 12 Billroth-I gastrectomies for gastric ulcer. Three patients had perforated duodenal ulcer. Operations on the small bowel were all for Crohn's disease, and operations on the large bowel were usually for carcinoma, although 3 were for chronic inflammatory disease of the bowel. The commonest operation on the biliary tree was cholecystectomy, which was always accompanied by an operative cholangiogram. Nine of the operations were for acute cholecystitis. There were 5 operations on the common bile-duct.

Preoperative antibiotics were administered in 41 patients: in 20 as part of preoperative bowel preparation, in 11 because of pre-existing chest infection, in 4 because of acute cholecystitis, and in the remainder for a variety of reasons, such as prophylaxis in patients with rheumatic heart disease. Antibiotics were used postoperatively in 94 patients, and in 9 this was a continuation of the antibiotic course started preoperatively. Both the preoperative and postoperative antibiotic cases were equally divided between the two treatment groups.

Table II.—THE SITE OF OPERATION

SITE OF OPERATION	NO. OF PATIENTS		
	Vi-Drape Group	Control Group	Total
Stomach and duodenum or jejunum	30	34	64
Small bowel only	3	3	6
Large bowel	20	12	32
Gall-bladder and bile-ducts	29	31	60
Other	2	3	5

Seventeen patients were recorded as having gross contamination of the wound by the intestinal contents: 4 from the perforated peptic ulcer, 9 from contamination with bile, and the remainder was due to the opening of an abdominal abscess or to leakage from the bowel. All of these patients received postoperative antibiotic therapy. Ten of the patients were in the Vi-Drape group and 7 were in the control group.

RESULTS

In the analysis of results it was decided to include all the patients with some wound infection, even those with mild infection, in the infected group. There were 20 wound infections, giving an overall infection rate of 12 per cent. Ten of these were in the Vi-Drape group (11·9 per cent) and 10 were in the control group (12 per cent). Five of these had only minor infections with wound redness but no suppuration, and 1 had infection in a gastrostomy drainage wound only and not in the main wound which was protected by the Vi-Drape. If these 6 are excluded, the incidence of infection in the remainder is 7·1 per cent (6 patients) for the Vi-Drape group and 9·7 per cent (8 patients) for the control group. Only 2 of the 20 patients were under 40 years old, while 4 were 80 years or more, showing the expected higher incidence of wound infection in older people. Since there were more older patients in the Vi-Drape group a higher incidence of wound infection in this group might have been expected. The infected wounds in relation to the operation site are shown in *Table III*, which also gives the incidence of infection for each site.

In the total series there were more large-bowel operations in the Vi-Drape group than in the control group, which in part explains the large number of wound infections in the large-bowel operations of the Vi-Drape group. Only 3 of the 17 patients with gross wound contamination at the time of operation developed a wound infection, 2 of whom were in the control group: 1 with a perforated duodenal ulcer and the other with acute cholecystitis. Only 1 out of the 10 patients with Vi-Drapes who had operative contamination developed wound infection, and this patient had carcinoma of the colon with a pericolic abscess.

Table III.—THE SITE OF OPERATION RELATED TO THE NUMBER OF INFECTED WOUNDS

SITE OF OPERATION	NO. OF INFECTED WOUNDS			PERCENTAGE INCIDENCE
	Vi-Drape Group	Control Group	Total	
Stomach and duodenum or jejunum	2	2	4	6·25
Small bowel	0	0	0	0
Large bowel	5	1	6	18·8
Gall-bladder and bile-ducts	3	5	8	13·3
Other	0	2	2	40

Table IV.—NON-INFECTION WOUND COMPLICATIONS

Vi-Drape Group (5)	*Control Group* (5)
Late haematoma; no infection	Bullae possibly due to adhesive plaster
Haematoma	Slight wound erythema (2 patients)
Dehiscence; sterile culture	Oedema of centre of wound (2 patients)
Tissue bruising	
Later development of fistula	

In addition to noting wound infection, the bacteriologist made a special mention about the wound in 10 other patients, 5 in each group. These findings are summarized in *Table IV*. In the opinion of the bacteriologist these wounds were not infected, but even if some or all of them were included with the wound-infection patients the results would not materially be affected.

DISCUSSION

Despite the facts that very stringent criteria were laid down for the diagnosis of wound infection and that the assessment was done by an independent observer, the overall incidence of wound infection in this series was low. Four other recent series are summarized in *Table V*. In by far the largest series, that recorded by Jepsen, Larson, and Thomsen (1969) from Copenhagen, 145 cases of purulent wound infection are reported in 706 operations (an incidence of 20·5 per cent).

A comparison of this series with other reported series shows some conflicting results. In a similar series to ours which was reported by Harrower (1968) a prospective trial was performed by allocating patients alternately to receive either impervious wound guards or permeable cloth wound guards after operation. In the control series of 97 patients there were 9 patients with major sepsis and 5 with minor sepsis, an overall infection rate of 15 per cent, whereas in the 127 patients who were treated with impermeable wound guards only 3 patients had wound sepsis, which was of a minor nature, an incidence of 2·4 per cent. In this report, however, no mention is made of the criteria of designation of wound infection, nor what steps were taken to ensure the objectivity of those recording the wound infection. Similar beneficial results following the use of Vi-Drape wound guards were reported by Ellis and others (1969), who allocated their patients to either control or Vi-Drape groups according to the last digit of their hospital number. In their control group they reported 30 patients with wound infection out of a total of 129 (an incidence of 23 per cent), whereas when Vi-Drape wound protectors were used there were only 4 patients with infection out of a total of 135 (an incidence of 3 per cent). Once again this report does not define wound infection or how objectivity of recording of wound infection was ensured. In another recent series by Maxwell, Ford, Peterson, and Richards (1969) a control trial was begun by treating alternate patients by either a plastic adherent skin drape alone or a plastic adherent skin drape plus a Vi-Drape wound protector. Later a third group was added in which only permeable towels were used. In a total of 202 patients having abdominal operations there were 35 wound infections (an incidence of 17·3 per cent). There were no significant differences in the wound infection rates between the three groups. With the plastic skin drape alone the incidence of wound infection was 14·6 per cent, when the plastic skin drape was used with a Vi-Drape protector the incidence was 18·2 per cent, and when skin towels alone were used the incidence was 21·8 per cent.

Table V.—SUMMARY OF RECENT SERIES INVESTIGATING WOUND INFECTION

AUTHOR	INCIDENCE OF WOUND INFECTION (per cent)				
	Site of Operation				
	Gastro-duodenal	Biliary	Bowel Small	Bowel Large	Miscellaneous abdominal
Harrower (1968)*	15	10	—	7·7	22
Ellis and others (1969)*	27	18·5	60	27	—
Maxwell and others (1969)	11	16	83	26	—
Jepsen and others (1969)	37	35	59		—
Present series	6·2	13·3	0	18·8	40†

* Only the patients in the control series are included. In both these reports the wound infection was almost absent in the plastic wound drape series.

† Only 5 patients.

The results of our study provide support for the view that plastic impermeable wound protectors do not significantly reduce the rate of wound infection in patients having abdominal operations involving an opening in the alimentary tract. However, the fact that the Vi-Drape wound protectors were used in a large number of elderly high-risk patients with an overall low incidence of wound infection suggests that there is no contra-indication to their use. Their use could be advocated in an attempt to prevent malignant cells seeding into the abdominal incision during operation for abdominal cancer (Smith and Hilberg, 1955).

During the course of this experimental trial the surgeons involved liked to use the Vi-Drape wound protectors as they kept the abdominal wound tidy and did not interfere with access or dissection.

Acknowledgements.—The Vi-Drape abdominal wound protectors were supplied by Parke, Davis and Company, who also assisted with the design of the trial and the preparation of the random selection schedule.

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TREATMENT OF ARTERIOVENOUS MALFORMATION BY ENDARTERIAL ELECTROCOAGULATION

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Whether some day it may be possible by electrochemical methods safely to dehydrate one of these angiomas cannot be foretold. Harvey Cushing (1928).

Summary

The successful treatment of an arteriovenous malformation in the parotid region is described. Endarterial electrocoagulation was used and damage to the facial nerve was avoided. The possible use of this method in other situations is discussed.

Most of the congenital arteriovenous fistulae affecting the head and neck lie within the cranial cavity, but a small proportion (1 : 20) are associated purely with branches of the external carotid artery and the corresponding veins. Amongst the latter group, arteriovenous malformations in relation to the masseter muscle are well recognized (Callander, 1920). The pathogenesis of these lesions has been discussed by Holman (1968).

Many therapeutic measures have been tried and these date back at least to 1757 when William Hunter (Holman, 1968) first recognized the true nature of an 'aneurysm by anastomosis'. They include simple ligation of the main feeding vessel, occlusion of all (or as many as possible) vessels feeding or draining the malformation, injection of sclerosants, radiotherapy, and the induction of artificial emboli to occlude feeding vessels (Cushing and Bailey, 1928; Luessenhop and Spence, 1960; Pool and Potts, 1965). The more ingenious latter methods are related in general to the inaccessibility of the lesions under consideration. The general consensus of opinion would appear to be that simple ligation of the major feeding vessel is, by and large, inadequate (Cushing and Bailey, 1928; Olivecrona and Ladenheim, 1957), and that surgical extirpation is the goal to be achieved if possible. It is of interest to note that one of Cushing's cases improved following spontaneous thrombosis (Cushing and Bailey, 1928).

Uncomplicated surgical excision of lesions lying deep to the parotid is not readily achieved. Olivecrona and Ladenheim (1957) claim that their case was the first reported where excision of an arteriovenous malformation of the parotid region was accompanied by the preservation of the 7th cranial nerve. This procedure resulted in temporary facial paralysis following a 5-hour operation (Dolietis, 1949). The subject of the present report is a case of arteriovenous malformation in the same situation which has been successfully treated without injury to the 7th nerve by a simple method that has not, as far as we can ascertain, been previously described.

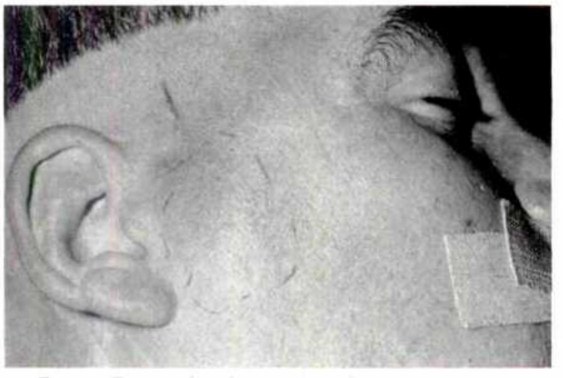
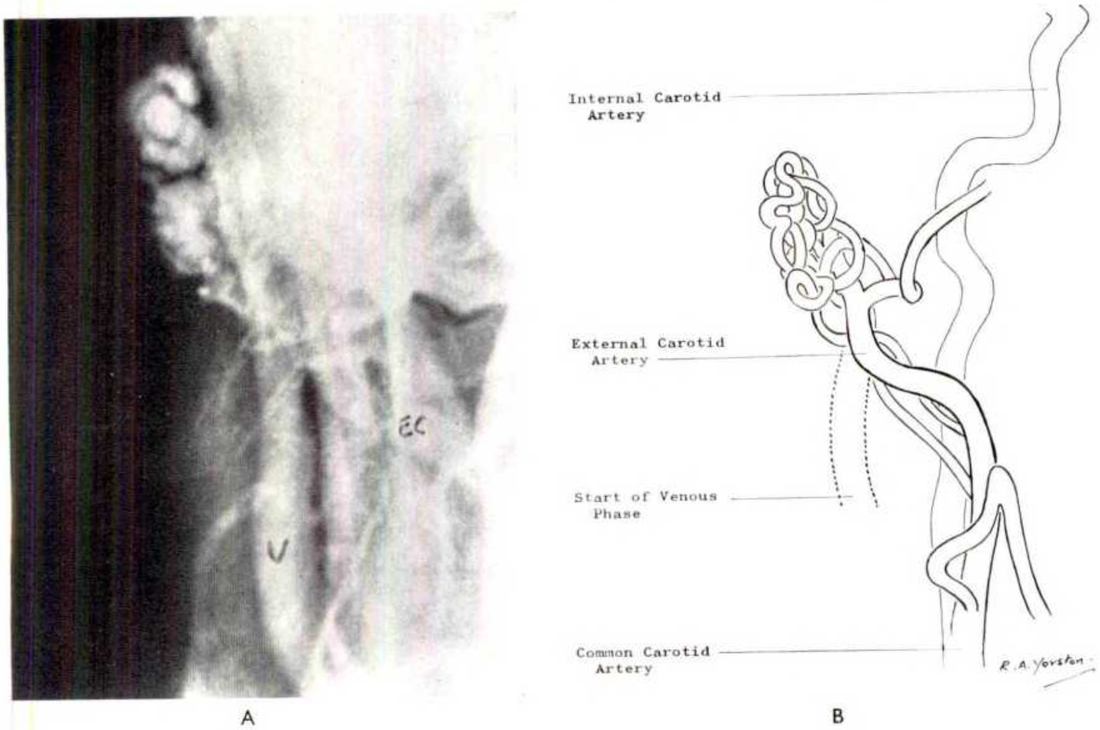


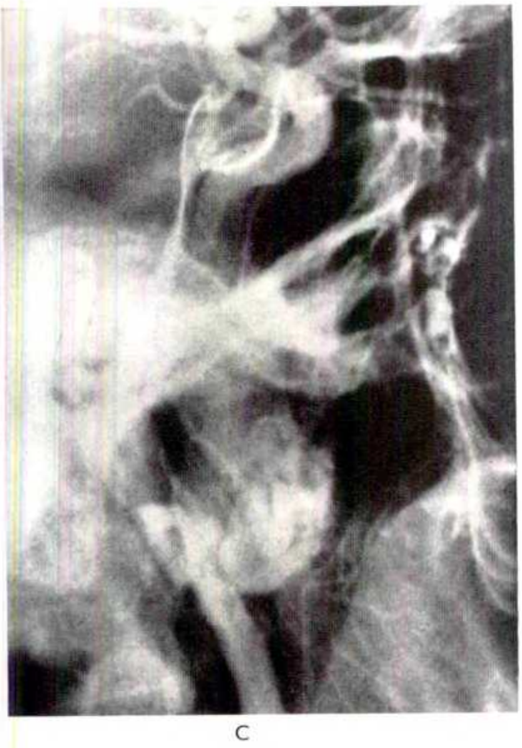
Fig. 1.—Preoperative photograph of the patient. The dotted line marks the limits of the pulsatile swelling. The vertical line above marks the position of the superficial temporal artery.

CASE REPORT

A fit 31-year-old male gave a 1-year history of distressing tinnitus, which was synchronous with his pulse, and a pulsatile swelling in front of his right ear. There was no history of trauma. Examination revealed a pulsatile swelling, 3 cm. in diameter, of the right parotid region (*Fig.* 1). Otological examination together with examination of the lower cranial nerves revealed no abnormality.

A right carotid angiogram revealed a well-demarcated arteriovenous malformation of the right parotid region. It was supplied by a greatly enlarged branch of the external carotid artery. There was early venous filling of two large





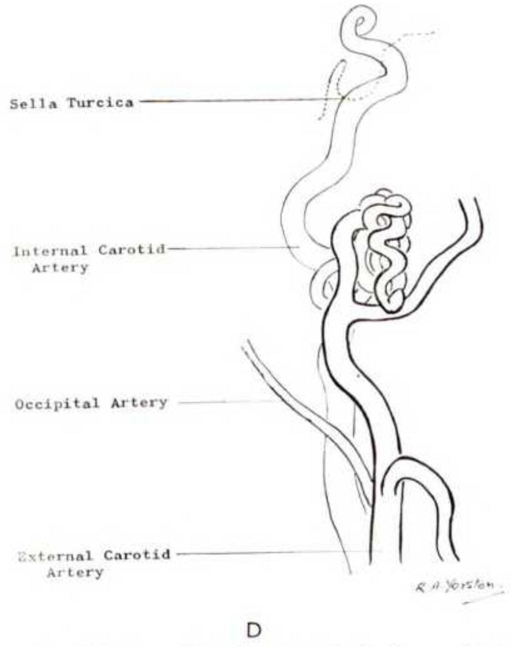


FIG. 2.—Right carotid angiograms and drawings made from tracings. The arteriovenous aneurysm in the parotid region is fed from the enlarged external carotid artery (EC) and is drained by a large vein (V). A, Anterioposterior angiogram. B, Diagram of the anterior aspect. C, Lateral angiogram. D, Diagram of the lateral aspect.

veins lateral to the mandible. No intracranial communication was demonstrated (*Fig.* 2).

In view of the relative inaccessibility of the lesion, the following surgical approach was devised. Through a crease incision the major vessels of the right side of the neck were exposed. Within the common facial vein, streams of arterial and venous blood were visible. There was a high division of the common carotid artery. After it has been established that occlusion of the termination of the external carotid artery resulted in control of the pulsation in the aneurysm, all branches of the external carotid artery peripheral to the superior thyroid were isolated and divided. A small cystodiathermy electrode was inserted into the uppermost part of the external carotid artery and was manipulated into several major feeding arteries in the malformation. The current was applied intermittently to prevent too great a local heat generation, which might have damaged local structures, particularly the facial nerve. This procedure was to some extent controlled by palpation. When endo-electrocoagulation was completed the external carotid was ligated.

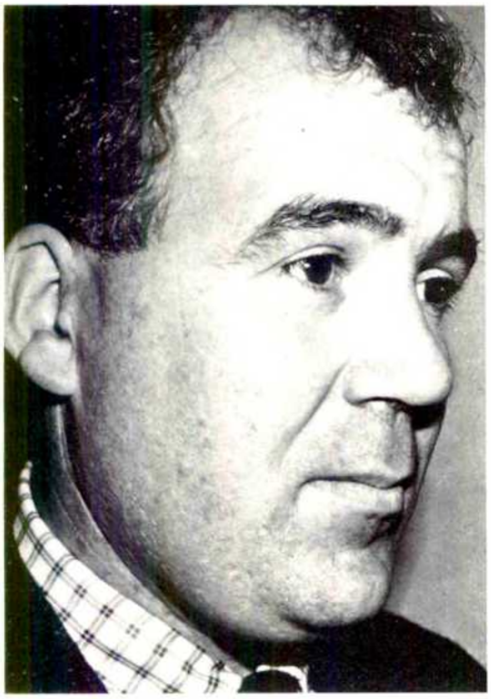


FIG. 3.—Postoperative photograph of patient. The swelling has disappeared.

Postoperatively, the tinnitus and swelling disappeared. The patient experienced trismus, suggesting that the malformation involved the masseter. Initial limitation of jaw opening soon resolved, although slight discomfort on chewing persisted for 4 months after operation. Two and a half years following the operation the patient remains well with no evidence of recurrence (*Fig.* 3).

DISCUSSION

Operation on extracerebral arteriovenous malformations is indicated for cosmetic, symptomatic, and haemodynamic reasons. The simple procedure described above would appear attractive, in that it is of a relatively minor nature and does not endanger adjacent important structures. Endo-electrocoagulation of extracerebral arteriovenous malformations is almost certainly without serious risk. This method of treatment may prove useful in some intracerebral malformations—in this situation radiological control may be desirable. The technique could also be used to coagulate the maxillary artery in conjunction with ligation of the external carotid artery for severe epistaxis.

Arteries, unlike veins, once completely blocked, seldom if ever recanalize. This different behaviour after thrombosis is attributable to the different anatomical arrangements of the blood-supply to their walls. In thrombosed arteries the vasa vasorum are necessarily occluded, whereas in thrombosed veins, blood (with fibrinolysin) can still enter the walls through the vasa venarum.

Acknowledgements.—We are indebted to Dr. H. T. Apsimon and Dr. R. A. Yorston for the angiograms and the diagrams.

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SHORT NOTES OF RARE OR OBSCURE CASES

PROLAPSE OF THE ILEUM THROUGH THE RECTUM AND ANAL CANAL

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SUMMARY

A case of prolapse of the ileum through a tear in the rectal wall and the anus is presented and 11 previous cases found in the literature are reviewed. The aetiology and the management of the condition are discussed.

INTRAPERITONEAL tears of the rectum are not uncommon in general surgical practice. They are frequently caused by the introduction of foreign bodies into the rectum, either by the patient himself or in the course of medical investigation. In the latter category are included perforation by a sigmoidoscope, by a barium enema (Hartman and Hills, 1957), or by a thermometer (Miller, 1962; Wilkinson, 1965).

Less frequently, intraperitoneal tears are caused by a sudden increase in intra-abdominal pressure. This can result from crush injuries, coughing, or even straining during defaecation. The usual course of events is for the bowel contents to contaminate the peritoneal cavity. It is unusual for a viscus in the peritoneal cavity to pass into the lumen of the bowel.

CASE REPORT

On 30 Nov., 1968, Miss C. D., a 90-year-old spinster, was referred to the Casualty Department of Kingston Hospital. She was confused and unable to give a detailed history, but it appeared that she had fallen the previous day striking her chest and upper abdomen. Since that time she had had vague central abdominal pain and had vomited on two occasions. The last occasion on which she had opened her bowels was on the day preceding the accident, when she passed a normal motion. She said that in the 10 months before the accident she had noticed a mass protruding from her anus after defaecation on several occasions. She had been able to replace this manually.

On examination, she was 4 ft. 10 in. in height (155 cm.), thin, and not in any obvious distress. Her pulse-rate was 80 per minute and her blood-pressure 150/80. No abnormality could be found in the cardiovascular or respiratory systems. Her tongue was furred but she did not appear dehydrated. Her abdomen was not distended, but there was marked tenderness over the lower abdomen, though no guarding or rigidity. There were no palpable masses. Bowel sounds were present in all areas and were normal. However, examination of her perineum showed loops of small intestine prolapsing through the anus (*Fig.* 1). The small intestine appeared viable, with visible peristalsis. Arterial pulsation could be seen in the mesentery.

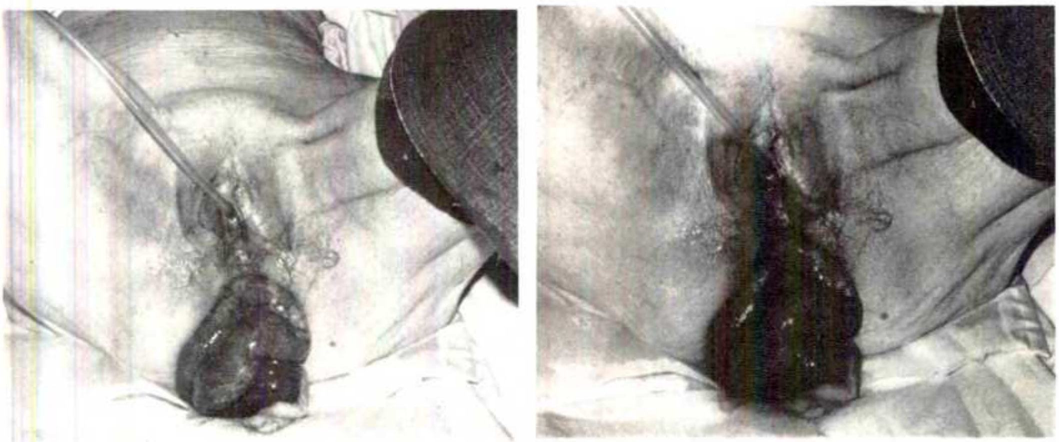

FIG. 1.—Coils of ileum protruding through the anal canal.

A diagnosis of prolapsed ileum through a tear in the colonic wall was made, and the patient was transferred to the operating theatre.

The patient was anaesthetized and examined in the lithotomy position. The loops of small bowel appeared fully viable and the pulsation in the mesentery was confirmed. A finger was inserted into the anus which was found to be patulous. A tear could be felt high up on the anterior wall of the rectum, through which the small bowel had prolapsed. The abdomen was opened through a right lower paramedian incision, and the ileum, after cleansing with Cetavlon, was withdrawn into the peritoneal cavity. The tear was found to be 3·8 cm. in length, lying longitudinally on the anterior rectal wall, 2·5 cm. above the peritoneal reflection (*Fig.* 2). The edges appeared to be viable, with no evidence of ischaemia or infection. There was no soiling of the peritoneal cavity and the other abdominal viscera all appeared normal. As the ileum, 45·7 cm. of which had passed through the rectal wall, appeared normal, no resection was necessary. A biopsy was taken from the edge of the tear, which was then closed in a transverse direction with two layers of 00 chromic catgut. Finally, a sigmoid colostomy was fashioned through an oblique incision in the left iliac fossa and the abdomen was closed in layers, leaving a Ragnall drain to the site of the suture line on the anterior rectal wall. Postoperatively the patient received intravenous fluids and she was given tetracycline 250 mg. q.d.s.

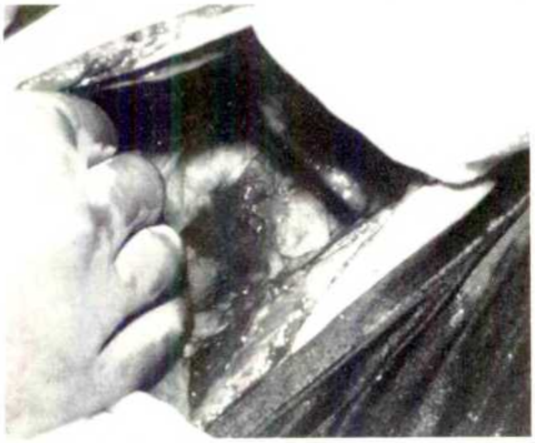

FIG. 2.—Anterior surface of the rectum showing the 3·8-cm. longitudinal tear.

Forty hours later the patient strained in an attempt to open her bowels and prolapsed a loop of ileum alongside her sigmoid colostomy. She was operated upon and the prolapsed loop of ileum was reduced into the abdominal cavity and the colostomy opening was narrowed with sutures to the peritoneum and the skin. Thereafter the colostomy functioned well and the patient was maintained on a normal diet. Subsequently the patient suffered several episodes of rectal prolapse—easily replaceable without anaesthesia.

A barium enema via the distal limb of the colostomy demonstrated no leakage at the site of the original tear. Accordingly, the sigmoid colostomy was closed 14 days later and normal defaecation was established. The patient continued to prolapse her rectum and 2 months following the first operation a Thiersch wire was inserted subcutaneously around the lower end of the anal canal. The patient was discharged 4 days later, and has had no further episodes of rectal prolapse.

REVIEW OF THE LITERATURE

We have only been able to find 11 similar cases reported in the world literature since 1900, and no similar case in the British literature. The main points are summarized in *Table I*.

Table I.—SUMMARY OF THE FEATURES OF 12 CASES OF PROLAPSE OF THE ILEUM REPORTED IN THE WORLD LITERATURE SINCE 1900

CASE NO.	AUTHOR	AGE AND SEX	RECTAL PROLAPSE	SITE OF TEAR	PRECIPITATING FACTOR	PROCEDURE	FATE OF PATIENT
1	Moulton (1901)	M.	Present	Rectum	Not stated	Nil	Died after 36 hours
2	Zena (1914)	14 F.	Absent	Rectum	Injury (by rock fall)	Resection rectum	Recovered
3	Guibe (1931)	78 F.	Present	Sigmoid	—	Resection; gangrenous ileum	Died after 2½ months
4	Guibe (1931)	77 F.	Present	Rectum	Fall	Suture of tear	Died after 5 days
5	Moskalenko (1934)	52 F.	Present	Rectosigmoid	Coughing on defaecation	Resection of ileum and suture of tear	Died after 24 hours
6	Erlikhmana (1937)	45 F.	Present	Sigmoid	Heavy lifting	Suture of tear	Died after 64 hours
7	McLanahan and Johnson (1945)	76 F.	Present	Sigmoid	Fall	Exteriorization of sigmoid	Died after 62 hours
8	Minkari and Turan (1961)	28 M.	Absent	Sigmoid	Defaecation	Resection of ileum and suture of tear	Recovered
9	Alvich and Lepow (1959)	58 F.	Present	Sigmoid	? Spontaneous	Resection of ileum and suture of tear; colostomy	Recovered
10	Henessey (1966)	63 F.	Present	Rectum	? Spontaneous	Suture of tear	Recovered
11	Rowse (1966)	38 M.	Absent	Rectosigmoid	Blow in a fight	Suture of tear	Recovered
12	Hall and Bradfield (1971)	90 F.	Present	Rectum	Fall	Suture of tear and sigmoid colostomy	Recovered

The condition is frequently associated with prolapse of the rectum, for in only 3 cases out of a total of 12 was this absent. The sex incidence was 9 female to 3 male, reflecting the increased incidence of prolapse of the rectum in the female. The age range varies from 14 to 90, our own case being by far the oldest. It is interesting to note that the patients in whom there was no rectal prolapse were the youngest of the series (*Cases* 2, 8, 11).

The precipitating factors resulting in prolapse of the ileum through the anus are varied. These were not recorded in 2 cases (*Cases* 1, 3) and a history of a fall was obtained in 3 (*Cases* 4, 7, 12). One case had a history of constipation, and the prolapse occurred on defaecation (*Case* 8). *Case* 5 prolapsed her ileum whilst coughing when defaecating in the squatting position. *Case* 2 was trapped by a rock fall. The prolapse followed heavy lifting in *Case* 6 and a blow on the abdomen in *Case* 11. No precipitating cause is mentioned in *Cases* 9 and 10, but both these patients were inmates of mental hospitals and were unable to give a clear history.

The site of the tear has always been in the distal large bowel, the sites being the sigmoid colon in 5 cases, the recto-sigmoid junction in 2, and the rectum in 5.

The operative procedures adopted have been basically similar in all cases, except for *Case* 1 in which no treatment was attempted. At operation the ileum has been replaced in the peritoneal cavity or resected if non-viable. The tear in the wall of the large bowel has been either sutured or a portion of the bowel resected. In some cases a proximal colostomy was formed (*Cases* 9, 12) and in 1 patient (*Case* 7) the sigmoid colon containing the tear was exteriorized.

In the pre-antibiotic era the condition was almost uniformly fatal, although it is notable that the case of Zena in 1914 made a remarkable recovery (Zena, 1937) and 1 patient of Guibe (1931) died 2½ months after her operation, having become cachectic, following a faecal fistula. However, the last 5 reported cases have all recovered, doubtless owing partly to the introduction of antibiotic therapy, blood transfusion, and general advances in postoperative care.

DISCUSSION

The factor initiating the passage of the small bowel through the wall of the sigmoid colon or the rectum seems to be an increase in intra-abdominal pressure. It is suggested that in the presence of prolapse of the rectum there is an area on the wall of the abdominal cavity that is unsupported by muscle, namely, the rectovesical or recto-uterine pouch, where the pelvic floor is weak and the anus is patulous. Accordingly, the wall of the sigmoid colon or rectum tears, the site depending on the degree of the rectal prolapse, and the ileum passes into the lumen of the rectum through the anus.

The judicious use of antibiotics, blood transfusion, and other supportive measures all contribute to the survival of the patient with prolapse of ileum through the anus. Early laparotomy is essential. Alvich and Lepow (1964) recommend that the loops of ileum which have prolapsed are divided inside the peritoneal cavity, and that they are then drawn through the rectum and out through the anal canal to avoid further contamination of the peritoneal cavity by non-viable bowel. However, recent cases (Henessey, 1966; Rowse, 1966) and the present case have shown that when the ileum is viable it can be safely preserved by reintroducing it into the peritoneal cavity after cleansing. If the edges of the tear are viable it can be closed in two layers, preferably in a transverse direction. If there is doubt concerning the integrity of the suture line or if the patient is old and enfeebled, a sigmoid colostomy is probably advisable. When prolapse of the rectum is present a further operation at a later date may be necessary to avoid recurrence.

Acknowledgements.—We would like to record our grateful thanks to Mrs. B. Meade for help with the translation of the Russian articles.

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BOWEL HERNIATION THROUGH A DEFECT OF THE BROAD LIGAMENT

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SUMMARY

This is the fifty-fourth reported case of a defect in the broad ligament and the forty-ninth associated with intestinal obstruction.

HISTORICAL REVIEW

Quain is accredited with the first description of a defect in the broad ligament which he noted at an autopsy in 1861 (Baron, 1948). The literature was comprehensively reviewed by Baron in 1948, who collected 45 previous cases and added 1 of his own, and since then only 7 further case reports have been published; 3 collected by Wills (1957), 1 by Bordenca (1959), 1 by Papas (1960), 1 by Rose (1963), and 1 by Johnson (1965), making a total of 53 cases. In 19 of these cases reported, the defect in the broad ligament was a sequel of a uterine suspension operation and may have been due to technical error (Baron, 1948; Wills, 1957). In the remainder there was no direct injury to the broad ligament. In 48 of the patients attention was drawn to the defect by the occurrence of intestinal obstruction or strangulation.

CASE REPORT

HISTORY.—Mrs. F. F., aged 41, a multipara with a previous history of three normal labours, suffering from abdominal pain of 36 hours' duration and vomiting of 24 hours' duration, was admitted to Leith Hospital on 1 April, 1970. The pain had awakened her from sleep on the morning of the day prior to admission. It was initially epigastric in position and 'sharp' in nature but by the following day had shifted to the suprapubic area and was 'like labour pains'. Eighteen hours after the onset of the pain a normal stool was passed. There were no urinary symptoms. Her menstrual periods had been regular over the past 5 years while she was on 'the pill', her last period having ceased 10 days previously and having been quite normal. There was no vaginal discharge, nor were there any other gynaecological symptoms or history of any previous gynaecological or other procedure.

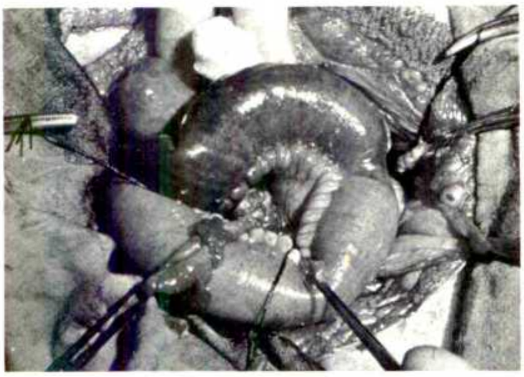

FIG. 1.—The defect in the broad ligament has been divided and the left ovary and Fallopian tube are held in Allis's forceps. The constriction ring in the bowel can be seen.

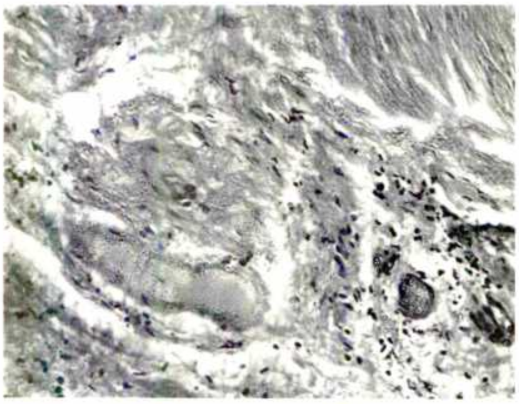

FIG. 3.—Section of the margin of the hole showing fibrous connective tissue. (× 150.)

EXAMINATION.—On examination the patient was a slightly plump woman, pale, anxious, a little dehydrated, and obviously in pain. Her temperature was 36·4° C., pulse, 136 per minute, and respiration rate, 20 per minute. Her face was drawn, her lips were dry, and her tongue was furred. The breath was not foetid. The systolic blood-pressure was 110 and the diastolic 50 mm.

The abdomen moved well in the upper half on respiration but to a lesser extent in the lower half, where there was also some distension but no visible peristalsis. There was true muscle guarding in the lower half of the abdomen. There were tenderness and rebound tenderness in both iliac fossae suprapubically—the maximum point of tenderness being in the left iliac fossa towards its most medial part. There was no tenderness or guarding in the upper abdomen. On auscultation the bowel-sounds were only slightly increased in frequency and volume. Rectal examination revealed diffuse tenderness but no masses were felt. Vaginal examination was not carried out.

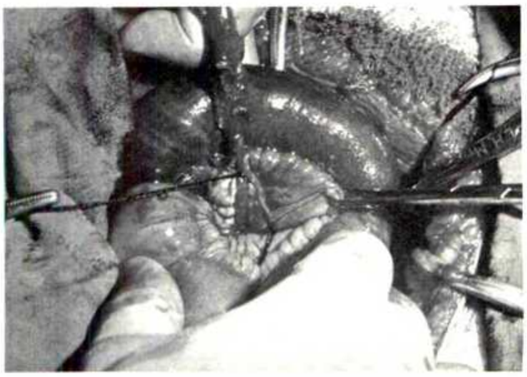

FIG. 2.—The hole in the broad ligament in process of repair with black silk sutures.

INVESTIGATIONS.—Haemoglobin was 136 per cent, P.C.V., 60 per cent, and W.B.C., 19,000 per c.mm. with 77 per cent neutrophils. Erect and supine abdominal radiographs showed that there were one or two small dilated loops of small bowel present and that there was a solitary fluid level in one of them. The appearances were those of a mechanical obstruction in the distal small bowel.

With the foregoing history, examination, and investigations, it was evident that the patient required a laparotomy.

OPERATION.—Preoperatively i.v. fluids were commenced and a nasogastric tube was passed.

On palpation of the abdomen under anaesthesia prior to incision of the skin, a mass, which was relatively mobile and lying to the left of the midline suprapubically, was revealed.

A right, lower, paramedian, rectus-displacing incision was therefore made. On opening the peritoneal cavity the following was found:—

1. There were 300 ml. of serosanguineous fluid in the peritoneal cavity.
2. There was a 2·5-cm. hole in the left broad ligament of the uterus with 7·6 cm. of terminal ileum approximately 2·5 cm. from the ileocaecal valve herniated through this hiatus from anterior to posterior. The herniated bowel was strangulated (*Fig.* 1).
3. The defect was through the broad ligament, with the round ligament, Fallopian tube, and mesovarium passing superiorly, the uterine wall medially, the levator ani muscle laterally, and the uterine artery, ureter, and vault of vagina inferiorly.

The following procedure was therefore carried out. The upper part of the left broad ligament of the uterus was ligated and divided to release the strangulated loop of bowel (*Fig.* 2). The bowel was covered with a warm pack, but on inspection some minutes later, pulsation had not returned to the mesentery and the bowel appeared non-viable. Resection of the bowel with end-to-end anastomosis using two layers of catgut was carried out. The hole in the mesentery was closed with catgut sutures. Attention was then turned to the defect in the broad ligament. The edges of the defect were rigid and sharp and were thought to be the constricting band which had caused the strangulation. A biopsy of the rim of the defect was taken for microscopy and the defect was repaired with interrupted black-silk sutures. A suction drain was brought out through a stab wound from the pouch of Douglas. The main wound was closed with tension sutures, continuous catgut for peritoneum and rectus sheath and interrupted black silk for skin.

PROGRESS.—The wound healed by first intention and the patient made a good recovery. She was discharged from hospital on the thirteenth day after operation and has remained free of symptoms.

PATHOLOGY.—Microscopy showed fibrous tissue and vascular connective tissue only (*Fig.* 3).

DISCUSSION

Internal hernias account for between 0·5 and 1 per cent of all intestinal obstructions (McIver, 1933; Wangensteen, 1955). The classic definition of an internal hernia is given by Treitz in 1857 (Bertelsen and Christiansen, 1967): 'an internal hernia is a hernia situated retroperitoneally'. In common usage, however, there are two types: first, that of retroperitoneal herniation of an abdominal organ through a hernial opening formed by a peritoneal fold, and second, that of herniation of a viscus through a defect in the mesentery or omentum (Bertelsen and Christiansen, 1967). Most of the hernias through the broad ligament fall into the second category, only 5 of the reported cases having a peritoneal sac.

Aetiology.—In patients who have had previous uterine suspension operations (19 out of 53 reported cases) the cause of the defect is probably failure to close the hole made in the broad ligament securely enough around the sling of the round ligament (Wills, 1957). In patients who have not undergone previous surgery the aetiology is more obscure. Our patient falls into this category and she had many of the features reported by authors mentioned in the historical review. The average age at operation was 42 years with a range of 16–79 years (Baron, 1948; Rose, 1963). Our patient was 41 years old.

In 11 out of 25 cases in which the relation to the layers of the broad ligament has been mentioned, the defect involved both layers, as in our patient. In the others one leaf only was involved. The defect was on the left side (as in our patient) in 11 out of 28 patients in whom this finding was recorded, with 14 on the right side and 3 bilaterally.

The relationship to the uterine adnexa is variable and the same relationship as in our patient was encountered in 3 out of 18 patients in whom the exact site was recorded.

Three explanations have been offered for spontaneous defects in the broad ligament. The first is that they occur secondarily to previous infection in the region of the broad ligament. This was probably valid only in the 2 described cases in whom there was evidence of previous pelvic inflammation, as most of the other patients, like ours, were singularly free from adhesions and other evidence of prior inflammation. The second explanation is that the defects are congenital anomalies and this must be invoked in the few patients who were nulliparous. The third explanation, that trauma to the broad ligament during pregnancy results in tears which heal leaving defects, would appear to apply to the majority of the patients including ours. This would explain the fact that 80 per cent of broad ligament defects have occurred in multiparous women and that the site of the defect is variable. There has been 1 report of the condition actually occurring in the eighth month of pregnancy. Bordenca (1959) reported a hernia of the sigmoid colon through the broad ligament in the eighth month of pregnancy.

Biopsy of the margin of the defect would seem to help in deciding which is the most valid of these three explanations. This has only been done in 1 previous case, the findings being quoted by Baron in 1948 as 'typical scar tissue'. In our patient the margin was made up of fibrous and vascular connective tissue. This is consistent with a traumatic tear which had healed satisfactorily in the past leaving the defect.

Acknowledgement.—We wish to thank Mr. I. E. W. Gilmour, under whose care this patient was admitted, for permission to publish this report.

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IDIOPATHIC PSEUDOMEMBRANOUS COLITIS SUCCESSFULLY TREATED BY SURGICAL EXCISION

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SUMMARY

A case is presented of acute idiopathic pseudomembranous colitis successfully treated by panproctocolectomy. The barium enema showed 'thumb printing', an appearance normally associated with ischaemic colitis. The histology of the specimen, however, did not confirm an ischaemic aetiology.

PSEUDOMEMBRANOUS enterocolitis was first described by Billroth in 1867 (Bloomfield and Walters, 1960). Since then there have been many accounts of cases affecting the small intestine (van Prohaska, Mock, Baker, and Collins, 1961) but only sporadic reports of inflammation confined to the colon (Hartmann and Angevine, 1956; Bloomfield and Walters, 1960; Goulston and McGovern, 1965). The aetiology is uncertain, but many authors draw a distinction between the staphylococcal variety which often follows antibiotic therapy and the non-infective forms for which an ischaemic aetiology has been postulated (Hardaway and McKay, 1959; Marston, 1962). Conservative treatment is usually recommended but the disease is often fatal and in many cases the diagnosis is made only at necropsy.

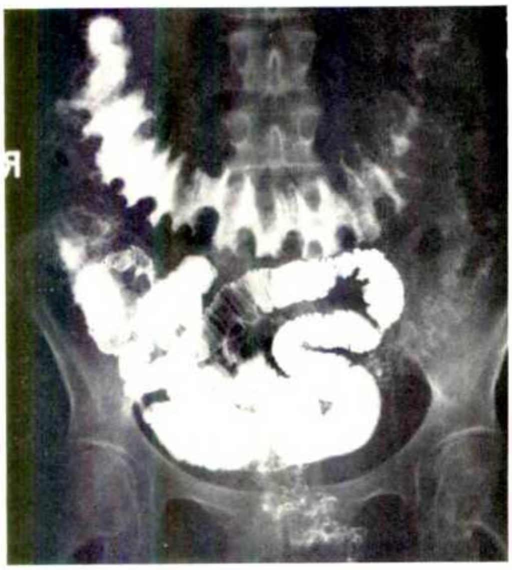

FIG. 1.—Barium enema showing 'thumb-printing' in the transverse colon and widespread 'polyposis'. Reflux into the ileum is also seen.

This report is of a patient with severe pseudomembranous inflammation confined to the colon which was successfully treated by surgical excision. There was no predisposing cause or evidence of infection but the barium-enema appearances were compatible with an ischaemic aetiology.

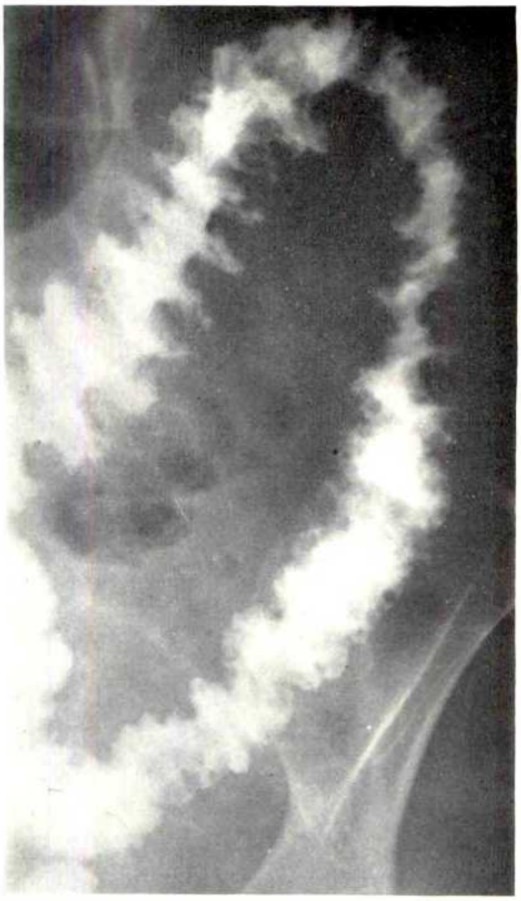

FIG. 2.—Barium enema showing the appearance of the left colon.

CASE REPORT

Mrs. E. B., a housewife aged 66 years, was admitted to St. Peter's Hospital, Chertsey, with a short history of diarrhoea of sudden onset. The bowels were opened up to twenty times daily, the motions being watery and offensive but without blood or mucus. There was a constant pain in the lower abdomen and anorexia but no nausea or vomiting. Previous to this admission the patient had been well apart from a herniorrhaphy and appendicectomy performed many years previously.

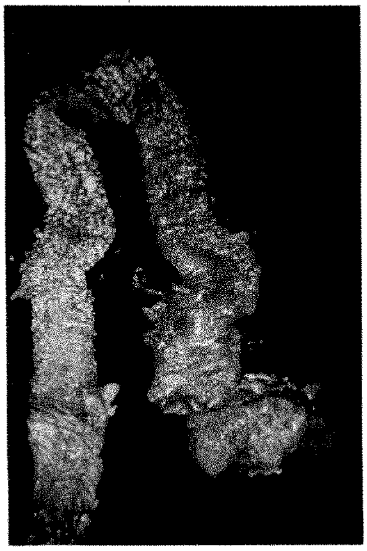

FIG. 3.—The opened specimen showing the colitis extending from the rectum to the caecum. The terminal ileum is spared.

On examination the temperature was raised (37·3° C.) and the pulse-rate was 100 per minute. There was tenderness in the right iliac fossa but no guarding, abdominal distension, or masses. Digital examination of the rectum was normal. Sigmoidoscopy was difficult because of the presence of liquid faeces, but large numbers of small, yellowish-white, raised nodules of an obscure nature were seen lining the rectal mucosa which appeared inflamed. A biopsy was taken which showed severe chronic inflammation but no other abnormality.

Investigations included the following: haemoglobin 15·2 g. per cent, W.B.C. 10,000 per c.mm., E.S.R. 10 mm. per hour, urea 24 mg. per cent, normal electrolytes and bicarbonate, and normal chest and plain abdominal radiographs. A provisional diagnosis of infective enteritis was made and the patient was treated by fluid and electrolyte replacement. No antibiotics were given pending the result of a stool culture. This showed no evidence of pathogens and therefore antibiotics were withheld.

During the next week the patient's symptoms and signs subsided, and 10 days after admission the patient was completely well. Repeat sigmoidoscopy was normal to 13 cm. but a repeat rectal biopsy still showed chronic inflammation with a thickened muscularis mucosa. The patient was discharged and remained well for 1 month when she was readmitted with a 3-day history of abdominal pain and severe diarrhoea. Again there was no blood in the motions and no nausea or vomiting. The diarrhoea was watery and offensive, containing some mucus, and occurred up to twenty times daily. The patient was febrile, her temperature being 37·3° C. Sigmoidoscopy again showed the presence of yellowish-white raised nodules, approximately 3 mm. in diameter, throughout the entire rectum. The mucous membrane was oedematous but there was no contact bleeding. Biopsy again showed non-specific chronic inflammation. Stool culture showed no evidence of pathogens, cysts, ova, or fungi. A barium enema was grossly abnormal showing 'thumb-printing' in the transverse colon, widespread appearances of polyposis coli, and reflux into the ileum (*Figs.* 1, 2).

Her diarrhoea and abdominal pain continued and she became exceedingly ill despite adequate fluid replacement and correction of electrolyte imbalance. A week after admission her condition was critical and a panproctocolectomy and ileostomy were performed. Following this operation a dramatic improvement took place and her postoperative recovery was uneventful. She has remained well for the past 2 years.

PATHOLOGY.—The specimen showed numerous soft yellowish nodules of mucopus throughout its length from the anal canal to the caecum (*Figs.* 3, 4). These nodules were from 2 to 7 mm. in diameter, in places forming confluent masses, and could be removed to reveal underlying superficial ulcerations. The mucosa between the lesions also showed a few minute ulcers. The bowel wall was generally thickened but there were no enlarged lymph-nodes. Histology showed generalized chronic inflammation throughout all coats, with foci of superficial necrosis of the mucosa covered by fibrin and mucopus, in which no protozoa, fungi, or bacteria could be demonstrated. There was no intramural haemorrhage and the lymph-nodes were unremarkable. The blood-vessels were normal and no malignancy was present. A diagnosis of pseudomembranous colitis was made.

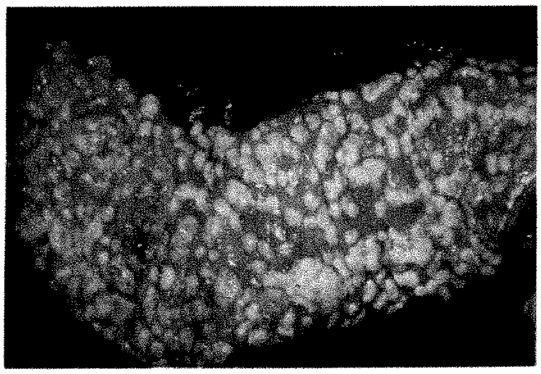

FIG. 4.—Close-up of the transverse colon showing the nodules of mucopus.

DISCUSSION

The pathological findings are those of the focal type of pseudomembranous colitis described by Kay, Richards, and Watson (1958). Goulston and McGovern (1965) claim that pseudomembranous colitis occurs in two groups of patients: those having primary disease of the colon, and those with generalized disease such as uraemia or septicaemia. They suggest that it is a separate entity from staphylococcal enterocolitis, which often follows antibiotic therapy or operation, but refute an ischaemic aetiology on histological grounds. Other authors agree that pseudomembranous colitis develops in association with pre-existing disease (Kleckner, Bargen, and Baggenstoss, 1952; Pettet, Baggenstoss, Judd, and Dearing, 1954; Birnbaum, Lauffer, and Freund, 1961). The above patient was unusual in that no other disease was present, no staphylococci were demonstrated, and no antibiotics had been given.

Penner and Bernheim (1939) were the first to suggest the possibility of local ischaemia causing the inflammation. Hardaway and McKay (1959) reproduced the clinical features and the histological appearances in dogs by causing intravascular clotting in the capillaries of the bowel mucosa. Marston

(1962) also reproduced similar histological appearances in dogs by occluding the superior mesenteric artery. Although the histological features in our patient did not suggest an ischaemic origin the barium enema showed multiple, rounded, filling defects in the transverse colon, a sign known as 'thumb-printing' (Lea Thomas, 1966). This has been described in human ischaemic colitis and is thought to be caused by mucosal oedema and submucosal haemorrhage consequent upon the ischaemia (Boley, Schwartz, Lash, and Sternhill, 1963; Marston, Pheils, Thomas, and Morson, 1966; Marcuson, Arthur, Chapman, and Marston, 1969). It does not appear to have been described in a non-ischaemic condition. The misleading appearance of 'polyposis' seen on the radiographs was caused by the nodules of mucopus.

The prognosis for patients developing pseudomembranous inflammation of the bowel is poor and the majority of reported series are of necropsy cases. Our patient was deteriorating rapidly despite vigorous fluid and electrolyte replacement and seemed certain to die had a conservative regimen been continued. Tanner and Hardy (1968) advocate surgical excision of the affected segment, but their 2 cases were of small-bowel inflammation. This report appears to be the first describing colectomy in the management of pseudomembranous colitis.

Acknowledgements.—We wish to thank Dr. C. F. Ross, Consultant Pathologist, St. Peter's Hospital, Chertsey, for his help in diagnosis, and Mr. T. W. Brandon of the Department of Photography, St. Thomas's Hospital, for reproducing the illustrations.

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A CASE OF DIAPHRAGMATIC HERNIA, ABSENT PERICARDIUM, AND HAMARTOMA OF LIVER

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SUMMARY

A case is described of a diaphragmatic hernia associated with a left pericardial defect and hamartoma of the liver. The possible embryological origin of the first two defects from premature closure of the duct of Cuvier is discussed. The radiographic changes of the absent pericardium are mentioned and the histology of the liver hamartoma is described.

DIAPHRAGMATIC hernia has been known since 1575 when it was described by Ambroise Paré (Rickham and Johnston, 1969). Baillie in 1788 (Moore, 1925) first accurately described a case of absent pericardium, although the earliest report was by Realdus Columbus in 1559 (Moore, 1925). Benign hamartoma of the liver which presented as a large tumour in an 18-month-old child was described by Rewell (1957).

Only 1 case of all three abnormalities found together has been recorded (Ladd, 1936). The histological description of the diaphragmatic sac was similar to our findings, but no explanation was given or name suggested. We feel that the case of Ladd, as in the present case, was a hamartoma of the liver.

CASE REPORT

A 10-day-old baby girl presented as a feeding problem from birth. Chest radiographs (*Fig.* 1 A) suggested left diaphragmatic paralysis; the mediastinum was a little displaced to the right. A urinary infection was found and, after a normal intravenous pyelogram and cystogram, was treated. She improved and was allowed home.

She was readmitted as an emergency at 6 months with a 3-day history of increasing cough and dyspnoea. On examination the baby was cyanosed. The temperature was 40° C. Respirations were grunting and the rate was 60 per minute. The pulse was 172 per minute. The left side of the chest was flattened and expanded minimally. Bowel-sounds were heard in the left lower chest. Radiographs (*Fig.* 1 B) showed the stomach to be in the left chest and the mediastinum displaced to the right.

A diagnosis of left diaphragmatic hernia was made and, after resuscitation, laparotomy was carried out through a left transverse incision.

A large left anterolateral diaphragmatic defect was found, which contained volvulated stomach, spleen, and some left lobe of the liver. The sac was thick and fleshy and bled briskly when cut. Three thickened lobules were found on the pleural surface looking like sequestrated lung. No left pericardium was seen. The heart appeared to lie in the pleural cavity. The left lung appeared small and filled half of the pleural cavity. Postoperatively the left lung did not fully expand and chest radiographs (*Fig.* 1 C) showed the mediastinum displaced well to the left. She was discharged 17 days after admission, clinically well but with radiographic changes (*Fig.* 1 D) as described.

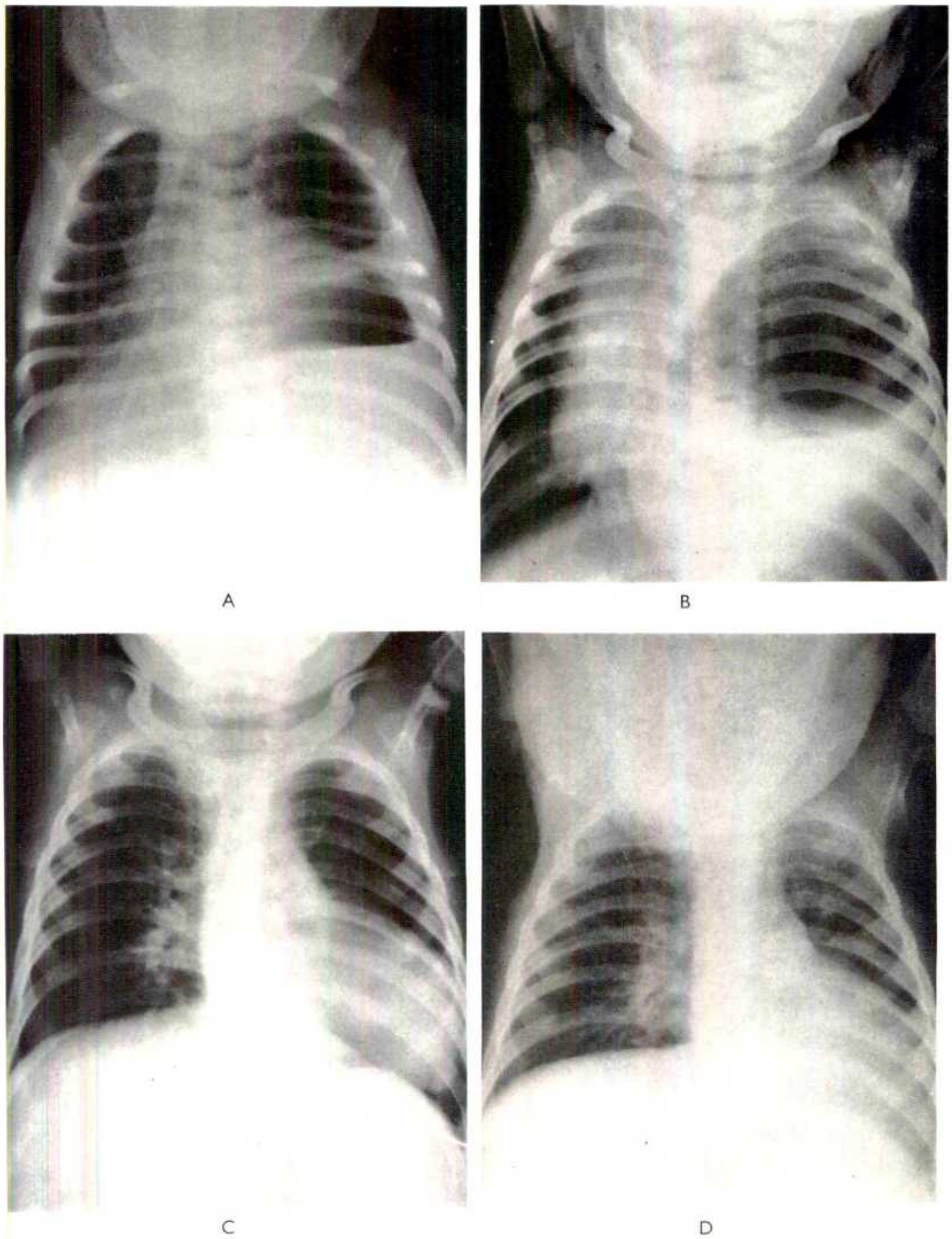

FIG. 1.—Serial radiographs before and after diaphragmatic hernial repair. A, 10 days old. B, 6 months old before operation. C and D, After operation.

PATHOLOGY.—The specimen taken at operation was a flattened hernial sac, 8 by 5 cm. Most of the tissue was fibromuscular in nature and 2 mm. thick, but there were three firm elevations on the pleural surface of the specimen, projecting 5 mm. above the surface. The cut surface was red and homogeneous.

HISTOLOGY.—A number of blocks was taken from the elevated areas and also from the intervening tissue, several of which represented a full thickness. The intervening tissue consisted of fibrous tissue interspersed amongst which were a small number of muscle-fibres. The appearance of the elevated parts was similar and differed only in the relative amounts of the constituents from place to place. Much of the tissue consisted of what appeared to be islands of well-differentiated liver cells in a fibrous stroma. There were also numerous ramifying bile-ducts which varied greatly in diameter. In places (*Fig.* 2) liver cells, bile-ducts, and fibrous stroma could all be seen together and it was possible to find areas in which the liver cells could be seen in continuity with the bile-duct epithelium.

FIG. 2.—Photomicrograph of diaphragmatic sac. (× 170.)

DISCUSSION

Congenital absence of the pericardium is usually left-sided; only rarely does it involve the right side. Deutsch, Yahini, Shem-Tov, and Neufeld (1970) described 116 cases including their own case. The present case and 4 of Tubbs and Yacoub (1968) bring the total number described to 121. Ladd's case (1936) was the first to be discovered during life.

Absent pericardium has been classified by Moore (1925). Complete absence of the left pericardium is harmless. Radiologically it should be considered, as it may be confused with other pathological conditions in the left-lung field.

Numerous associated defects have been described (Tabakin, Hanson, Tampas, and Caldwell, 1965). Diaphragmatic hernia is one of these. Risel (Moore, 1925) described 3 such cases found at post-mortem examination, but they were associated with multiple congenital defects. Keith (1910) described 3 cases of diaphragmatic hernia through the central tendon into the pericardial cavity. In the event of absence of the left pericardium, this type would not easily be distinguished from our own case. His type of hernia was probably due to persistence of the infracardiac bursa.

To explain the defect of absent pericardium embryologically Moore (1925) suggests that it may arise as the result of early closure of the left duct of Cuvier, which conforms with the propensity of this defect to be left-sided. However, the pulmonary ridge lying just medial to the Cuvierian duct gives rise to both the pleuropericardial and the pleuroperitoneal membranes, so the association of both absent pericardium and diaphragmatic hernia is explicable on this basis.

It is generally considered that the endodermal cells of the hepatic diverticulum give rise to the parenchyma of the liver, whilst the capsule and fibrous stroma are derived from the mesoderm of the septum transversum. Elias (1955) considers that there is a contribution to the hepatic parenchyma from the septum transversum. Meyenberg (1918) has suggested that even some of the small bile-ducts arise from the mesoderm derived from the septum transversum. Rewell (1957) described a benign hamartoma of the liver in an 18-month-old girl, and regarded the hamartoma as taking its origin from well-differentiated mesenchymal cells. The histological appearance encountered here would appear to be in accord with his view.

In Ladd's case (1936) with deficiency of the pericardium associated with diaphragmatic hernia, he described numerous duct-like structures in the histological examination of the hernial sac although he does not mention the presence of differentiated liver cells. It is felt that this appearance, like our case, may be a liver hamartoma.

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PERFORATION OF A PEPTIC ULCER IN DUPLICATED ILEUM

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SUMMARY

A case of perforation of a peptic ulcer in a tubular duplication of the ileum is presented with a brief review of the relevant literature.

THE term 'duplication' appears to have been first used by Fitz in 1884 and has now widely replaced such terms as 'enterocystoma', 'enterogenous cyst', 'ileum duplex', or 'giant diverticulum' which have more limited connotations (Gross, Holcomb, and Farber, 1952) and for which a classification has been proposed by Smith (1960).

Duplications have certain characteristics in common. They occur anywhere along the course of the gastro-intestinal tract, are spherical or tubular in shape, and have a wall which reproduces the normal bowel structure. The mucosal lining may possess microscopic features of one or more than one specific region of the bowel. The outer muscular and serosal layers of the duplication may be shared by the normal bowel along part or all of its length. They may communicate with the normal lumen, in which case the lesion is usually tubular, or they may not communicate, in which case the lesion is cystic. The majority of duplications tend to lie within the leaves of the mesentery and to share the blood-supply of the adjacent normal bowel.

Duplications are named according to the segment of normal bowel with which they are in contact or communication, not according to the type of bowel which they resemble either macroscopically or histologically.

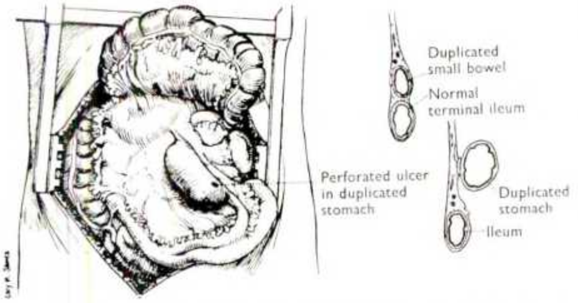

FIG. 1.—Appearance of the duplicated bowel at operation, showing a sac-like 'stomach' with a perforated ulcer, and cross-sectional drawing to show the relation of the 'stomach' and distal duplicated bowel to the mesentery of the normal ileum.

The present case is classified as a 'communicating tubular duplication of ileum'. Duplications are uncommon but not rare, and from a review of several hospital series totalling 168 cases (Donovan and Santulli, 1947; Gross and others, 1952; Moore and Battersby, 1952; Sieber, 1956; Mellish and Koop, 1961) those in relation to the ileum are found to occur most frequently. Of these, almost half contain some areas of heterotopic gastric mucosa. Anaemia from occult blood-loss is the usual presenting feature of peptic ulceration in these duplications, but frank perforation is very rare. This case is presented as a rare complication of an uncommon condition, treated surgically with success.

CASE REPORT

G. S., aged 7 years, presented with the clinical features of generalized peritonitis. He was born on 19 July, 1962, with a benign cystic lymphangioma on his back which was removed 10 days later and from which he has had no subsequent disability. At each of two subsequent annual follow-up visits he was found to be underweight for his age and to be slightly anaemic. He remained underweight for his age, lethargic, and pale for the next 5 years. One month prior to admission he complained of stabbing abdominal pains and vomiting. The vomiting continued intermittently despite symptomatic treatment and the abdominal pains became more severe. He was referred for a paediatric opinion, at which time nothing specific was found other than an iron-deficiency anaemia (Hb., 7·6 g. per cent). Thirty-six hours later he collapsed with sudden generalized abdominal pain.

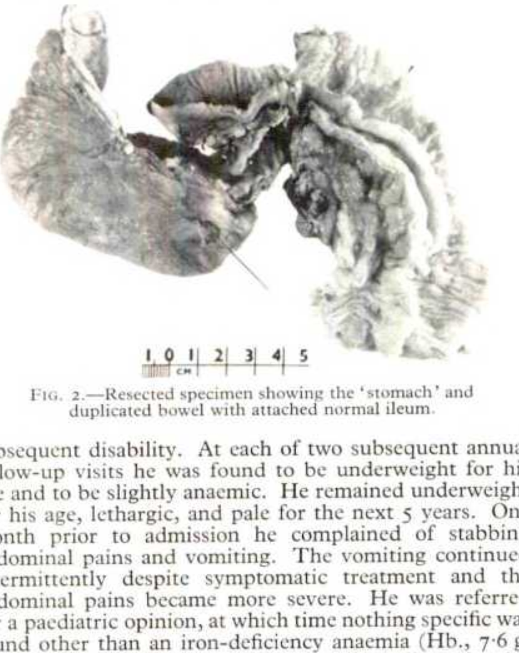

FIG. 2.—Resected specimen showing the 'stomach' and duplicated bowel with attached normal ileum.

EXAMINATION.—He was a pale underweight boy with obvious signs of peritonitis. Haemoglobin on admission was 7·4 g. per cent. After urgent fluid replacement he was submitted to laparotomy.

OPERATION.—The abdomen was explored through a right paramedian incision. One hundred ml. of blood-stained peritoneal fluid were sucked out from the peritoneal cavity. The bowel was mobilized to reveal the lesion shown in *Fig.* 1. The appearance was of a miniature 'stomach' and small bowel attached to the mesentery of the terminal ileum. The 'stomach' contained a perforated ulcer proximal to a constriction which felt like a stenosed 'pylorus'. The duplicated small bowel approached the normal terminal ileum and passed between the two leaves of its mesentery for a distance of 8 cm. before the two parallel lumina communicated (*Fig.* 2). The duplicated 'stomach' was filled with altered blood which looked like 'coffee grounds' and whose *p*H was 3.

The duplicated bowel was resected along with 15 cm. of normal terminal ileum and the two ends were anastomosed. The patient made an uninterrupted recovery, and oral iron therapy has since corrected his anaemia. Thorough examination failed to reveal any other congenital malformations although slight abnormalities were found on analysis of the palmar dermatoglyphics. This showed three whorls and seven ulnar loops in the fingerprints. On the palms, all triradii were normally situated except for a distal displacement of the right t triradius to a t' position. Palmar flexion creases were normal. Thenar patterns were absent, and there was a right hypothenar arch and a left hypothenar mutant loop. This last feature is rare and present in only 1 of 500 normal controls.

PATHOLOGY.—The duplication consisted of a cystic structure, 12 cm. long and 4 cm. in diameter, in communication with a tube, 12 cm. long and 1·5 cm. in diameter (*Fig.* 2). The 'cyst' was lined by rugose gastric-like mucosa. Most of the wall was 0·5 cm. thick but this increased up to 1·2 cm. at one end where a narrow lumen communicated with the duplicated small bowel. A perforation, 0·3 cm. in diameter, was present just proximal to the narrowed segment. Like the 'cyst' the duplicated small bowel had a complete muscular wall up to 0·5 cm. proximal to its communication with the normal ileum where the two parallel lumina were separated only by a thin mucosal web.

Histological examination showed the large cystic structure to be lined by mucosa indistinguishable from normal gastric mucosa. The perforation was through an active peptic ulcer with marked adjacent fibrosis and infiltration with polymorphs, macrophages, plasma-cells, and fibroblasts. The attached duplicated 'small bowel' had the appearance of normal ileum.

DISCUSSION

Little is known of the pathogenesis of enteric duplications although several mechanisms for their formation have been proposed. Lewis and Thyng (1907) considered that they might arise from the buds of intestinal epithelium which they sometimes found in the submucosal connective tissue of human embryos and foetal rabbits and pigs. Bremer (1944) suggested that tubular duplications might develop from the abnormal persistence of fluid-filled vacuoles, first described by Johnson in 1913, which form among epithelial cells during the 'solid stage' in the development of the intestine. However, neither hypothesis explains the almost invariable position of the duplications on the mesenteric side of the intestine. McLetchie, Purves, and Saunders (1954) reported the association of vertebral anomalies and alimentary diverticula, and concluded that there was abnormal adherence of the endoderm to the neuro-ectoderm in the early embryo with subsequent mesenchymal development around these buds of epithelium which later canalized to form duplications. Of the cases reviewed, Donovan and Santulli (1947) reported one similar to the present case in that there was a long tubular duplication with well-defined subdivisions into 'stomach' and 'bowel', but with the additional intriguing feature of a cord-like projection extending cephalad from the 'stomach' to the base of the small-bowel mesentery, with a wall histologically indistinguishable from that of common bile-duct. Moore and Battersby (1952) noted an old perforated ulcer in a 'diverticulum' which was plugged by omentum, and a similar finding was described by Donovan and Santulli (1947). Black and Benjamin (1936) report a necropsy finding of peritonitis from a perforated peptic ulcer in a tubular jejunal duplication in a patient who also had an intrathoracic 'enterogenous cyst'.

Cystic duplications usually present as an abnormal mass but there are no characteristic clinical features of communicating tubular duplications, although the diagnosis might be considered as an alternative to 'Meckel's diverticulum' in a patient presenting with abdominal pains, failure to thrive, and anaemia from occult blood-loss. Meckel's diverticulitis was in fact the diagnosis proposed by the general practitioner on referral of this child to hospital.

Acknowledgements.—I would like to thank Mr. H. J. Espiner, F.R.C.S., for permission to publish this case and Dr. R. Blight for his assistance with the pathology. I also thank Dr. T. David for his assessment and interpretation of the dermatoglyphics.

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REVIEWS AND NOTICES OF BOOKS

Malignant Tumors in Organ Transplant Recipients. By I. PENN, M.B., B.Ch., F.R.C.S., Colorado. Pp. 51, with 12 illustrations. 1970. Berlin: Springer-Verlag. DM.24.

THIS small monograph is concerned with malignant tumours in organ-transplant recipients.

Transplantation of organs has much to contend with, and a vast literature has accumulated in world medical literature concerning the relationship between immunity and cancer. Now another hazard has reared its ugly head—namely, the occurrence of malignant disease in patients who have received organ transplants.

The author has been at some pains to produce evidence to show that cancer does occur more frequently in experimental animals and in humans who have been subjected to organ transplantation.

Manuel d'Osteosynthèse. Technique A.O. By M. E. MÜLLER, Berne, M. ALLGÖWER, Basle, and H. WILLENEGGER, Liestal. 10½ × 7½ in. Pp. 296 + viii, with 306 illustrations. 1970. Paris: Masson et Cie. 150F.

PENDING the publication of a new edition of their well-known book on operative treatment of fractures, the authors wrote this preamble on the techniques of internal fixation according to the principles of A.O. The result is a very welcome atlas. Biological and mechanical principles of internal fixation are clearly illustrated by diagrams. The text is brief, concise, and of necessity a little dogmatic. An excellent case is made for the use of drill, tap, and screws, instead of self-tapping screws. Good illustrations of internal fixation of fractures are given. Treatment of non-union is outlined and internal fixation of osteotomies and of arthrodesis is illustrated.

Cardiovascular Surgery, 1970. By EARLE B. MAHONEY, M.D., New York. 10⅝ × 7⅜ in. Pp. 158. Illustrated. 1971. New York: The American Heart Association, Inc. $5.

THIS monograph is Number 34 to be published by the American Heart Association. It contains a series of articles covering almost every aspect of cardiac surgery as practised today in the various clinics of America.

A large number of the articles deal with congenital heart conditions in infants. Various operations using prostheses make interesting reading. Balloon closure of ventricular septal defects and other interesting operative procedures are well described.

Many research projects dealing with animal hearts are included in this book. Some very useful information is given on the rehabilitation following cardiac surgery.

This monograph will interest all clinicians, but especially cardiologists and cardiac surgeons.

Surgeons' Decisions. By H. L. DUTHIE, Professor of Surgery, University of Sheffield. 7 × 4¼ in. Pp. 112 + vii, with 28 illustrations. 1971. Edinburgh: Oliver & Boyd. 37½p.

THIS small paperback is a mine of information which cannot be found in the standard textbooks of surgery.

Professor Duthie has written chapters on all the major fields of surgery, and his lucid style of writing is one which will appeal to many classes of readers who want to know more about surgeons and their craft.

The illustrations, all line drawings, are quite a feature of this book.

The price of this small book is remarkably cheap and we look forward to seeing more of this type of surgical literature.

Psychiatric Aspects of Organ Transplantation. Edited by PIETRO CASTELNUOVO-TEDESCO, M.D., Torrance, California. 10 × 7 in. Pp. 172. 1971. New York: Grune & Stratton Inc. $7.75.

THIS book is in reality a reprint from the February, 1971, issue of *Seminars in Psychiatry* published by Henry M. Stratton of New York. It contains some fifteen chapters, all of which deal with the different aspects of psychiatric complications occurring in patients who have undergone cardiac, renal, or lung transplantation.

As one would expect, the majority of the papers in this book come from America, yet there is one from Belgium and one from England. Professor Alec Paton, of Birmingham, contributes the last chapter in this volume in which he considers the moral and ethical questions which surround the surgical extension of life and the donation and reception of organs in transplantation.

The problems of the relatives and the general practitioner with regard to donors are fully discussed.

This book brings a new angle on the subject of organ transplantation in man.

Gathorne Robert Girdlestone. By J. TRUETA. 8½ × 5½ in. Pp. 101 + viii, with 8 illustrations. 1971. Oxford: Published for the Girdlestone Orthopaedic Society by the Oxford University Press. £1·50.

PROFESSOR TRUETA has put the medical profession in his debt by writing such an interesting account of the life of G. R. Girdlestone. It is true that he knew his subject well as he worked with Girdlestone at Oxford and eventually held the same post as Girdlestone, namely, Nuffield Professor of Orthopaedic Surgery, at Oxford.

One of the interesting features of this book is the inclusion of letters written by Sir Robert Jones to Girdlestone and the replies. These letters give the reader a first-class insight of both these men and their burning interest in the care of crippled children.

Girdlestone will always be remembered as an outstanding orthopaedic surgeon and the founder of the Wingfield Morris Orthopaedic Hospital, which today is known as the Nuffield Orthopaedic Centre. Lord Franks, a patient of Girdlestone, writes a foreword to this book and whole-heartedly recommends it, and so does the reviewer.

Progress in Pediatric Surgery. Vol. 2. Edited by P. P. RICKHAM, W. Ch. HECKER, and J. PRÉVOT. 8¾ × 5½ in. Pp. 178 + vii. Illustrated. 1971. Berlin: Urban & Schwarzenberg. DM.45.

THE editorship of this interesting paperback comes from England, Germany, and France, an excellent combination as far as paediatric surgery is concerned.

The papers which comprise this book were delivered in July, 1970, at the Alder Hey Children's Hospital, Liverpool, where a postgraduate course on recent advances in neonatal surgery took place.

Such subjects as recent advances in the surgery of the diaphragm in the newborn, surgery of oesophageal atresia, intestinal obstruction, anorectal abnormalities, renal cystic disease in children, and exstrophy of the bladder are included.

This book demonstrates in no uncertain way the importance of paediatric surgery and that special centres are required to deal with neonatal surgery.

The illustrations are excellent.

Engineering and Living Systems. Interfaces and Opportunities. By D. R. RUTSTEIN, M.D., Harvard, and M. EDEN, Massachusetts. 9 × 5¾ in. Pp. 320. 1971. London: The M.I.T. Press. £5·85.

THIS book rightly calls for closer co-operation between medicine and engineering, which includes mathematics and the use of computers. Such items as artificial internal organs, bio-engineering curricula, diagnostic instrumentation, image processing and visualization techniques, neurophysiology, sensory aids, skeletal prostheses, and subcellular engineering are discussed at length in this book.

If all branches of medicine and surgery are to progress in the future a much closer appreciation is necessary of all the newly invented engineering products.

The book also highlights the importance of mathematics in the medical curriculum.

Basic Practical Surgery. By C. BARRIE WILLIAMS, M.D., F.R.C.S., Bristol. 7¼ × 4¾ in. Pp. 180, with 107 illustrations. 1971. Bristol: John Wright & Sons Ltd. £1·75.

THIS cheap paperback is the ideal book for the student of today, for it gives the reader all the basic facts concerning modern-day surgery. It is written in a clear, concise way and the illustrations, all line drawings, are excellent. This is a book for the student to carry in his pocket for ready reference. There are some blank pages at the end of the book for notes, a real asset for the student. This is by far the best book on basic practical surgery that has so far been published.

Fractures of the Mandible. By H. C. KILLEY, F.D.S. R.C.S. (Eng.), F.D.S., H.D.D. R.C.S. (Edin.), L.R.C.P. (Lond.), M.R.C.S. (Eng.), F.I.C.S., London. Second edition. 8¾ × 5½ in. Pp. 74, with 42 illustrations. 1971. Bristol: John Wright & Sons Ltd. 75p.

THIS excellent paperback now appears in a second edition. The author's clear decisive style and the excellent illustrations make this an ideal book for students, and the price is well within the pocket of all students. Both dental and medical students will find this book of real use in this traumatic age. The book is well printed and there is a full bibliography at the end.

Full Dentures. The Treatment of the Edentulous Patient. By ALAN MACK, M.D.S. (U. Durh.), F.D.S. R.C.S. (Eng.), London. 8¾ × 5½ in. Pp. 105, with 130 illustrations. 1971. Bristol: John Wright & Sons Ltd. £1·70.

THIS excellent paperback is No. 13 of the well-known Dental Practitioner Handbooks published by John Wright & Sons Ltd. of Bristol. It is one of the best in the series, for it gives the reader an admirable account of the 'why' and the 'wherefore' of full dentures. The book is comprehensive and complete. From the examination of the patient, conditions before extraction, impressions, centric occlusion, to the finished denture—all are described in a vivid and clear style. The illustrations throughout the book are excellent. A useful bibliography is to be found at the end of the book.

Fractures of the Middle Third of the Facial Skeleton. By H. C. KILLEY, F.D.S. R.C.S. (Eng.), F.D.S., H.D.D. R.C.S. (Edin.), L.R.C.P. (Lond.), M.R.C.S. (Eng.), F.I.C.S., London. Second edition. 8¾ × 5½ in. Pp. 78, with 39 illustrations. 1971. Bristol: John Wright & Sons Ltd. 90p.

THE second edition of this excellent paperback is very welcome, for it contains a wealth of useful information concerning the treatment of the all-too-common injuries of the middle third of the facial skeleton.

In this age of trauma, road-traffic accidents are on the increase and motor-cyclists and motorists are constantly involved, and facial injuries are common.

This book, which is well illustrated with clear drawings, reveals the importance of the co-operation of the dental surgeon with the plastic surgeon to achieve good results.

The cost of this useful book is most moderate.

Anatomy of the Brain and Spinal Medulla. By NEVILLE G. SUTTON, M.B., Ch.M., D.S., F.R.C.S., F.R.A.C.S., Brisbane. 8½ × 5½ in. Pp. 162 + viii. Illustrated. 1971. London: The Butterworth Group. £2·80.

THERE can be no doubt whatever that medical students find that anatomically the brain and spinal cord are the most difficult parts of the body to understand. This being so, this small manual will be welcome as it sets out in a clear and practical way the essential points in the anatomy of the brain and spinal medulla. The illustrations, for the most part line drawings, are good and not too detailed. The X-ray pictures, including ventriculograms and angiograms, are excellent. This is a book that every medical student will find essential for his preclinical studies of anatomy. Final-year students will find this book of value in their surgical anatomy programme.

Plastic and Reconstructive Surgery. Edited by J. T. HUESTON, M.B., M.S. (Melb.), F.R.C.S., F.R.A.C.S., Melbourne. 9½ × 7 in. Pp. 1300. Illustrated. 1971. London: The Butterworth Group. £18·60.

THE numerous papers in this large work were presented in Melbourne in February, 1971. The editor must be congratulated in getting this volume published some six months after the papers were delivered.

There is a pleasing photograph of Mr. B. K. Rank, who was the President at this important international gathering.

This volume deals with various conditions which are discussed in ten sessions.

Session I deals with malignant melanoma, and some seven papers are included which detail the many and varied factors concerned in this disease. Facial paralysis is also considered under this section and the various plastic treatments are dealt with in detail.

Session II gives a very good survey of facial injuries and their treatment.

Session III is concerned with the treatment of cleft lip and palate. This is a large section and the modern methods of dealing with this condition are described and beautifully illustrated. Hypospadias is also considered at length.

Session IV discusses nasal deformities, correction of protruding ears, and the reconstruction of the ear.

Session V surveys tendon surgery and soft-tissue and skeletal repair of the hand.

Session VI deals with Dupuytren's contracture, rheumatoid hand surgery, and congenital abnormalities of the hand.

Session VII is concerned with basic science studies, and deals with skin-grafting from every aspect.

Session VIII is a most comprehensive survey of burns and their treatment.

Session IX is devoted to the reconstruction of facial defects and is interesting and practical.

Session X, a very large section of the book, is concerned with aesthetic surgery and general techniques.

One of the features of this large volume is the excellence of the illustrations, especially the clinical pictures depicting conditions before and after operative intervention.

This is an excellent reference volume dealing with plastic and reconstructive surgery.

Oral Diagnosis. Oral Medicine. By DAVID F. MITCHELL, B.S., D.D.S., Ph.D.; S. MILES STANDISH, D.D.S., M.S.; and THOMAS B. FAST, D.D.S., M.S.D., Indianapolis. Second edition. 10 × 7 in. Pp. 458 + xi. Illustrated. 1971. London: Henry Kimpton. £8·30.

THE authors of this large work rightly insist that oral diagnosis/oral medicine is the foundation upon which the dental curriculum as well as dental practice rests. There are four large sections to this volume: Section 1 is a very complete introduction to oral diagnosis, while Section 2 is concerned with comprehensive clinic oral diagnosis, which includes radiographic examination. Section 3 gives a very interesting account of the recognition and management of oral *pathosis*. This is a curious word and one with which we are not familiar. Section 4 is taken up with treatment planning and patient management.

The illustrations are uniformly good throughout the book. It is interesting to note that the stethoscope can be used in the diagnosis of a fracture of the lower jaw.

This book will be useful not only for students but also to resident medical officers and casualty officers.

Diseases of the Breast. By C. D. HAAGENSEN, M.D., Columbia. Second edition. 10⅕ × 7⅕ in. Pp. 829 + xvi. Illustrated. 1971. London: W. B. Saunders Company Ltd. £14·90.

THE second edition of this large work appears some fifteen years after the original one, and considerable progress has been made in this interval with regard to cancer of the breast in particular. This new volume is comprehensive and is beautifully illustrated with clinical pictures, pathological specimens of breast conditions, and photomicrographical material. It is stimulating to find such a wealth of original drawings. The operative techniques are clear and enhance the written word.

The mature clinical acumen of the author is seen in the whole presentation of this work.

There is a complete author index at the end of the book, but it is a pity that there are some mistakes in the names of the British authors. There is also an extensive index.

Many surgeons will find this work an excellent reference volume on diseases of the breast.

Transperikardiale Operationen an den Hauptbronchien und Lungengefassen. By L. K. BOGUSCH, A. A. TRAVIN, and J. L. SEMENENKOW, Moscow. 10⅔ × 7 in. Pp. 232. Illustrated. 1971. Stuttgart: Hippokrates Verlag. DM.148.

THIS book on transpericardial surgical procedures on the main bronchus and the pulmonary vessels originated in Moscow and has been translated into German. There is a detailed anatomical description of the mediastinum in relation to the surgical project. Preoperative investigations and anaesthetic problems are discussed in detail. The second part of the book analyses the author's experience with 42 patients who underwent such surgical procedures, usually for advanced tuberculosis, where other standard operations had resulted in fistulae and persistent infection. There were 6 deaths.

The book is well illustrated and the colour reproductions are excellent. The translation is rather stiff and at times difficult to follow. The book is beautifully produced, but at over £15 it is expensive. It will be of interest to a rather small number of surgeons involved in this highly specialized field.

The Immunobiology of Transplantation. By RUPERT BILLINGHAM and WILLYS SILVERS, University of Pennsylvania. 9 × 5¾ in. Pp. 209 + xiii. Illustrated. 1971. London: Prentice-Hall International Inc. £2.

THIS paperback is one of the 'Foundations of Immunology' series edited by Abraham G. Osler and Leon Weiss. This series provides an authoritative treatment of important problems in major research areas where rapid development of new information requires an integrated and reliable evaluation.

This book provides an excellent account of the immunological problem in the operation of transplantation.

Consideration is given to the genetic determination of the fate of grafts, the genetics of histocompatibility in man, and weak histocompatibility factors. The problems of thymus and transplantation immunity and immunological tolerance are discussed at some length. There is an excellent chapter on immunosuppression at the end of the book.

This is a useful book and one that will be read by pathologists, physiologists, and research workers who are dealing with transplantation of organs.

Atlas of Ear Surgery. By WILLIAM H. SAUNDERS, M.D., Columbus, Ohio, and MICHAEL M. PAPARELLA, M.D., Minneapolis. Second edition. 10¾ × 8½ in. Pp. 390 + ix. Illustrated. 1971. London: Henry Kimpton. £14·40.

THE second edition of this comprehensive atlas of ear surgery will be welcomed by students and postgraduates alike. The drawings, mostly line, are clear and concise; every detail in the various and many operative techniques on the external, middle, and internal ear are excellent. The second chapter in the book is concerned with dissections of the temporal bone, and the way in which this bone can be removed from the skull of the cadaver. It is only by making himself familiar with the minute anatomy of the temporal bone that the would-be aural surgeon can hope to be able to operate on pathological conditions.

Aural surgery has made vast strides since the Second World War and the various operations involving stapedectomy are now perfected.

Decompression of the seventh cranial nerve by an antral or a transcranial approach is described in detail.

This volume should be in every medical school library, for it is the best atlas of ear surgery that has so far been produced.

Modern Trends in Surgery—3. Edited by W. T. IRVINE, B.Sc., M.D., Ch.M., F.R.C.S., London. 8½ × 5½ in. Pp. 325 + x. Illustrated. 1971. London: The Butterworth Group. £3.

THIS third volume in the series of 'Modern Trends in Surgery' contains some very interesting articles from surgeons in this country and in America.

The articles range over a wide field, from the treatment of shock to the treatment of malignant tumours of the paranasal sinuses. The value of radiotherapy in the treatment of oesophageal cancer is discussed at some length and some favourable results are reported. Articles on rectal prolapse, cancer of the breast, surgical treatment of coronary artery disease, and the topical use of 5-fluorouracil cream for skin cancer are outstanding.

Senior students and postgraduates preparing for higher degrees or diplomas will find this paperback of real value.

The printing and illustrations of this book are excellent and the price is quite moderate.

Amputees and their Prostheses. By MOHINDER A. MITAL, M.D., M.Sc.Bio., and DONALD S. PIERCE, M.D., F.A.C.S., Boston. 9¾ × 7¼ in. Pp. 214 + x, with 58 illustrations. 1971. Edinburgh: Churchill Livingstone. £6·50.

Two World Wars and the increase in road-traffic accidents all over the world have extended the number of amputations performed. In this book a brief outline of the amputee services at Massachusetts General Hospital is presented and then the whole wide subject of the causes and treatment of amputation cases comes under review. The various levels of amputation are considered in detail and the impact of amputation on the patient and society is discussed at some length.

The prosthesis is considered: concepts, components, fabrication, and limitations are all included.

The pre- and postoperative treatment is considered in a practical way.

The book is illustrated with clear and concise line drawings.

A useful reference volume.

Glossaire d'histopathologie des tumeurs humaines. By RENE GÉRARD-MARCHANT, Anatomopathologiste de l'Institut Gustave-Roussy. 8¼ × 5¾ in. Pp. 144 + vi. 1971. Paris: Masson et Cie. 42F.

THIS glossary offers a short and clear histological description of the benign and malignant tumours of the body tissues, though colonic and rectal tumours are omitted.

The author has been successful in creating uniformity in the nomenclature.

The book is very useful for specialists and general practitioners who are not too familiar with tumour pathology and are in need of a quick orientation after the reports of the pathologist are received.

The Structure and Support of Contemporary Residency Programs in Surgery. Edited by HAROLD G. BARKER, M.D., New York. 9 × 6 in. Pp. 290 + xxi. Illustrated. 1971. Springfield, Ill.: Charles C. Thomas. $12.50.

THIS volume contains the papers which were presented at the Thirteenth Annual Meeting of the Allen O. Whipple Surgical Society which was held in the University of Pennsylvania. The large number of contributors cover the whole field of surgical training programmes in a very critical and comprehensive style.

The volume is divided into four parts: Part 1 is devoted to the development of surgical training programmes; Part 2 deals with the important problem of financial support for surgical training programmes; Part 3 is concerned with the federally insured patient in surgical education; while Part 4 deals with the problems and solutions for graduate surgical education.

As one would expect with the affluent society in America, they seem to be entering an era when many members of their society are asking for a modification of the traditional health care. More and more people want personal physician's and surgeon's services and are willing to pay for them.

This book, which is full of useful information, presents the problems which are causing some concern in the training and payment of the interns in American hospitals.

Nephron Failure: Conservation, Substitution, Replacement. By JOHN B. DOSSETOR, B.M., Ph.D., F.A.C.P., F.R.C.P., Edmonton, and M. HENRY GAULT, M.D., C.M.M.Sc., F.A.C.P., Montreal. 9¾ × 6¾ in. Pp. 303 + xi. Illustrated. 1971. Springfield, Ill.: Charles C. Thomas. $19.75.

THIS is a useful monograph which fills in many facts which are often hard to find in one single book. 'Nephron failure' is a name that will soon be universally used instead of 'renal failure'.

Many physicians and surgeons have patients suffering from renal failure under their care and this book will be of great value to them and to all clinicians. It covers the whole wide field of renal failure. The drugs used in the treatment of renal failure are discussed in detail, including the corticosteroids and immunosuppressive drugs.

Neurorenal syndromes come under review. Haemodialysis and peritoneal dialysis are discussed in full.

The final chapter is an attempt to put the logistics of the whole renal failure problem into current perspective.

The illustrations throughout the book are good and have been well chosen. This book will appeal to all clinicians, to research workers, and especially to urologists.

Surface and Radiological Anatomy. Fifth edition. Edited by W. J. HAMILTON, M.D., D.Sc., F.R.C.S., F.R.C.O.G., F.R.S.E., Emeritus Professor of Anatomy in the University of London; G. SIMON, M.D., F.R.C.P., D.M.R.E. (Cantab.), F.F.R., Radiologist to the Diagnostic X-ray Department, St. Bartholomew's Hospital, and to the Brompton Hospital; and S. G. IAN HAMILTON, M.A., M.Chir. (Cantab.), F.R.C.S., Consultant Surgeon, Royal Cornwall Hospital, Truro, Cornwall. Pp. 397 + x. Illustrated. 1971. Cambridge: W. Heffer & Sons Ltd. £6.

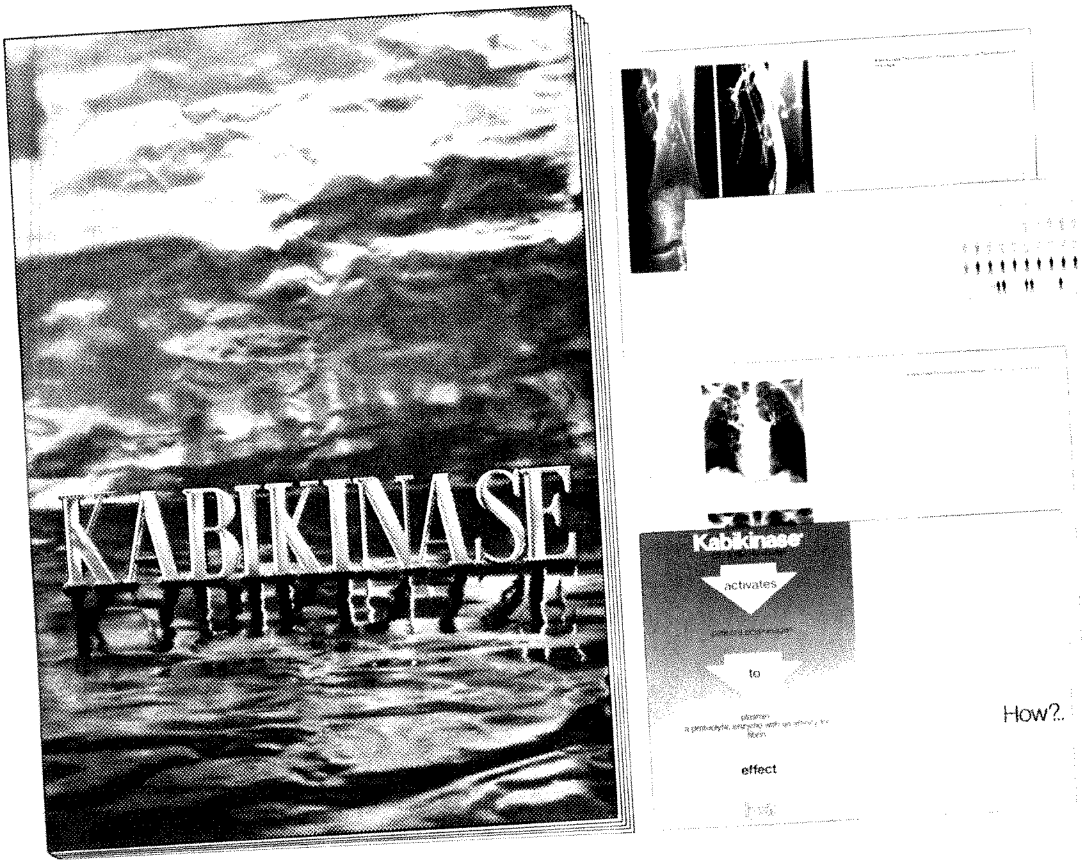
THIS is one of the really useful books for the student today, and its value will be appreciated throughout his medical career. It can be used by the student in his undergraduate days; it can be used by the postgraduate who wishes to polish up his surface and radiological anatomy before he sits for higher diplomas or degrees; it will also be useful for ready reference in the library of any doctor.

There are many unique features in this volume and the most important is the excellence and the beautiful reproductions of the numerous illustrations, which number nearly five hundred. The drawings of A. K. Maxwell are outstanding and could not be bettered. It is stimulating to see so many new and original illustrations.

The editorial trinity have established a wonderful text; the association of an anatomist, a radiologist, and a surgeon seems to be ideal.

The book is divided into sections which enable it to serve as a complement to the study of anatomy in the cadaver both for preclinical and postgraduate students. Much of the book could be studied with profit by students of physiotherapy, radiotherapy, and physical education, and all who use radiology to investigate man in health or disease will find it an invaluable guide.

The first edition of this book appeared in 1938, and since then it has gone from strength to strength. The book is a great credit to British medical literature.



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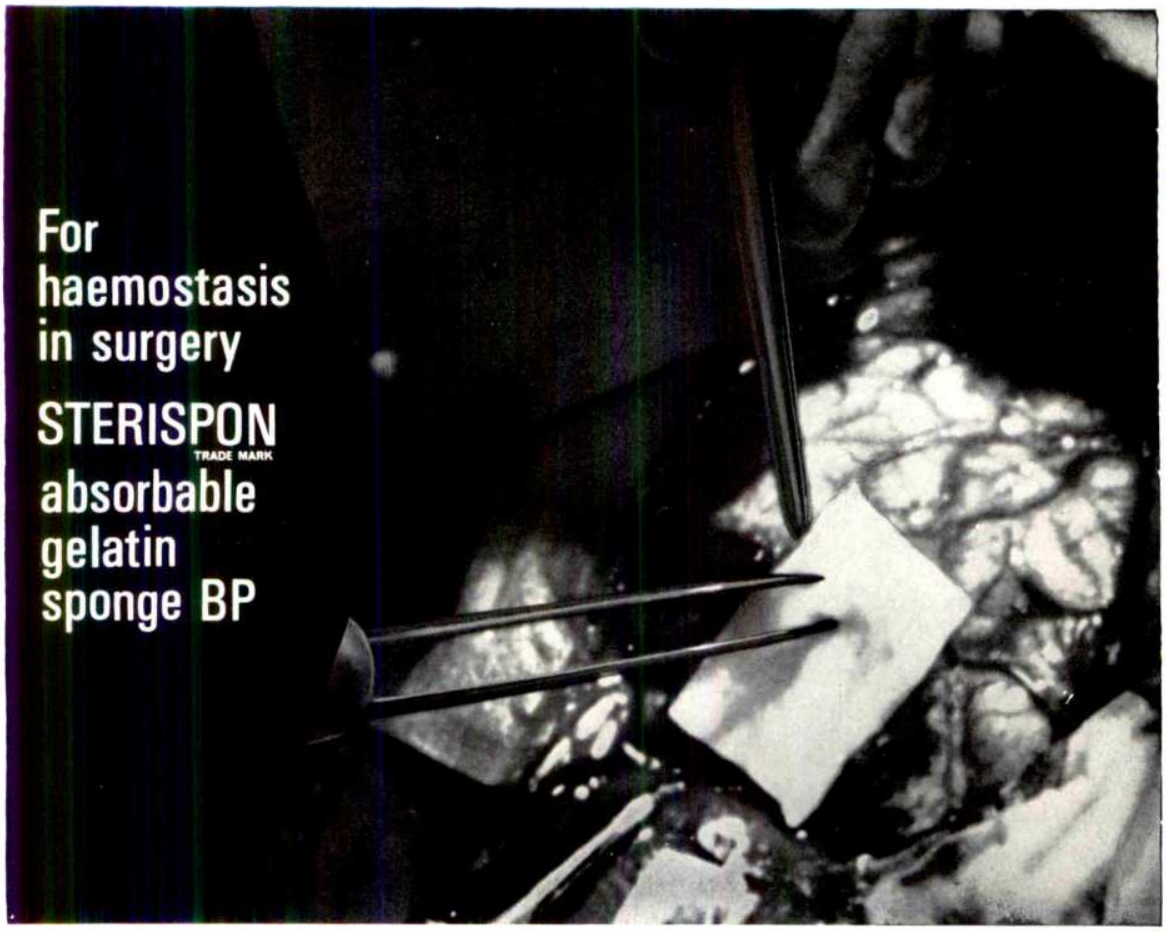

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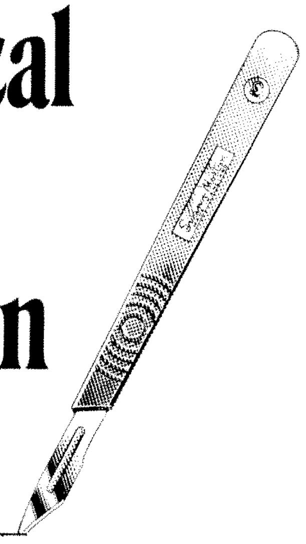

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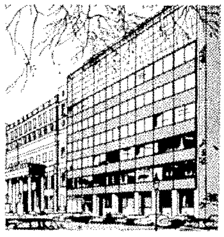

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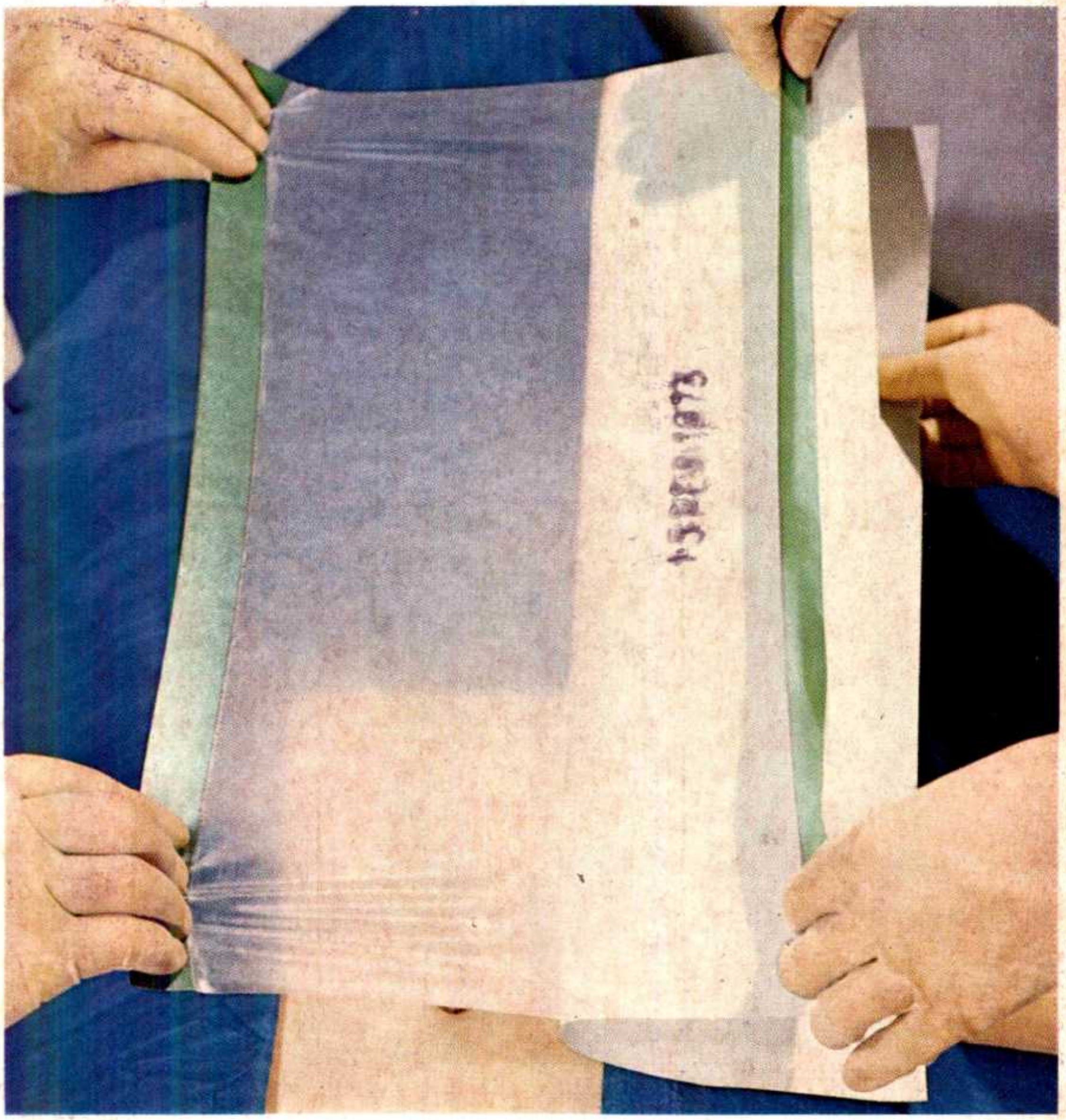

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CONTENTS

PAGE

ORIGINAL PAPERS

The Battered Buttock Syndrome—Fat Fractures - *B. F. Meggitt and J. N. Wilson* 165

Ligation of the Left Renal Vein in Splenorenal Anastomosis without Impairment of Renal Function *John S. Simon, Ashley A. Brown, and Harvey B. Ross* 170

Rectal and Colonic Ulceration in Behçet's Disease - *D. W. Empey* 173

The Maintenance of Maldescended Testicles within the Scrotum using a Dartos Pouch *W. J. Pryn* 175

Peritonitis from Amoebic Liver Abscess - *E. Q. Archampong* 179

New Instruments for Microvascular Surgery - *Robert Acland* 181

Wound Antibiotics in Gastro-intestinal Surgery - *T. A. M. Stoker and Harold Ellis* 184

Kidney Preservation for Transportation *Geoffrey M. Collins, Lionel C. J. Hartley, and Gordon J. A. Clunie* 187

The Value of Frusemide in 110 Consecutive Prostatectomies - *C. R. Williams* 190

The Effect of Oral Supplementation of Zinc Sulphate on Primary Wound Healing in Rats *U. I. Lavy* 194

Acute Intramural Abscess of the Pyloric Antrum—Localized Phlegmon *Gordon Gillespie and Gordon H. MacPherson* 197

The Obliteration of Perforating Veins in the Leg - *R. J. Bentley* 199

Mortality in Missile Wounds of the Head - *Adelola Adeloye* 201

Comparative Evaluation of Preoperative and Operative Radiology in Biliary-tract Disease *D. J. Grundy, P. A. King, and G. Lloyd* 205

Mediastinoscopy - *J. Gunstensen and J. D. Wade* 209

Argentaffin-cell Tumour of Meckel's Diverticulum *E. L. Jones, H. Thompson, and J. Alexander Williams* 213

The Effects of Intermittently Applied External Pressure on the Haemodynamics of the Hind-limb in Greyhound Dogs - *S. Sabri, V. C. Roberts, and L. T. Cotton* 219

The Effect of Intermittently Applied External Pressure on the Haemodynamics of the Lower Limb in Man - *V. C. Roberts, S. Sabri, A. H. Beeley, and L. T. Cotton* 223

A New Non-invasive Technique for Assessment of Superficial Femoral Artery Obstruction *J. P. Woodcock, R. G. Gosling, and D. E. FitzGerald* 226

The Fate of Aortic Valve Homografts *P. E. A. Savage, D. G. Clayton Jones, A. E. Thompson, and D. N. Ross* 231

SHORT NOTES OF RARE OR OBSCURE CASES

Crossed Renal Ectopia without Fusion associated with Carcinoma of the Renal Pelvis *J. E. Castro and M. Handley Ashken* 235

Aortic Aneurysm following External Cardiac Massage - *C. P. Mayers* 238

Leiomyoma of the Oesophagus with Calcification - *Phillip Huddy and Gordon Griffiths* 239

A Case of Traumatic Rupture of the Thoracic Aorta associated with Hypothermia *M. R. Thompson* 243

The Non-absorbable Cystic Duct Ligature - *A. Gunn* 245

REVIEWS AND NOTICES OF BOOKS

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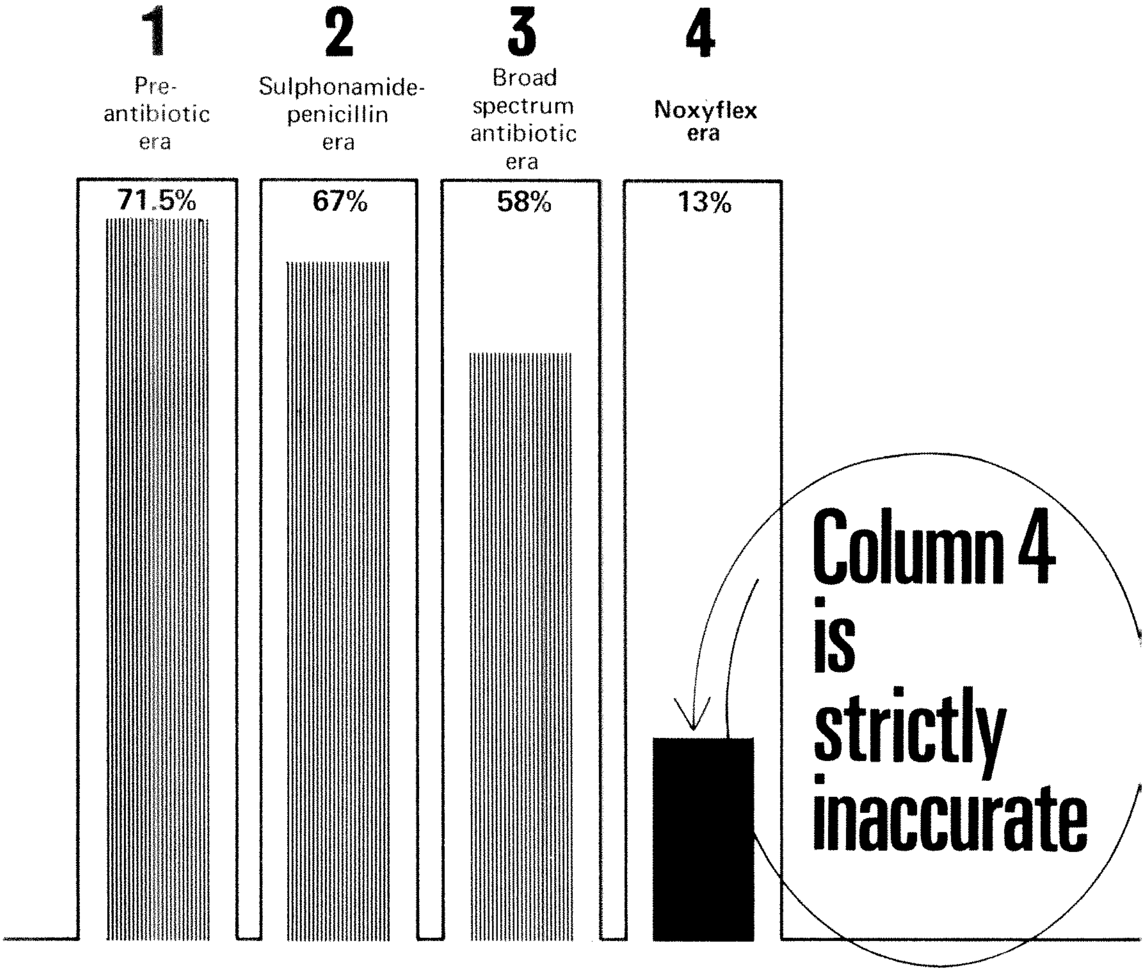

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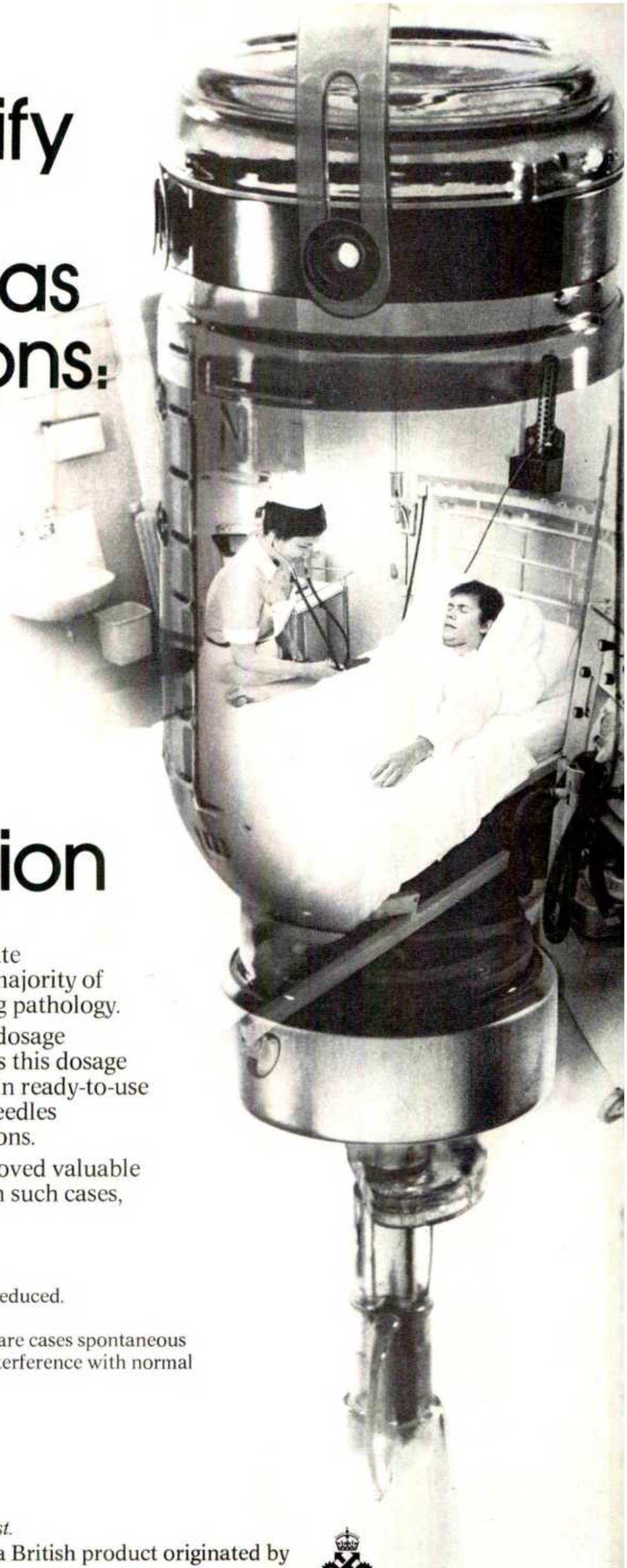

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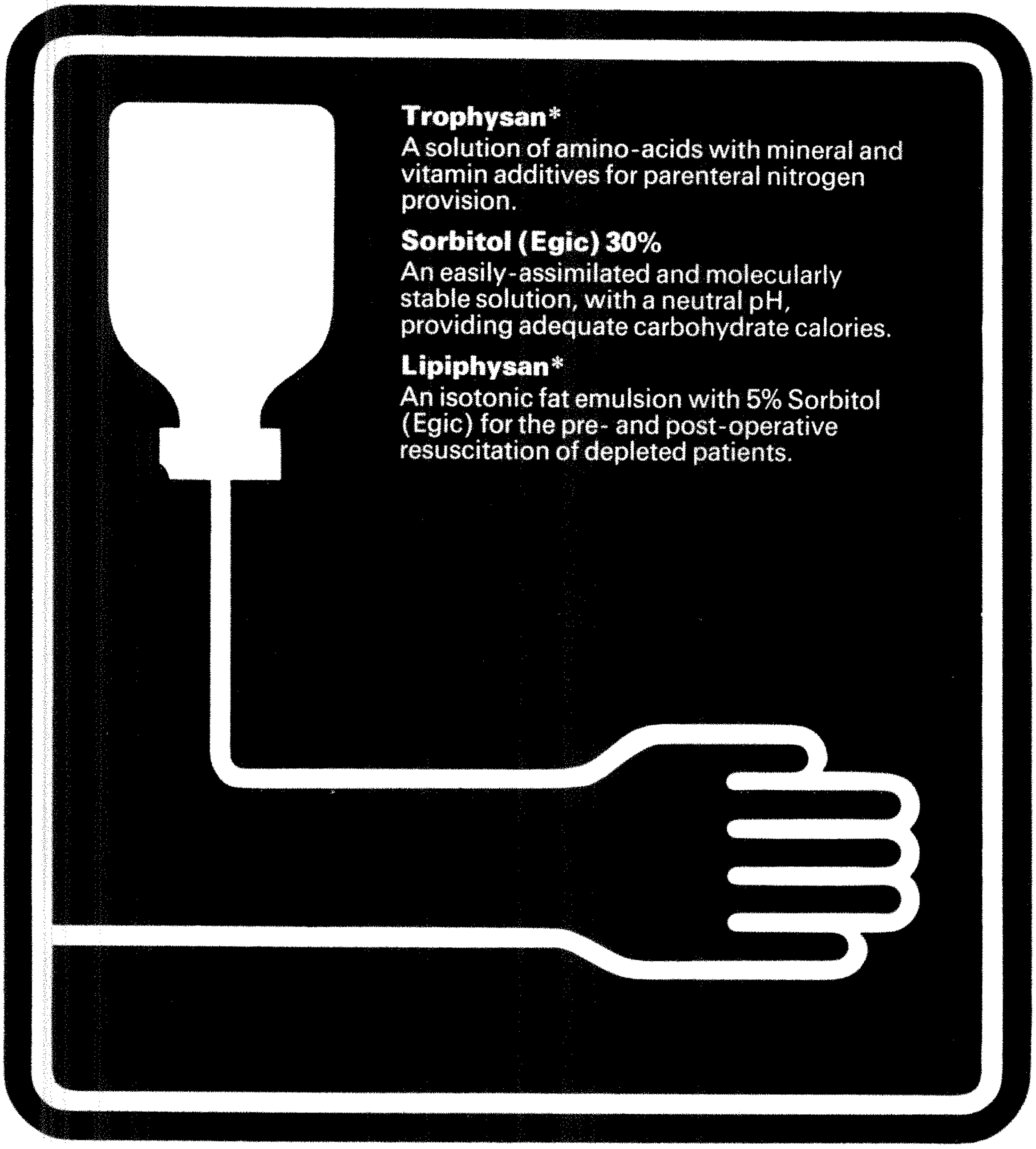

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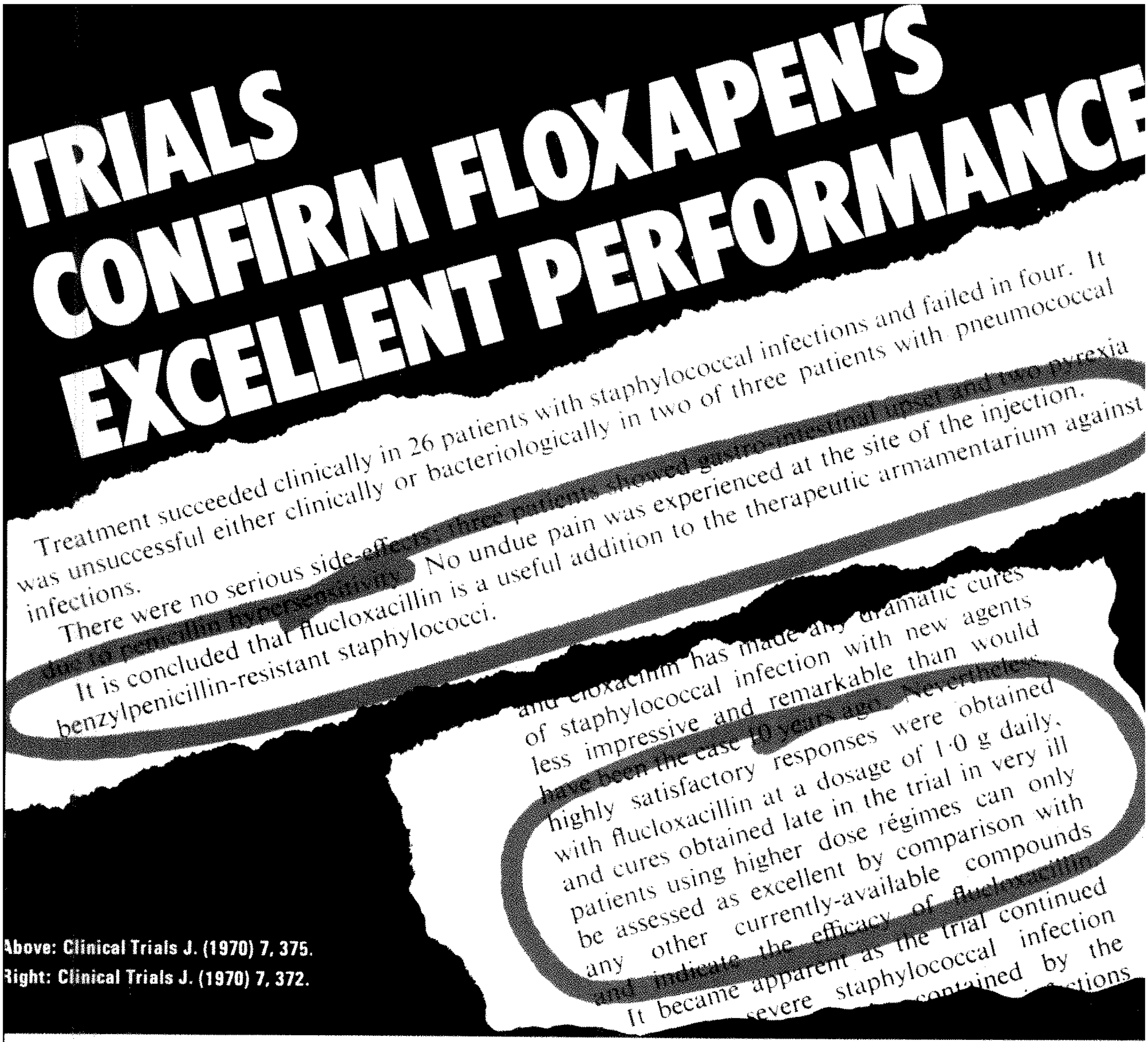

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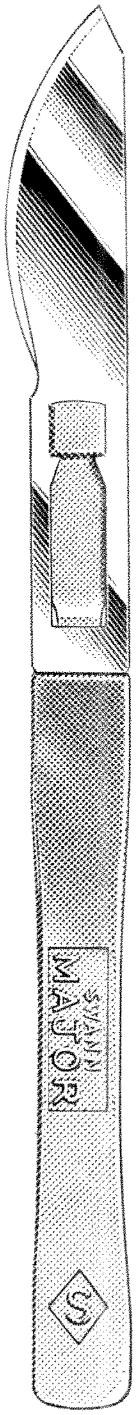

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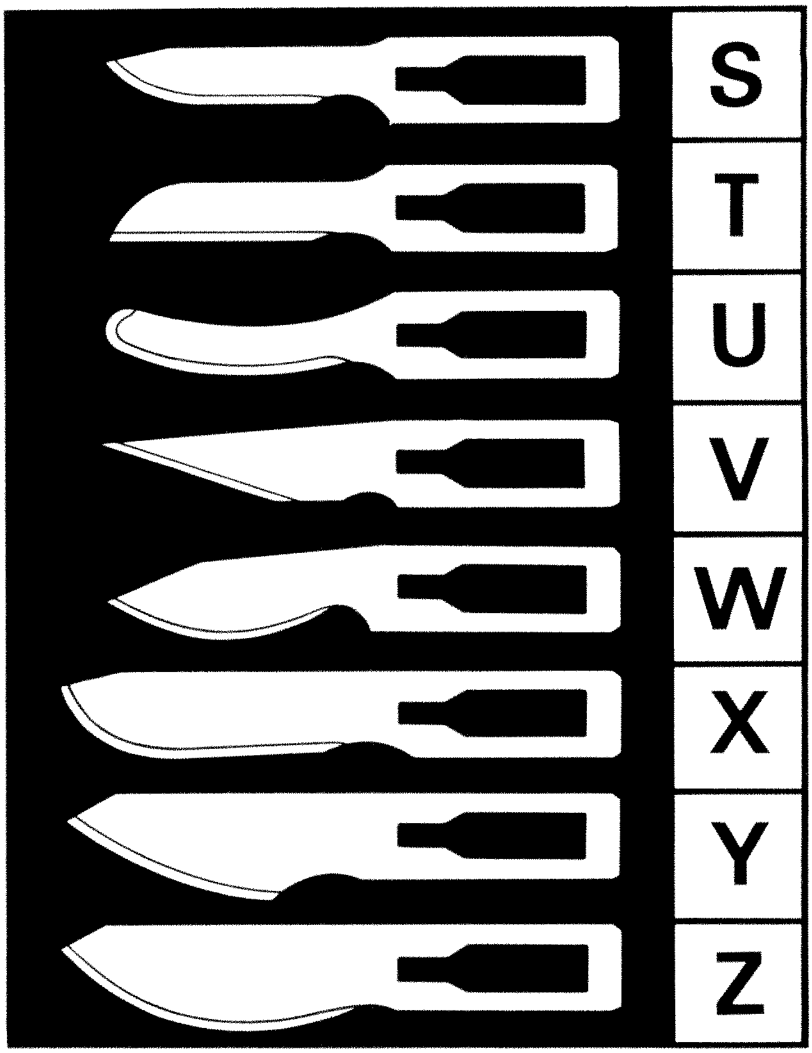

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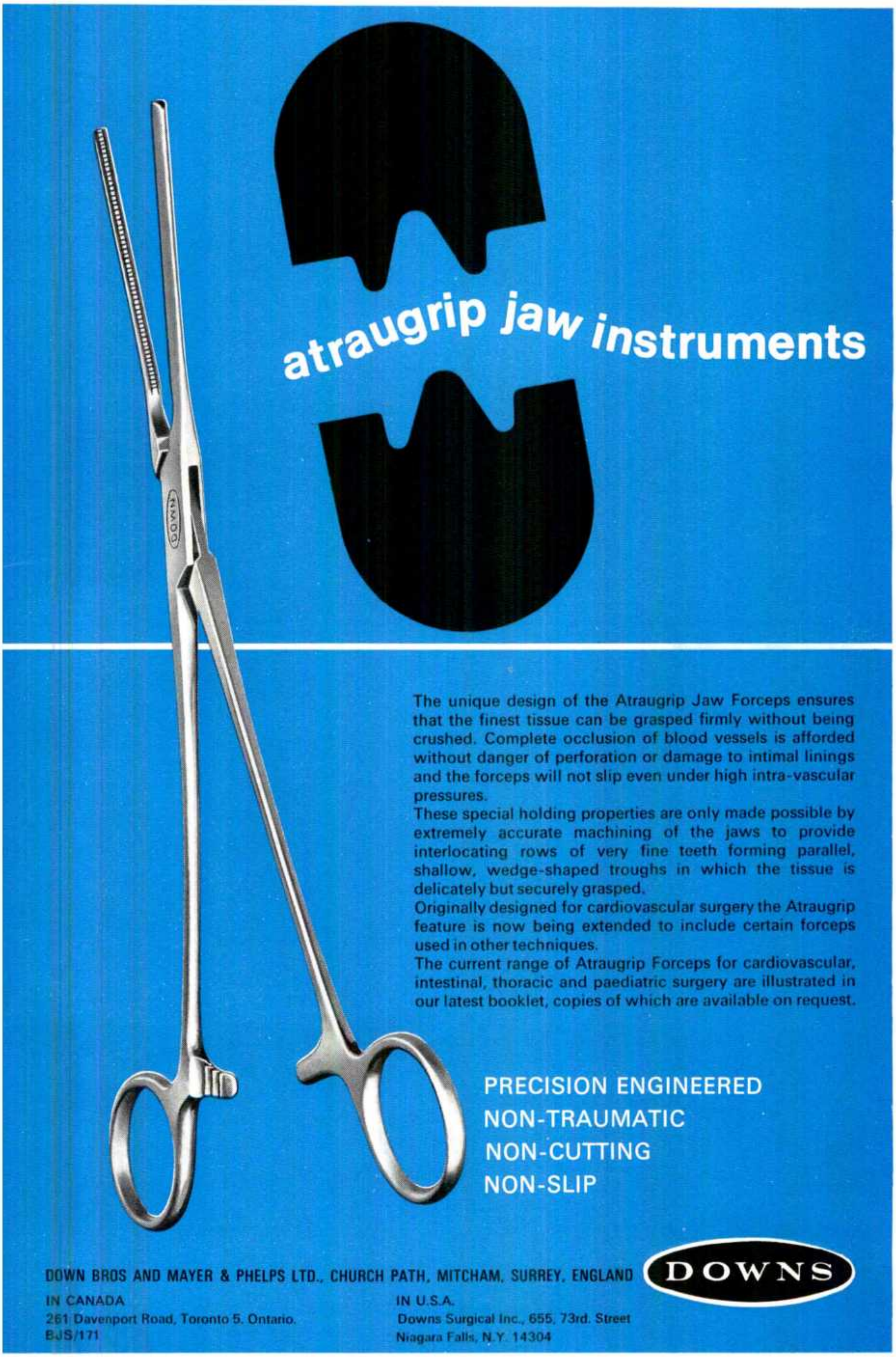

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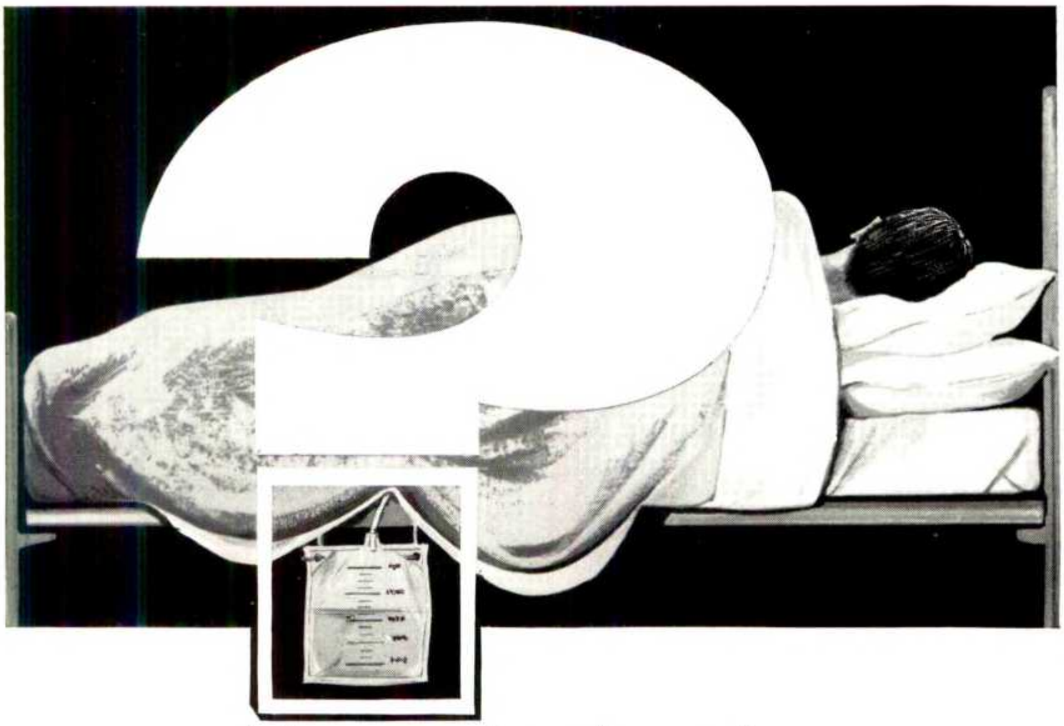

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THE
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ORIGINAL PAPERS

THE BATTERED BUTTOCK SYNDROME—FAT FRACTURES

A REPORT ON A GROUP OF TRAUMATIC LIPOMATA

By B. F. MEGGITT and J. N. WILSON
THE ROYAL NATIONAL ORTHOPAEDIC HOSPITAL, LONDON AND STANMORE

SUMMARY

1. A group of 12 women with traumatic fat swellings around the buttock region is presented.

2. The structure of the subcutaneous tissue and the mechanism in formation of the lipomata are described.

3. Treatment of the essentially cosmetic deformity is discussed and excision of the lipomatous mass is advised when symptoms indicate this.

THE fat covering in man gives roundness to the body and serves to transform unsightly straight lines and irregularities of the deeper structures into more graceful contours. Its greater importance, however, is that by virtue of its resilient, sponge, rubber-like composition this panniculus adiposus provides a protective lining and anchorage to the skin. It acts as a buffer between external pressures on the surface and the deeper tissues beneath. Alterations in this tissue layer through abnormal fat deposition may occur generally as nutritional or endocrine forms of obesity, or locally as fat neoplasms—the lipomata. There is, however, another group of local fat tumours which has a traumatic aetiology and is the subject of this paper.

The 12 cases reported in this series occurred in women, and the lesions were situated in the gluteal, trochanteric, or lower lumbar fat pads. They were mostly the result of blunt trauma and have been variously labelled 'battered buttock syndrome', 'fat fracture', or 'traumatic lipoma'.

As far as we can tell, this condition has not been reported previously in the literature. This is possibly because, not being very common, it has been misdiagnosed as a resolving haematoma. However, with the increase in road-traffic accidents, the condition is likely to become more frequent and, as the residual deformity may often be large, corrective surgical treatment may be required.

CASE REPORTS

Case 1.—A 21-year-old woman was referred from the neurology department complaining of a large tender swelling over the right buttock which was painful on walking. Six months previously she had been knocked down by a car in a road accident and had sustained severe concussion with transient paraparesis. There had also been extensive bruising of the right thigh with a laceration anteriorly that had been sutured. When the bruising had absorbed, the large swelling had remained. Examination confirmed a large, flabby, tender mass just below the greater trochanter, and a hollow deficiency just anteriorly with a 7·5-cm. scar in the lower part (*Fig.* 1). There was no weakness of the abductors.

At operation under general anaesthesia, using a long, anterior, curved incision, the subcutaneous fat was found to have been split obliquely across the trochanter region and it formed a large mass inferiorly. An adventitious bursa was found extending down on the deep fascia from the greater trochanter to the underpart of the fatty tumour. Repair of the defect was undertaken with difficulty by advancing the lower fat mass anteriorly after scarifying the bursa. The fat itself could not be flattened, but a cosmetic improvement which was very acceptable to the patient was obtained, although a bulge remained (*Fig.* 2). The tenderness and pain were completely relieved.

Case 2.—A 25-year-old woman was referred complaining of a lump on the right thigh which produced a dragging pain on walking and was tender to lie on. Two years previously she had been thrown out of a car in a traffic accident and had fallen heavily on to the right thigh and buttock. She had developed extensive bruising with haematoma formation, requiring aspiration of 100 ml. blood from the buttock. When the bruising had eventually settled, the residual lump had become apparent and had remained unaltered over the following 2 years. Local examination showed a large, soft, tender mass

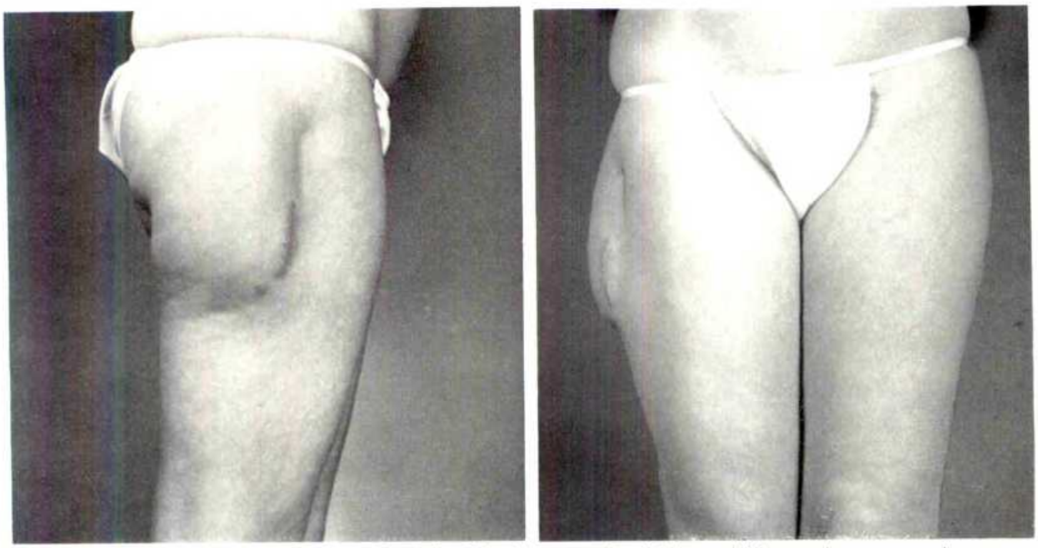

FIG. 1.—*Case* 1. Preoperative fat mass in the right thigh with an anterior deficiency visible over the greater trochanter.

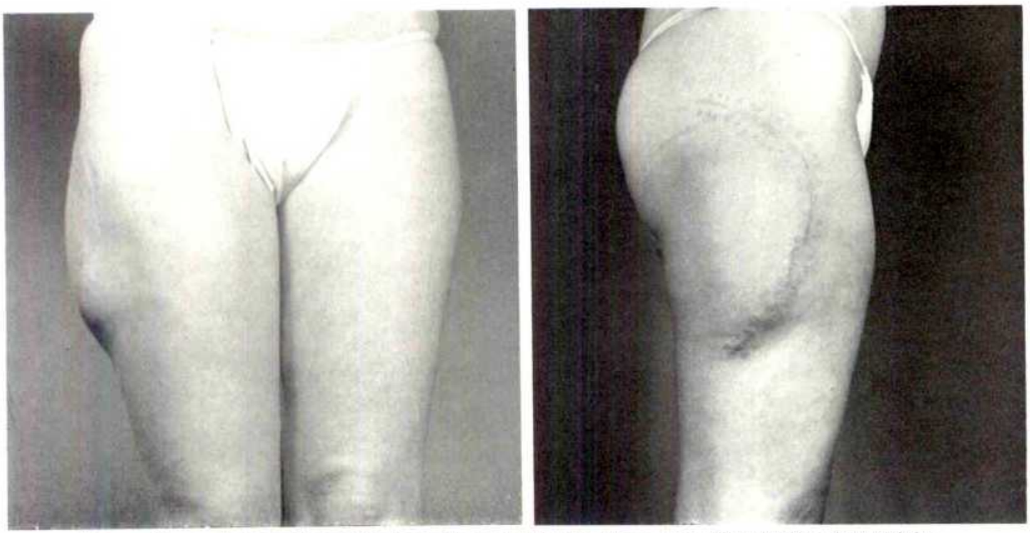

FIG. 2.—*Case* 1. Postoperative result of repair by advancing the fat mass over the greater trochanter defect.

(22·5 × 17·5 × 3·7 cm.) protruding from the lateral aspect of the right thigh (*Fig.* 3). There was a large deficiency which was palpable above the mass.

At operation under general anaesthesia a large fibro-fatty mass was excised through a curved horizontal incision (*Fig.* 4), as an advancement repair was not possible. An adventitious bursa beneath the tumour was also removed and found to contain fifteen large, free fat lobules (*Fig.* 4, inset).

The deformity was considerably improved, with restoration of the smooth thigh contour (*Fig.* 5). The aching pain produced by walking and rolling on the area was completely relieved.

Case 3.—A 35-year-old woman was referred with a large swelling (20 × 15 × 3·7 cm.) just below the right trochanter following a glancing impact by a car in a road accident 6 months previously. There had been considerable bruising around the buttock initially, with a painful limp for 4 months. This had settled, leaving the swelling in which a dragging aching pain had developed with walking, which was severe enough to require surgical relief if possible.

At exploration under general anaesthesia a large fibro-fatty mass was excised through a curved anterolateral incision. The subcutaneous fat was seen to have been split transversely just below the trochanter and it had retracted inferiorly. It had formed a conglomerate mass, free from its deep fascia attachment, with a pseudobursa underlying it. After removing all the excess fat the skin was sutured, leaving a vacuum drain. An almost normal thigh contour was obtained with complete relief of the aching pain.

Case 4.—A 6-year-old girl was admitted to hospital having been knocked down by a lorry. She was found to have sustained severe concussion, fractures of the pubic rami and right tibia, and extensive bruising of the righ

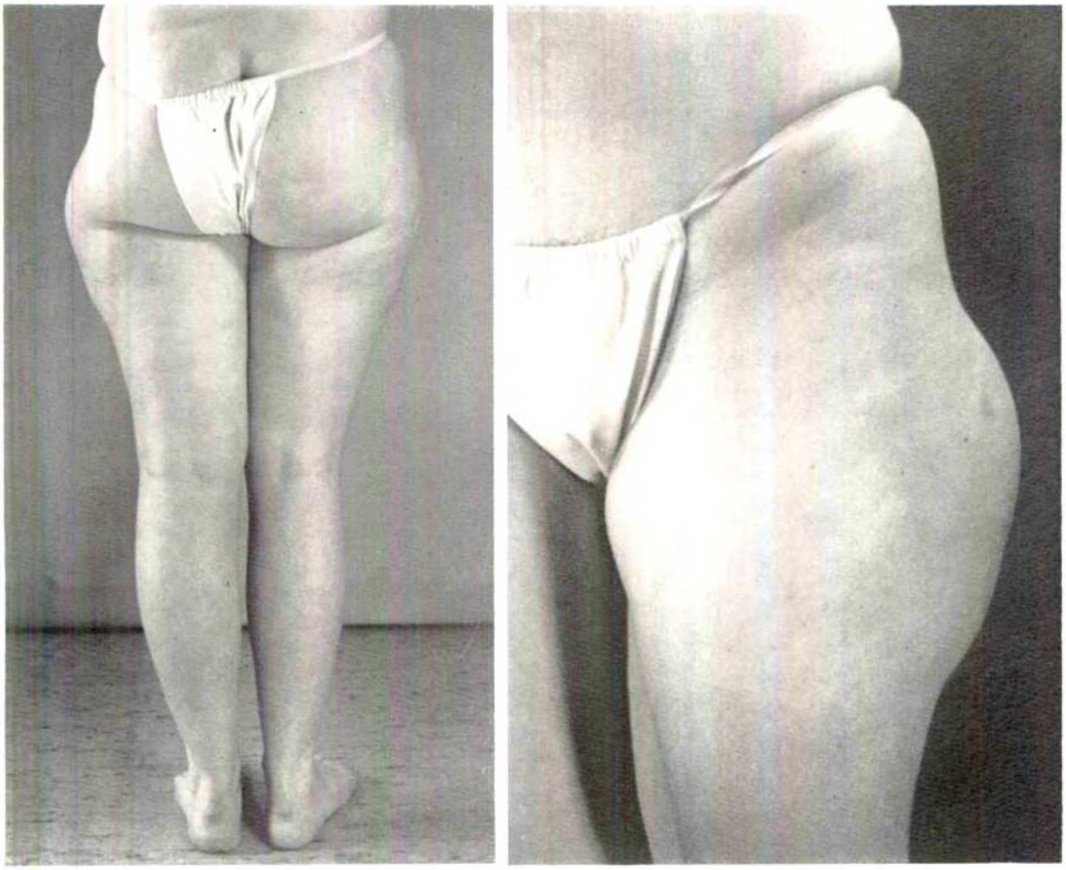

FIG. 3.—*Case* 2. Preoperative mass in the left buttock with the fat fracture defect shown above.

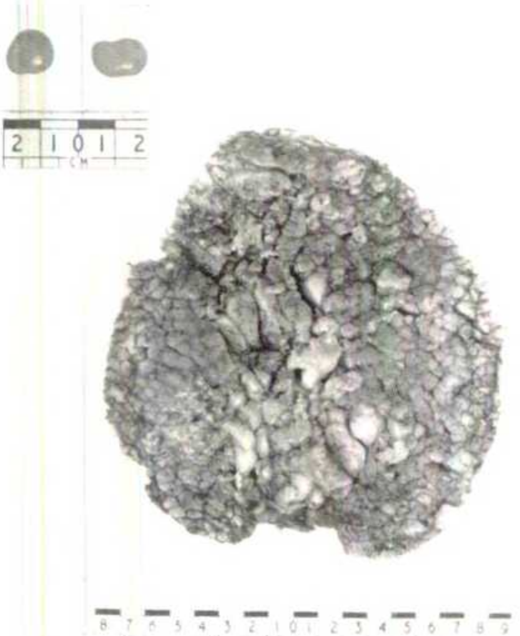

FIG. 4.—*Case* 2. Lipoma mass excised at operation. *Inset*, Two of the free fat lobules from the underlying bursa.

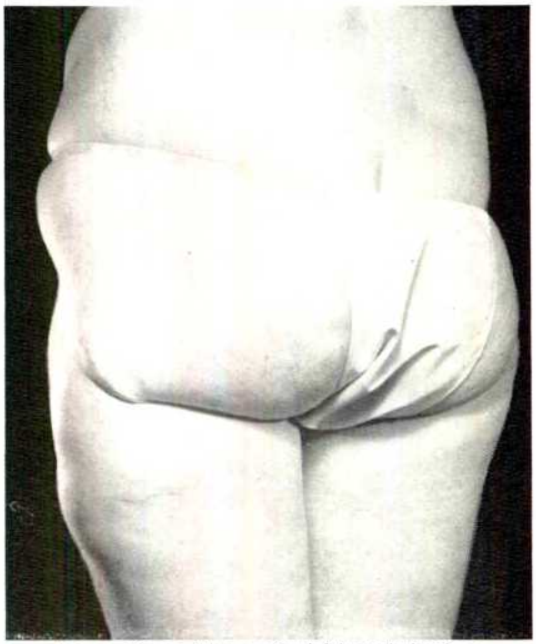

FIG. 5.—*Case* 2. Postoperative left buttock showing a good cosmetic result.

buttock. Three months later she had made a good recovery from the head injury and fractures, but was left with a large prominent swelling over the right lateral buttock (*Fig*. 6). There was a palpable transverse deficiency in the right upper buttock where a wide section of the gluteal fat had retracted laterally, producing the large deformity. At follow-up examinations over the past 12 months the size of this swelling has not altered very much. It is hoped that the swelling will get relatively smaller as the child grows, and no operation has been advised as yet.

Cases 5, 6, 7, 8, 9, and 10.—These cases are all similar to *Case* 3, being women aged between 25 and 60 years who presented with large fatty lumps in the buttock or lateral thigh of 6 months to 3 years' duration. These lumps were all the result of direct impact either from a car or from falling heavily on to the buttock, as in *Cases* 9 and 10, who were thrown out of a car on crashing. Extensive bruising occurred in all patients similar to that in *Case* 5 (*Fig*. 7), which on absorption revealed the fat fracture and a lipomatous mass below, as in *Case* 2 (*Fig*. 3). The main symptom was cosmetic deformity, but occasionally aching pain or tenderness was present. Once the nature of the swelling was understood, none of these patients was sufficiently worried to make further surgery necessary.

Case 11.—A 42-year-old woman was referred with a large tender swelling in the left lateral thigh. This had appeared immediately after a fall on to the hip region which had occurred 3 weeks earlier. There had been no bruising, but on examination there was a 10-cm. scar down the anterolateral trochanteric region. The patient had undergone two explorations of the greater trochanteric

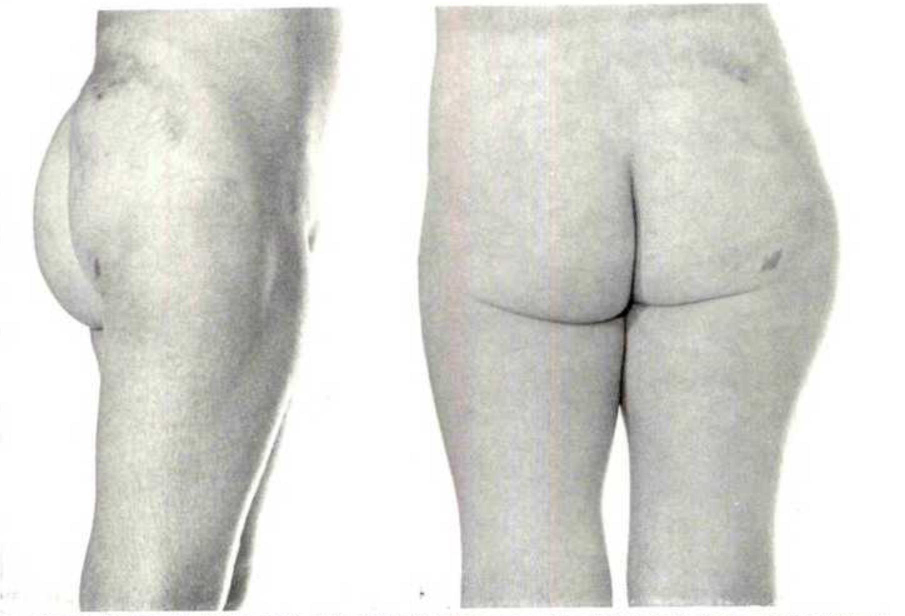

FIG. 6.—*Case* 4. Downward displacement of the right gluteal fat mass with a defect visible in the superior buttock.

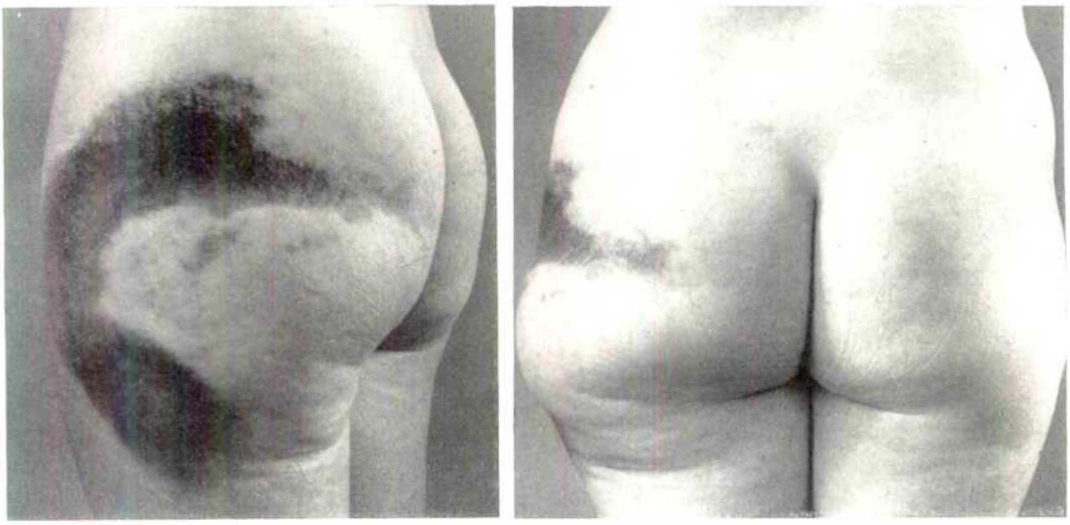

FIG. 7.—*Case* 5. 'Battered buttock' 2 weeks after injury, with the fat swelling being revealed as the bruising absorbs.

region 4 and 17 years previously for persistent pain, when non-specific bursitis was the only finding. It was in this operative area that the fat splitting had occurred (pathological fat fracture). Over the next 4 weeks the tenderness completely settled and no further treatment was required.

Case 12.—This case had a similar pattern to that in *Case* 11, but the lesion was much higher, occurring in the lumbar region posteriorly. The patient, a 56-year-old woman, was admitted to hospital following a road accident when she had been struck in the low back by a car. There was some local swelling and bruising in the lower left lumbar region and radiographic examination showed fractures of the left transverse processes of the fourth and fifth lumbar vertebrae. Over the following 4 months the back pain and tenderness settled, leaving a fatty swelling in the lower left lumbar region with a defect just above. The patient was not unduly concerned by the cosmetic deformity and no further treatment was indicated.

DISCUSSION

The structure of the panniculus adiposus would seem from a biomechanical consideration to be well adapted to maintain a resilient cushion system over the body surface for handling normal body loads. The individual fat lobules form the compressile units and are contained under some pressure by the fibrous capsule and septa which compose the tension elements. The lobules are arranged in layers of two to four deep with separating horizontal fibrous septa supported by vertical septa anchoring the epidermis to the deep fascia (gluteal or lata). This arrangement can be readily appreciated in the buttock during standard approaches to the hip region, and the fat lobules will be seen to pout where the fibrous compartments have been opened by the incisions. The whole region has a rich, fine, vascular network with larger vessels traversing the deep fascia.

Under normal body loads, local pressure produces flattening of the lobules and transference of the weight over a wider area, but the fibrous supporting septa prevent lateral migration of the fat. On release, this compression/tension system enables the tissue to return to its resting shape and position. If sudden excessive force is applied locally, such as impact from a moving vehicle (as in 9 of the cases described) or heavy falling on to the area (as in the 3 other cases reported), the fat compartments are burst open with rupture of the septa and shearing off of the anchorage between the skin and the deep fascia. Also, with local vascular damage, a varying amount of bruising and haematoma formation occurs, as in all of the present cases except for *Case* 11. The end-result is the battered buttock picture with fat fracture and traumatic lipoma formation after retraction of the detached subcutaneous tissue into the buttock or thigh. After the bruising and haematoma have been absorbed, the tissue defect above and the fat swelling below produce the typical deformity. It is a characteristic of fat tissue that it does not undergo local resorption or regeneration (the principle of abdominal apronectomy and some forms of mammoplasty), and hence the deformity is permanent in adults at least.

It is interesting to note that all the patients were female. This might be coincidence—or that women are more cosmetically conscious than men. However, it is a characteristic feature that women are more endowed with subcutaneous fat than men, especially around the buttocks and thighs. This may render the skin fascia anchorage weaker, with more liability to splitting and to the formation of larger lipomata. All the patients described here were well covered, but none was grossly overweight.

The main symptom in all the reported cases was local deformity, with aching and tenderness occurring early, but mostly settling later. Four patients with large swellings, tenderness, and local pain requested surgical treatment, and this was undertaken in 3; the fourth, a 6-year-old-girl, is still being followed up as it is thought that the swelling may well recede with general body growth.

Treatment of these traumatic lipomata may be by surgical repair or excision. The former proved partially successful in *Case* 1 where some cosmetic improvement was obtained by advancing the swelling into the defect. However, this was not possible in *Cases* 2 and 3 where the fat formed a localized fibro-fatty mass by retraction (*Fig.* 4) and could not be stretched or advanced sufficiently. Correction of the deformity by wide excision of the fatty mass gave good results in these 2 cases, with complete relief of the tenderness and pain. In the other 6, however, the deformity gave little trouble and no further treatment was necessary once the nature of the swelling was understood.

Acknowledgements.—Our thanks are due to Mr. N. T. Holden, Enfield, and Mr. R. C. Howard, Norwich, for permission to include their patients, and to the staff of the Photographic Department of the Institute of Orthopaedics.

LIGATION OF THE LEFT RENAL VEIN IN SPLENORENAL ANASTOMOSIS WITHOUT IMPAIRMENT OF RENAL FUNCTION

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SUMMARY

This paper draws attention to the fact that the left renal vein or one of its major tributaries may be ligated without apparent impairment of function of the left kidney. This information has been of great value in constructing splenorenal shunts in operations for portal decompression. Other situations in which this information might be of value are suggested.

END-TO-SIDE anastomosis of the splenic vein to the left renal vein is an accepted method of portal decompression. Occasionally, owing to abnormal anatomy of the renal vessels, an end-to-side anastomosis is technically unsatisfactory if not impossible. Previously, when this situation was encountered, a left nephrectomy was performed and the free end of the renal vein was used for an end-to-end anastomosis with the splenic vein. This technique proved technically easier, having two free mobile vessels to be brought together (Hunt, 1958). It did, however, mean sacrifice of the left kidney.

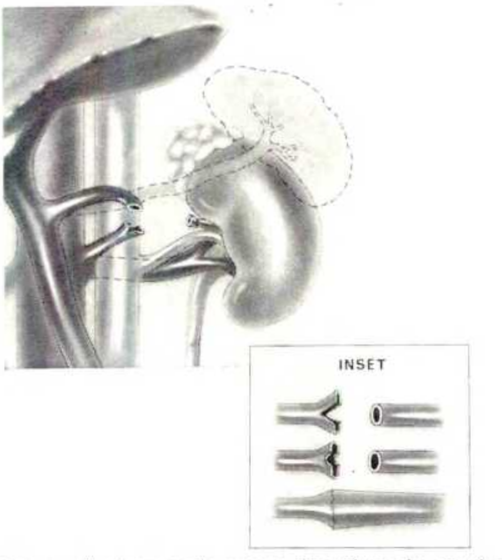

FIG. 1.—A circum-aortic venous ring where the anterior venous limit is used for an end-to-end splenorenal anastomosis. The inset shows how the vein(s) may be tailored if necessary.

In more recent years end-to-end anastomoses have been performed with preservation of the left kidney. Thirteen such cases have been carried out at St. Bartholomew's Hospital, using the entire left renal vein in 5 and a major tributary in 8. This paper emphasizes the already known fact that in certain instances the left renal vein may be ligated and divided without apparent embarrassment to the left kidney. It also points out a clinical situation in which ligation of the left renal vein may be of use.

ANATOMY

The left renal vein is more commonly anomalous than the right, probably in part owing to its greater length, and there is frequent deviation from the textbook picture of the left renal vein crossing the aorta and entering the hilum of the left kidney as a single vessel. The left renal vein may form a circum-aortic venous ring, from which there may be further branching of the anterior or posterior limbs (*Fig.* 1). There may be multiple segmental tributaries entering the left renal vein in any part of its course. It is, however, rare for more than one left renal vein to enter the inferior vena cava. Anson, Cauldwell, Pick, and Beaton (1947) point out: 'Complexity in the venous arrangement is the result of the Y-shaped bifurcation of the renal vein, or of communication with neighbouring veins or of these circumstances combined. Intricacy of this nature is characteristic of the left side.'

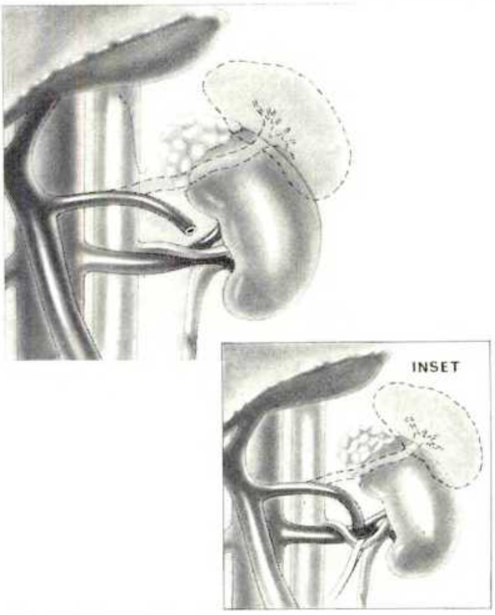

FIG. 2.—The renal artery lying anterior to the renal vein. The inset shows that the artery must be retracted away from the site of the end-to-side anastomosis and when released would interfere with the lie of the anastomosis.

A single left renal artery usually lies behind the left renal vein, allowing the standard end-to-side splenorenal anastomosis to be completed without undue interference. Owing to the segmental origin of the kidney the left renal artery may have important branches in front of the renal vein. Occasionally the entire left renal artery lies anterior to the vein, making coaptation of the renal and splenic veins difficult and interfering with the lie of the anastomosis (*Fig.* 2).

Table I.—DETAILS OF 8 SURVIVING PATIENTS WHO HAD AN END-TO-END SPLENORENAL SHUNT FOR PORTAL DECOMPRESSION

CASE	TYPE OF SHUNT	AGE AT TIME OF SHUNT (years)	DURATION OF SHUNT (years)	BLOOD-PRESSURE	BLOOD-UREA NITROGEN	URINALYSIS	INTRAVENOUS PYELOGRAM	COMMENT
1	End-to-end	39	$3\frac{1}{2}$	110/75	36	N.A.D.	Normal	Easier coaptation; left spermatic vein ligated
2	End-to-end	31	3	120/70	21	N.A.D.	Duplex left collecting system. Otherwise N.A.D.	Easier coaptation
3	End-to-end	18	$2\frac{3}{4}$	115/70	35	N.A.D.	Normal	Easier coaptation; left ovarian vein preserved
4	Partial end-to-end	14	2	118/78	16	N.A.D.	Normal	Two large branches tailored (as shown in *Fig.* 1) for easy coaptation
5	Partial end-to-end	60	$4\frac{3}{4}$	180/110	23	N.A.D.	Normal	Triple renal vein; highest branch used for easy coaptation
6	Partial end-to-end	11	$15\frac{1}{2}$	120/80	21	N.A.D.	Left peripelvic cyst. Otherwise N.A.D.	Circum-aortic ring; anterior branch used
7	Partial end-to-end	19	$6\frac{1}{2}$	110/70	20	N.A.D.	Normal	Early bifurcation to two renal veins; superior branch used
8	Partial end-to-end	56	$5\frac{3}{4}$	N.A.D.*	N.A.D.*	N.A.D.	Would not attend	Renal artery in front of three renal veins; middle vein used

N.A.D. = No appreciable disease.

* Per general practitioner.

It was noticed that when the left renal vein was occluded with a vascular clamp there was little or no venous congestion of the left kidney. Hollingshead and McFarlane (1953), in animal experiments, demonstrated by arteriography that after gradual surgical occlusion of the left renal vein the stellate and capsular veins of the kidney assumed the major role in collateral flow. They also found significant collateral flow via the lumbar, gonadal, and ureteric vessels. Erlik, Barzilai, and Schramek (1965) ligated the left renal vein in cadavers and did arteriograms showing venous drainage via the suprarenal and inferior phrenic veins above, by the gonadal and lumbar veins (second and third) below, and by a retro-aortic plexus of veins ultimately associated with the lumbar vessels behind.

Whether the bulk of the drainage is via capsular vessels or via the fixed collaterals is probably governed by the chronicity of the occlusion, the suprarenal, gonadal, and lumbar plexus of veins probably being more important in acute occlusion. These vessels usually enter the left renal vein at about 6 cm. from its junction with the inferior vena cava. Thus, if a left renal vein is to be ligated the ligature should be placed within 6 cm. of this junction with the inferior vena cava, although this was not always done in the present series (*Case* 1).

Cases have been reported of thrombosis of the inferior vena cava, including the renal veins, with pyelographic evidence of left renal function (Erlik and others, 1965). This is not true of the right kidney which has few anastomotic vessels available for the development of a collateral circulation.

MATERIALS AND METHODS

Thirteen patients have undergone an end-to-end splenorenal shunt for portal decompression at St. Bartholomew's Hospital over the past 16 years. Of these, 5 patients have had complete transection of the left renal vein, and 8 patients have had transection of a major branch of the left renal vein. Five of the patients died of various causes which were primarily related to their underlying liver disease. Where available, the pathology of these cases has been reviewed.

Renal function was evaluated in 7 living patients by estimation of blood-urea nitrogen, urinalysis, and measurement of blood-pressure, and 1-, 3-, and 5-minute hypertensive intravenous pyelograms were carried out. It is appreciated that these tests do not produce a delicate evaluation of the function of a single kidney, but arteriography and differential ureteric catheterization were considered to be unjustified in otherwise well patients. One patient (*Case* 8) could not come to hospital for the necessary examinations and declined to have an intravenous pyelogram.

RESULTS

Table I shows the details of the 8 patients who are alive with end-to-end splenorenal anastomoses. It is noteworthy that all of these patients are alive and well with no problems which are related to the left kidney.

These patients have had shunts for lengths of time varying from 2 to 16 years. All the patients had normal blood-urea and normal urinalysis. One patient was found to be hypertensive and is currently being treated with Aldomet. An accurate preoperative blood-pressure was not available for this patient; she entered the hospital in shock, and she was shunted as an emergency. In all the cases the intravenous pyelogram, where available, showed prompt bilaterally equal excretion of contrast material. There was no variation in the renal size. One patient (*Case* 2) showed a left duplicated collecting system which was unchanged from her preoperative intravenous pyelogram. A second patient (*Case* 6) showed a peripelvic cyst which was not seen on an intravenous pyelogram which was taken 15 years previously. Anatomical variations which prompted an end-to-end anastomosis are listed in *Table I*, but in some of the later cases an end-to-end anastomosis was performed because of the ease of the method rather than because of a distinct abnormality in the renal vasculature.

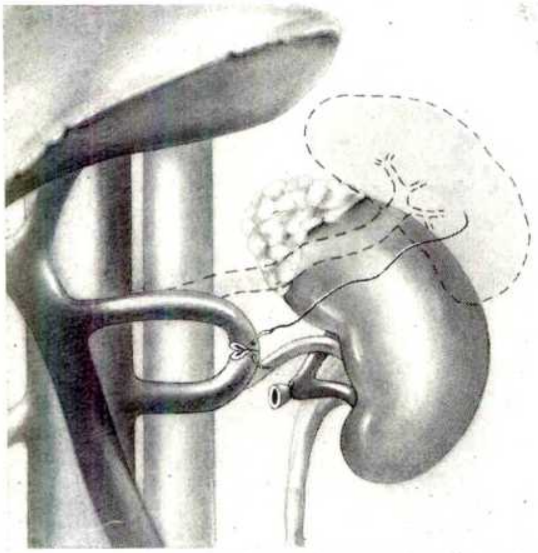

FIG. 3.—An end-to-end splenorenal anastomosis utilizing the entire left renal vein.

Table II lists the patients who had an end-to-end splenorenal anastomosis and who later died. Again, none of the patients had symptoms referable to the left kidney. Blood-pressure, urea nitrogen, and urinalysis were unchanged pre- and postoperatively in all instances. Post-mortem examinations were done on 2 patients: one (*Case* 13) showed normal kidneys bilaterally; the other (*Case* 9) showed left hydronephrosis. This patient, however, showed an abnormal left kidney with somewhat delayed excretion on the preoperative intravenous pyelogram.

DISCUSSION

It has been pointed out by others that the left renal vein may sometimes be divided without detriment to the left kidney. This paper confirms this finding and suggests an instance where the manœuvre may be of some importance. Since anomalies of the left renal vasculature are quite common, the surgeon doing splenorenal anastomoses will find instances when an end-to-side splenorenal shunt may be technically quite difficult. This may be due to the anatomical position of the vein, for example, located behind the artery (*Case* 8, *Fig.* 2), or due to the branching of the vein, making an end-to-side anastomosis difficult and tedious. It may also be found that having two completely divided ends of vessels gives more mobility for making the anastomosis (*Fig.* 3). In such instances an end-to-end anastomosis may be done without undue concern for the left kidney. A non-crushing vascular clamp is applied to the left renal vein and this is left in place for approximately 15 minutes while completing the dissection of the splenic vein. On application of the clamp the kidney may become mildly congested, but this is not common and is not a progressive phenomenon. In no instance in the present series was it necessary to abandon an end-to-end anastomosis because of the appearance of the left kidney. In

Table II.—DETAILS OF 5 PATIENTS WHO HAD AN END-TO-END SPLENORENAL SHUNT FOR PORTAL DECOMPRESSION AND WHO LATER DIED

CASE	TYPE OF SHUNT	AGE AT TIME OF SHUNT (years)	DURATION OF SHUNT (years)	BLOOD-PRESSURE		BLOOD-UREA NITROGEN		URINALYSIS		COMMENT	POST-MORTEM FINDINGS
				Pre-operative	Post-operative	Pre-operative	Post-operative	Pre-operative	Post-operative		
9	End-to-end	47	1⅓	120/70	105/70	30	25	N.A.D.	N.A.D.	Easier coaptation	Hepatoma; slight hydronephrosis (left); kidney otherwise N.A.D.
10	End-to-end	9	1¼	115/70	118/70	27	13	N.A.D.	N.A.D.	Cystic fibrosis; easier coaptation	No post-mortem examination; cystic fibrosis
11	Partial end-to-end	52	1½	180/95	160/94	35	28	N.A.D.	N.A.D.	Double vein: superior, inferior; lower (inferior) branch divided into anterior and posterior limb; anterior inferior branch used; died in coma	No post-mortem examination; died in coma
12	Partial end-to-end	72	7 months	120/70	140/70	13	20	N.A.D.	N.A.D.	Renal vein abnormal and segmental; lower branch used	No post-mortem examination; haematemesis
13	Partial end-to-end	42	1	130/80	130/90	25	24	N.A.D.	N.A.D.	Anterior and posterior renal vein in circum-aortic plexus; anterior vein used	Bilateral normal kidneys on histology

N.A.D. = No appreciable disease.

cases where a major tributary was utilized the clamp was applied to the tributary in the same fashion.

It is not suggested that end to end is a more effective method of anastomosis in achieving portal decompression than end to side; it is probable that there is no functional difference between the two. We wish to point out that in certain anatomical situations the construction of an end-to-side anastomosis may be very difficult and that in these instances division of the left renal vein or one of its major tributaries does not cause any apparent damage to the left kidney.

Situations may arise in which this knowledge may be of value in other procedures: both in the field of portal hypertension and also in other branches of general surgery. For example, when attempting a portacaval anastomosis, occasionally the portal vein is too short to bring down to the inferior vena cava. In such instances the left renal vein has been used to form the anastomosis with the portal vein (Simeone and Hopkins, 1967). Another example is in vascular surgery when resecting an abdominal aneurysm. If the left renal vein were damaged in obtaining proximal control or might prevent satisfactory proximal anastomosis, then it would be important to know that the left renal vein could be ligated (Szilagyi, Smith, and Elliott, 1969).

Acknowledgement.—We wish to thank the Department of Medical Illustration, St. Bartholomew's Hospital, for the preparation of the illustrations.

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RECTAL AND COLONIC ULCERATION IN BEHÇET'S DISEASE

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SUMMARY

Two patients with Behçet's disease and involvement of the gastro-intestinal tract are described. One patient presented with rectal bleeding and perianal pain, and later developed peritonitis due to perforation of the sigmoid colon. The second patient developed rectal bleeding 4 years after the diagnosis of Behçet's disease, and examination showed this to be due to an ulcer in the anal canal. Behçet's disease should be considered as a possibility, albeit rare, in the differential diagnosis of rectal and colonic ulceration.

In 1937 the Turkish dermatologist, Behçet, first described the clinical syndrome of inflammation in the eye with ulceration in the mouth and genital tract. Characteristically, it is a chronic disease with relapses throughout life. It occurs most frequently in the age-group 15–40 years and is slightly commoner in males. The histopathology is generally non-specific ulceration. The more severe disabilities come from involvement of the eye and central nervous system, and these can lead to blindness or death. The classic triad is not always seen but the diagnosis can still be made even if not all of the features are present at any one time. The missing symptom may develop in later years. In addition to the characteristic triad of symptoms, Behçet's disease may have more widespread manifestations such as arthralgia, erythema nodosum, pyrexial attacks, and thrombophlebitis. Gastro-intestinal involvement has been reported infrequently.

It is the purpose of this paper to present 2 patients in whom intestinal ulceration was a prominent feature, and in the first case it was the presenting system.

CASE REPORTS

Case 1.—Miss M. E., a laboratory technician aged 25 years. This patient presented to the surgical out-patients' department at the Gordon Hospital on 7 Sept., 1969, complaining of 1 month's progressive perianal pain which was aggravated by defaecation. One week prior to attending the hospital she had noticed blood on the outside of her stool. Also she had been feeling tired and anorexic, and had lost 2·25 kg. in weight. Apart from tonsillectomy as a child and pneumonia at the age of 14 years, her general health had been good. One year previously she had been found to be anaemic (haemoglobin 58 per cent) and had been treated with oral iron. Six months previously she had given blood for research purposes and had been told that she had very low iron stores.

On examination the patient was pale, with two aphthous ulcers on the uvula and a painful fissure in ano. These were the only abnormal clinical findings.

The patient was admitted to hospital for investigation. At sigmoidoscopy and proctoscopy under general anaesthesia an acute posterior fissure and an anterior rectal ulcer were found. The ulcer was 3 cm. across with overhanging edges. The remaining mucosa was granular to 15 cm., but no other lesions were found. The ulcer was biopsied, and the histology showed: 'Ulceration with dense collections of plasma cells, lymphocytes, and some polymorphs, and areas of tissue necrosis. There is some vasculitis, but polyarteritis nodosa or allergic vasculitis are not likely because of the lack of eosinophils in the section.'

The next day the patient developed generalized aches and pains with shivering, anorexia, tachycardia, and pyrexia (37·8° C.). Blood cultures were negative. Two days after admission an ulcer developed on the right pinna, and then others rapidly appeared on the back of the neck, the right lateral border of the tongue, and over the right scapula. These ulcers were punched out with necrotic bases, the largest being 2·5 cm. in diameter. She also had some transient dysphagia but a barium swallow was normal. In view of the typical appearances of the lesions a provisional diagnosis of Behçet's disease was made.

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INVESTIGATIONS.—The haemoglobin was 9·6 g. per 100 ml., E.S.R. was 84 mm. in the first hour (Wintrobe), and W.B.C. was 5400 per c.mm., with a normal differential. A film showed a hypochromic anaemia with toxic granulation of the polymorphs and a shift to the left. Biochemical tests revealed the following: urea 38 mg. per 100 ml., bilirubin 0·5 mg. per 100 ml., alkaline phosphatase 9 K.A. units, serum glutamic oxalo-acetic transaminase 10 U., and serum glutamic pyruvic transaminase 12 U. Examination of the plasma proteins revealed a total protein content of 6·5 g. per 100 ml. (albumin 2·9 g. per 100 ml., α_1-globulin 0·4 g. per 100 ml., α_2-globulin 0·8 g. per 100 ml., β-globulin 0·8 g. per 100 ml., γ-globulin 1·6 g. per 100 ml., fibrinogen 611 mg. per 100 ml.).

The serum iron was 19·5 μg. per 100 ml. The Wassermann and Kahn reactions were negative. The antinuclear factor was negative to 1 : 20. A xylose absorption test was normal, and a chest radiograph was also normal. Swabs from the cutaneous ulcers grew *Staphylococcus aureus*.

The patient was treated initially with a course of erythromycin and novobiocin for 10 days and this resulted in a slow but definite improvement in the cutaneous ulceration. She was given oral iron, folic acid, and ascorbic acid for her anaemia, and was discharged to continue this medication on 14 Oct., 1969, when her haemoglobin was 10·2 g. per 100 ml. At this time the cutaneous ulcers had healed and she had no perianal symptoms.

The patient remained well for 3 weeks, but on 2 Nov. she was readmitted with a 6-hour history of severe upper abdominal pain which became generalized. She had vomited five times but her bowel action was normal. On examination she was pale, ill, and dehydrated. The cutaneous ulcers were healed. Her pulse was 112 per minute and her blood-pressure was 110/70 mm. Hg. The abdomen was rigid, and rebound tenderness, particularly in the left iliac fossa, was noted. Bowel-sounds were absent, and rectal examination demonstrated marked tenderness anteriorly.

A diagnosis of peritonitis was made, and at laparotomy faecal peritonitis from a perforating ulcer at the apex of the sigmoid colon was found. The rest of the large bowel and the other viscera were normal, apart from an intense peritoneal reaction. The sigmoid colon was mobilized and exteriorized by a Paul-Mikulicz procedure, and after irrigation of the peritoneum the abdomen was closed. The ulcerated area was excised with a wide margin, and histology showed: 'Chronic inflammation and ulceration of all layers of the colon. No recognizable mucosa is seen. There is marked serositis. Appearances are similar to those seen in the rectal biopsy, and are entirely compatible with a diagnosis of Behçet's disease.'

Postoperatively the patient made a slow but satisfactory recovery and her colostomy functioned normally. No gross abnormalities were found by a barium enema which was performed 1 month later, and a barium meal and follow-through were normal. She was discharged on 16 Dec. when she was feeling well.

The patient was subsequently admitted twice with subacute large-bowel obstruction, which on both occasions was due to constipation, and the obstruction responded to conservative therapy.

Five months later the colon was shown to be normal by further barium studies, and the patient was admitted for closure of the colostomy on 3 May, 1970. At sigmoidoscopy and proctoscopy prior to operation the rectum was found to contain a large amount of pus, and the ulcer which had previously been noted was healed. The mucosa was friable and bleeding. An extraperitoneal closure of the colostomy was performed and the patient made a good recovery. Biopsies of the colon taken at operation showed non-specific inflammation only.

Three weeks after operation an abscess developed at the previous colostomy site, and after drainage it was clear that a fistula had developed from the colonic lumen to the skin. On 22 July an examination under anaesthesia, proctoscopy, and sigmoidoscopy to 20 cm. were performed. There was an ulcer, 4 cm. long, in the anal canal. There were no ulcers above this point but the mucosa was granular and friable. A low fistula was laid open and a posterior sphincterotomy was performed.

At the present time there is only a small amount of discharge from the fistula and the patient's bowel action is normal. She is still anaemic (haemoglobin 10·5 g. per 100 ml.) and the E.S.R. is currently 48 mm. in the first hour (Wintrobe).

Case 2.—Mrs. E. S., a telephonist aged 57 years. This patient was diagnosed as having Behçet's disease in March, 1966, when, having previously been well, she gave a 6-month history of recurrent mouth ulcers and sore throats. At that time she had extensive ulceration of the fauces, tongue, and lips, and had developed a deep-vein thrombosis in the right leg with pulmonary emboli.

INVESTIGATIONS.—The haemoglobin was 10·6 g. per 100 ml., W.B.C. was 23,400 c.mm. with a normal differential, and E.S.R. was 50 mm. in the first hour (Wintrobe). Wassermann and Kahn reactions were negative. No lupus erythematosus cells were present.

The patient was treated with 5 mg. prednisone twice daily, but she continued to be troubled by recurrent ulcers, new ones appearing on the right ankle in February, 1967, and in the natal cleft in April, 1968. Biopsy of the ankle ulcer showed non-specific inflammatory changes only.

In spite of treatment with corticosteroids the patient continued to experience relapses and remissions, and in November, 1969, she was readmitted with rectal bleeding which had occurred for the first time. Examination under anaesthesia was performed and an ulcer 4 cm. across was found high on the left side of the anal canal. Sigmoidoscopy to 22 cm. and proctoscopy were otherwise normal, and the bleeding appeared to have arisen from the ulcer. A biopsy showed non-specific ulceration only.

The patient was treated for 4 weeks in hospital, and she received initially 60 mg. prednisone daily which was gradually reduced to 20 mg. daily. She was discharged to continue on this dose and remains well on follow-up with no further rectal bleeding.

DISCUSSION

Diseases involving the gastro-intestinal tract may often be associated with skin lesions. Ulcerative colitis and some malabsorption syndromes are examples of this, and Mountain (1970) has emphasized the occurrence of cutaneous ulceration in Crohn's disease.

The occurrence of gastro-intestinal symptoms in patients with Behçet's disease has been described infrequently. Oshima, Shimizu, Yokohari, Matsumoto, Keno, Kagami, and Nagaya (1963), reporting the clinical features of 85 patients with Behçet's disease, found that 40 per cent had symptoms such as diarrhoea, nausea, or abdominal pain, and 1 case had proved jejunal ulceration. Jensen (1944) was the first to recognize the association of Behçet's disease and disease of the bowel when he described ulcerative colitis occurring in 2 patients who were known to have Behçet's disease. Cottini and Randazzo (1956) made similar observations and even suggested the use of the term 'cutaneous muco-intestinal syndrome'. Other cases of colitis as a manifestation of Behçet's disease have been described by Bechgaard (1940), Boe, Dalgaard, and Scott (1958), and Ramsay (1967).

The occurrence of rectal and colonic ulceration and perforation of the bowel, as happened in the first of our 2 patients, have only rarely been reported (Ono and Yamamoto, 1962; Somemura, Nishio, Nishida, Hashimoto, and Matsuhara, 1963; Tsukada, Yamazaki, Iyo, Nishio, Hashimoto, and Matsuhara, 1964). Curth (1964) described a man with a 5-year history of Behçet's disease who then developed rectal ulcers, sloughing of the rectal mucosa, and multiple colonic perforations necessitating proctocolectomy.

The aetiology of Behçet's disease remains uncertain, but amongst those factors which have been suggested are venereal diseases, tuberculosis or staphylococcal infections, and viral infections. Allergic or auto-immune processes and thromboses of small veins have also been invoked as causes. Because the pathological appearances are entirely non-specific the diagnosis is always based upon the association of the various clinical features.

Although more common in the Orient, the incidence of Behçet's disease in this country is probably greater than is usually quoted. Many cases may be missed because no specific inquiry is made about symptoms such as vulval ulceration in patients with other manifestations such as aphthous ulceration of the mouth. The information is often not volunteered by the patient because of modesty or the feeling that it is irrelevant.

The treatment of Behçet's disease is much disputed and usually not very successful. Heavy doses of corticosteroids are often used (as with our second patient) to suppress severe manifestations, but they have not been shown to be of any value in slowing the course of the disease. Immunosuppressives have been proposed as a rational treatment, and Cunliffe and Menon (1969) have used phenformin and ethyl oestriol with some success.

Now that the other features, such as polyarthralgia, thrombophlebitis, and gastro-intestinal symptoms, are accepted as part of the overall clinical picture in Behçet's disease, more cases will be diagnosed in general medical and surgical clinics. The differential diagnosis of rectal ulcers is large (Madigan and Morson, 1969); our first patient demonstrates that Behçet's disease should be borne in mind as one of the less common causes of this condition.

Acknowledgements.—I am grateful to Mr. M. Naunton Morgan and Dr. Peter Emerson for permission to publish details of patients under their care, to Dr. Martin Lewis for the histology reports, and to Dr. Lavinia Loughridge and Mr. J. E. Hale for their help and encouragement.

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THE MAINTENANCE OF MALDESCENDED TESTICLES WITHIN THE SCROTUM USING A DARTOS POUCH

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SUMMARY

A method of maintaining a testicle within the scrotum in the operation of orchidopexy for maldescent using a dartos pouch is described.

THAT orchidopexy is required for maldescent of the testicles is well documented (Wangensteen, 1935; Pace and Cabot, 1936; Mimpriss, 1938; Gilbert and Hamilton, 1940; Gross and Jewett, 1956; Scott, 1962; Collins and Pugh, 1964; Altman and Malament, 1967; Cohn, 1967; Dow and Mostofi, 1967; Hecker and Heinz, 1967). This paper is concerned only with the maintenance of the mobilized testicle within the scrotum in orchidopexy.

For orchidopexy to have the optimum of success the operation should be carried out at the age of 5 years, as histological development of the testicle is only a little delayed at this age (Scott, 1962; Cohn, 1967; Hecker and Heinz, 1967), the macroscopic structures are sufficiently developed to handle easily, and there is minimal interference with schooling. Certainly the operation should be completed before puberty. In cases with troublesome hernia, surgery may be indicated earlier.

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At operation any tension placed on the cord structures to maintain the testicle within the scrotum must be slight, neither interfering with the venous return from nor the arterial supply to the organ. The testicle should be placed in the scrotum on its own side so that it is unable to return to the groin and is not left riding high. The operation should be finalized in one stage, should be simple to carry out, and should cause only the minimum of postoperative discomfort.

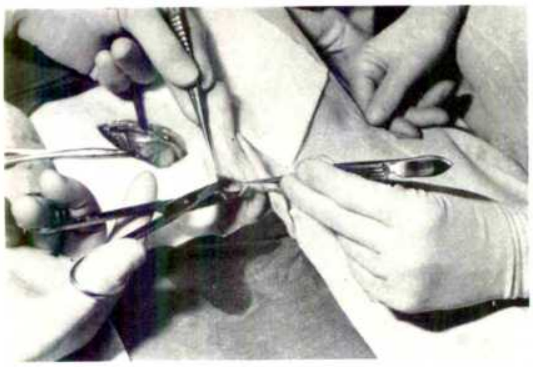

FIG. 1.—Formation of a pouch between scrotal skin and dartos muscle.

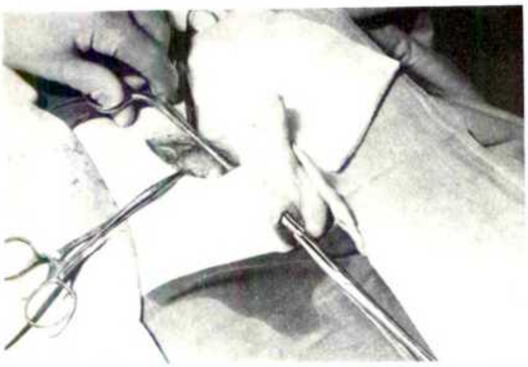

FIG. 3.—Method of introducing haemostats for the withdrawal of the testicle from the groin to the pouch.

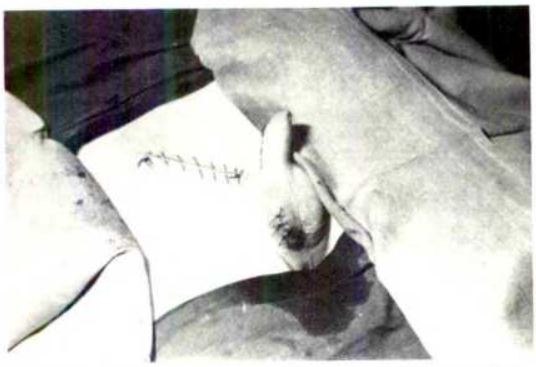

FIG. 5.—The appearance at the termination of the operation.

Using these criteria the following operative procedure using a dartos pouch to maintain a maldescended testicle within the scrotum has been devised.

OPERATIVE TECHNIQUE

Under general anaesthesia the maldescended testicle is mobilized through the usual groin incision (Bevan, 1899; Browne, 1933; Poole Wilson, 1939; Gross and Jewett, 1956; Hand, 1957). A finger is passed from the groin wound into the scrotum and the scrotal wall is stretched. A short vertical incision is made through the skin only near the apex of the scrotal wall on the same side as the maldescended testicle. By blunt dissection using scissors or a haemostat a pouch sufficiently large to accommodate the testicle is formed between the scrotal skin and the dartos muscle (*Figs.* 1, 2).

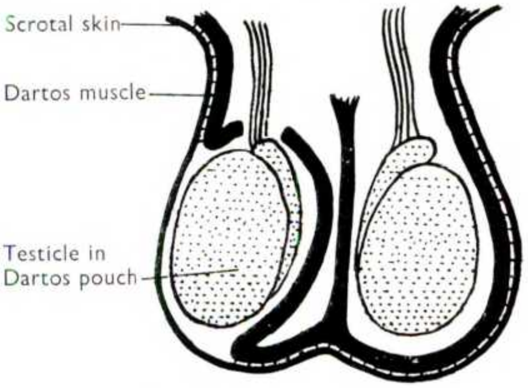

FIG. 2.—The dartos pouch.

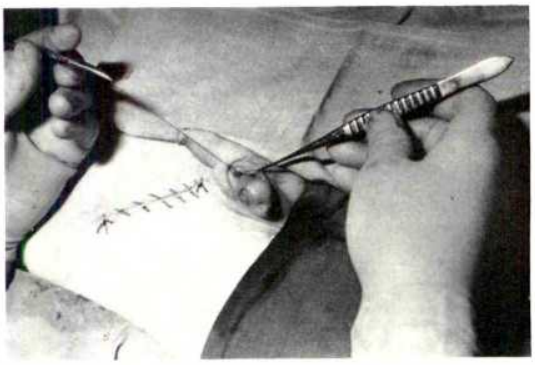

FIG. 4.—Approximation of the edges of the opening in the dartos pouch.

A closed haemostat is passed from the groin wound into the scrotum and through the centre of the dartos of the newly formed pouch. The hole in the dartos is stretched by opening the haemostat. A second haemostat is now grasped by its point by the first haemostat and is withdrawn into the groin wound (*Fig.* 3). This second haemostat is used to grasp the gubernacular tissue attached to the testicle, which is then drawn into the scrotum through the hole in the dartos pouch without twisting or pulling unduly on the cord.

One or two sutures are inserted to approximate the gap in the dartos sufficiently to prevent the testicle from returning to the groin, but equally they should be quite loose enough to prevent circulatory embarrassment of the testicle (*Fig.* 4). It is sometimes

CASE	AGE AT OPERATION (years)	SIDE OF MALDESCENT	ASSOCIATED HERNIA	COMPARATIVE PREOPERATIVE SIZE OF AFFECTED TESTIS	POSITION OF TESTIS OBTAINED AT OPERATION	LENGTH OF FOLLOW-UP	COMPARATIVE SIZE AND POSITION OF TESTIS AT LAST FOLLOW-UP	ADDITIONAL COMMENTS
1	12	Left	No	Both testes small but equal	Well down	3½ yr.	Both testes small, but equal in size and well down	Not yet at puberty. Possible genetic defect. Has an associated deficiency in pseudocholinesterase
2	15	Left	Yes	Smaller	Well down	3 yr.	Testis well down but remains smaller	—
3	6	Right	Yes	Equal	Well down	2½ yr.	Well down and equal in size	—
4	5	Right	No	Equal	At scrotal neck	2 yr.	Well down and equal in size	—
5	26	Left	No	Both testes smaller than normal but equal	At scrotal neck	1¾ yr.	Well down, equal in size, but both testes smaller than normal	Normal sperm count and is a father
6	9	Bilateral	No	Equal	Well down	1¾ yr.	Well down and equal in size	—
7	24	Right	No	Small	At scrotal neck	—	—	Lost from follow-up, having moved from a caravan site without trace after being turned down for military service
8	11	Right	No	Equal	Well down	1½ yr.	Well down and equal in size	Also has a very highly retractile left testis
9	15	Left	No	Smaller	Well down	1 yr.	Well down but remains smaller	—
10	8	Left	Yes	Equal	Well down	11 mth.	Well down and equal in size	Also has a very highly retractile right testis
11	8	Left	Yes	Equal	Well down	11 mth.	Well down and equal in size	A perineal left testicle
12	10	Right	Yes	Equal	Well down	10 mth.	Well down and equal in size	—
13	8	Right	No	Equal	At scrotal neck	10 mth.	Well down and equal in size	—
14	15	Right	Yes	Equal	Well down	9 mth.	Well down but right testis slightly smaller than left	There is a left-sided varicocoele. Normal sperm count
15	10	Left	Yes	Small	Well down	9 mth.	Well down but remains equally small	—
16	14	Right	Yes	Smaller	Well down	8 mth.	Well down but remains smaller	—
17	16	Right	Yes	Smaller	Well down	8 mth.	Well down and near equal in size	—
18	11	Left	No	Equal	Well down	7 mth.	Well down and equal in size	—
19	17	Right	No	Equal	Well down	7 mth.	Well down and equal in size	Previous right orchidopexy elsewhere for undescended testis. Testis lying over pubic tubercle prior to this second operation
20	15	Right	No	Equal	Well down	7 mth.	Well down and equal in size	—
21	15	Left	No	Smaller	Well down	7 mth.	Well down but remains smaller	Previous bilateral orchidopexy at age 13 elsewhere. Right testicle well in scrotum but left smaller and lying over pubic tubercle prior to this second operation
22	15	Right	No	Equal	Well down	6 mth.	Well down and equal in size	—
23	6	Bilateral	No	Equal	Well down	6 mth.	Well down and equal in size	—
24	15	Right	No	Equal	At scrotal neck	6 mth.	Well down and equal in size	—
25	18	Right	Yes	Small	Well down	6 mth.	Well down but remains equally small	—

easier to place these sutures before drawing the testicle into the pouch, and to tie them afterwards.

The scrotal skin and the groin wounds are closed (*Fig.* 5) and the skin sutures are removed in 5–7 days.

DISCUSSION

Over the past 3½ years, 27 orchidopexies for maldescent using the dartos pouch method to maintain the testicle within the scrotum have been carried out in 25 patients (*Table I*).

The operation is simple, and even if the cord is short and the testicle is left riding high in the scrotum at operation the gentle continuous pull of the dartos pouch allows for gradual elongation of the cord structures without disturbance to the vascular requirements of the testicle, which will subsequently be found to lie well within the scrotum. This was seen in *Cases* 4, 5, 13, and 24 (*Table I*); the outcome of *Case* 7 is unknown, having been lost to follow-up. None of these 5 cases had associated inguinal hernial sacs.

In this series no testis has atrophied following operation, though those testes which were small prior to orchidopexy remained so.

Postoperative discomfort was minimal.

The dartos pouch operation compares very favourably with other techniques which have previously been described.

The advantages of the trans-septal operation (Ombrédanne, 1910) are similar. Of necessity, the testicle lies on the opposite side in the same anatomical scrotal department as its neighbour, though the final cosmetic result is usually highly satisfactory. This method, however, is unsuitable for short cord cases and bilateral maldescent.

In cases with a short cord and a high-riding testicle, operations using a simple purse-string suture at the neck of the scrotum (Bevan, 1899), or a fibrous band between the floor of the scrotal tunnel and the pectineus (Browne, 1949), leave the testicle riding high and vulnerable to trauma.

Other methods of maintaining maldescended testicles within the scrotum in which traction is applied for several days via a suture placed in the tunica albuginea through the scrotal skin and attached to the thigh of the same or opposite side by direct stitching, elastic bands, or appliances are also described (Cabot and Nesbitt, 1931; Wangensteen, 1932). These operations are often uncomfortable and are subject to accidental, sudden, or prolonged pulling or tugging on the traction suture which is liable to result in injury to the testicular vessels with subsequent testicular atrophy.

Also, as shown in *Cases* 19 and 21 (*Table I*), when the traction suture is removed, or if it cuts out, it is not infrequently found that the testicle retracts to lie over the pubic tubercle, where it remains, becoming vulnerable to trauma with subsequent reoperation being necessary.

The Keetley-Torek operation (Keetley, 1894; Torek, 1909) should no longer be carried out, for of necessity a second operation is required, it is uncomfortable, the testicular blood-supply is often jeopardized, and small boys not infrequently fail to wash the crutch between the scrotum and the thigh.

Many of the cases in this series were regrettably referred for surgical treatment when they were well past the optimum age for orchidopexy (*Table I*). Those who had past puberty were all potential recruits for the Services and had been found at routine medical examination prior to acceptance or otherwise to have maldescent of the testicle.

A plea is put forward for greater diligence in seeking out and referring cases of maldescent of the testicle for surgery in early childhood, for which the dartos pouch operation is recommended.

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PERITONITIS FROM AMOEBIC LIVER ABSCESS

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SUMMARY

Four consecutive cases of peritonitis from rupture of amoebic liver abscess presenting late with the condition have been described. After treatment involving intensive resuscitation with adequate fluid therapy, ampicillin and hydrocortisone, and early laparotomy all 4 cases survived. The likelihood of this result recurring by chance is calculated at 0·3 per cent ($P < 0·05$).

The conclusion is drawn that now that surgery is safer and metronidazole is available as a rapidly acting non-toxic amoebicide, perhaps amoebic abscesses should no longer be regarded differently from other hepatic abscesses, at least when they rupture into the peritoneal cavity.

AMOEBIC liver abscess is a common complication of amoebiasis in areas of high endemicity of the disease. While the incidence of peritonitis from rupture of these abscesses has been diminishing since the advent of the potent systemic amoebicide metronidazole, there has been no appreciable decrease in the mortality. De Bakey and Ochsner (1951) reported an incidence of intraperitoneal rupture of 10 per cent with a 75 per cent mortality. More recent authors (Schiff, 1956; Adi, 1966) report a similar disquieting mortality. The factors which are responsible for this state of affairs are not readily evident. It is for this reason that the survival of 4 consecutive patients presenting late with the condition is reported.

CASE REPORTS

Case 1.—A farm labourer, aged 35 years, presented with a 2-month history of fever and intermittent pain in the right hypochondrium. Three years previously he had suffered a similar attack which had been treated conservatively. He had never had diarrhoea. Two days before admission he had developed a severe attack in which the abdominal pain had become generalized with vomiting and prostration. On admission he appeared mildly shocked, his blood-pressure was 90/60, his pulse-rate was 120 per minute, and he showed evidence of anaemia and weight-loss. There was generalized tenderness of the abdomen with guarding and moderate distension, but no masses were palpable. A plain radiograph showed two small radio-opaque calculi in the gall-bladder area. Peritonitis probably arising from inflammatory biliary disease was suspected.

Laparotomy revealed large quantities of thick amoebic pus which were traced to two abscesses in the right lobe of the liver. There were several adhesions and pockets of abscesses in the peritoneal cavity, indicating previous minor episodes. Two calculi were palpable in the gall-bladder, confirming the radiographic findings. The liver abscess was evacuated and the peritoneum was drained.

The patient responded well to specific anti-amoebic treatment with metronidazole (800 mg. thrice daily for 5 days) and emetine hydrochloride (60 mg. i.m. daily for 7 days). Four months later he had a cholecystectomy, from which he made an uneventful recovery. When last seen 3 months ago the patient was well and was continuing at work.

Case 2.—A heavy-duty lorry driver, aged 47 years, presented with fever, abdominal pain, and vomiting of 3 days' duration. Six weeks previously he had consulted his private doctor complaining of abdominal pain and bouts of diarrhoea, passing mucus, blood, and pus, which had settled on symptomatic treatment. On examination the patient was very pale with a tinge of jaundice (bilirubin 1·6 mg. per cent). He was shocked with a pulse-rate of 126 per minute and a blood-pressure of 70/50; his temperature was 37·7° C. Signs of peritoneal irritation were evident. The liver was grossly enlarged and exquisitely tender and there was a fluctuant swelling in the epigastrium which was continuous with the liver.

A diagnosis of peritonitis from rupture of an amoebic abscess was made and was confirmed by the aspiration of thick amoebic pus by diagnostic paracentesis. Intensive resuscitation was carried out in an attempt to prepare the patient for laparotomy, and after 24 hours of intravenous fluid therapy (1·5 litres isotonic saline, 1 litre dextrose saline, 1 litre dextran 40, and 2 U. blood), tetracycline (2 g. i.v.), hydrocortisone (1·2 g.), chloroquine (300 mg. i.m.), and metronidazole (1·2 g.) anti-amoebic therapy, his blood-pressure was barely 95/70 and his pulse-rate was 100 per minute.

He was not considered fit for general anaesthesia and therefore laparotomy was carried out under a bilateral intercostal regional block. Large quantities of pus were found and were traced to a large amoebic abscess of the left lobe of the liver. The right lobe was free of abscesses and there were no amoebic lesions in the rest of the gastro-intestinal tract. Peritoneal toilet was performed and the abscess cavity was irrigated with emetine hydrochloride solution. The abdomen was closed with drainage.

The patient's immediate postoperative course was stormy, with high pyrexia, rigors, and abdominal distension, and in spite of intensive anti-amoebic and antibiotic therapy this persisted for 10 days. The drainage site also continued to discharge large quantities of thick creamy pus. He gradually recovered from this poor physical state and left hospital after 6 weeks, all his wounds having healed.

The patient was readmitted a month later with recurrence of abdominal pain and fever, and the reappearance of a swelling in the epigastrium. On examination he had a large, tender, hepatic swelling but the rest of the abdomen was normal. The recurrent amoebic abscess was treated with repeated aspirations and the instillation of emetine hydrochloride, with very little improvement. At a second laparotomy a large loculated right lobe abscess was evacuated. There was an associated subphrenic collection which was drained. The patient had an uneventful recovery. When last seen he was back at work and was well.

Case 3.—A labourer, aged 27 years, was admitted with a 2-year history of recurrent upper abdominal pain. Each episode of fever had been accompanied by vomiting and weight-loss, culminating with the discharge of pus through a sinus in the epigastrium. On the present occasion the pain had spread rapidly throughout the abdomen and had been followed in 24 hours by jaundice.

On examination the patient was not shocked but was pale and emaciated. His pulse-rate was 110 per minute and his blood-pressure was 100/70. His abdomen was generally tender with guarding and absent bowel-sounds. There was a partially closed sinus in the epigastrium. Peritonitis from intra-abdominal rupture of an amoebic liver abscess was thought to be likely, and the patient was subjected to immediate laparotomy. This revealed several loculated pockets of amoebic pus with numerous adhesions. The pus was evacuated and the abdomen was drained by means of two corrugated rubber drains in the iliac fossae. The patient responded satisfactorily to anti-amoebic and antibiotic treatment (metronidazole 1·2 g. per day for 7 days and tetracycline 1 g. per day for 5 days). He was discharged on the sixteenth postoperative day.

Case 4.—The patient, a 30-year-old trader, presented in similar fashion to *Case* 1, complaining of intermittent pain in the right hypochondrium and epigastrium of 6 weeks' duration, which was not associated with bowel disturbance. He was admitted during an attack which had started 24 hours previously. He was anaemic and mildly shocked, and signs of peritonitis were evident in his abdomen. In the light of the experience of the previous cases a diagnosis of ruptured amoebic abscess was quickly arrived at and was confirmed at laparotomy. The patient's recovery after peritoneal toilet and drainage and chemotherapy (consisting of metronidazole 1·2 g. per day for 5 days and tetracycline 1 g. per day for 5 days) was rapid. He was discharged after a fortnight in hospital.

DISCUSSION

Intraperitoneal rupture remains the most dreaded complication of amoebic liver abscess. Manson (1917), Castellani and Chalmers (1919), Rogers (1922), and Manson-Bahr (1943) all regarded it as almost inevitably fatal, and Schiff in 1956 still recorded a mortality of 75 per cent. Adi (1966) found in Nigeria a mortality of 67 per cent in cases with free leakage into the peritoneal cavity. An important factor predisposing to rupture in the hepatic lesion and to the poor prognosis is delayed or inadequate treatment (Biggam and Ragab, 1931). Poor nutrition or diminished host resistance associated with other diseases contributes to an unsatisfactory outcome, and the persistence of these conditions in many tropical countries is responsible for the continuing high mortality. The encouraging outcome of the cases described here is probably partly due to the improved nutritional status of the patients and their relative youth. However, early surgical intervention was undoubtedly important in determining the result.

Rupture is more commonly seen in abscesses of the left lobe of the liver, probably because of its smaller size and more complete peritoneal cover. This together with delayed diagnosis of abscesses of the left lobe on account of their more hidden localization (Alkan, Kalmi, and Kalderon, 1961) considerably increases the mortality from these abscesses. Alkan and others (1961) reported intraperitoneal rupture in 4 of 8 cases of abscesses of the left lobe; 1 of the 3 deaths in the series was from intraperitoneal leakage. In the left lobe, rupture occurs more often on the inferior surface (*Cases* 2 and 4) as opposed to that in the right lobe (*Case* 1) where the abscess tends to point on to the superior or anterior surface. In both places a slower pace of abscess development and leakage makes for localization by adhesions, with improvement in the outlook.

Wilmot (1962) described three forms of clinical presentation of intraperitoneal rupture of amoebic abscess:—

1. Sudden perforation with signs of widespread peritoneal soiling, carrying the highest mortality.
2. A gradual leak with localized abscess.
3. A gradual process without localization, causing chronic generalized peritonitis.

The first category, which is typified by *Case.*
2, and 4, is unfortunately the most frequently s
and the differentiation from other forms of p
tonitis presents some difficulty. The large liver
Case 2 and the preceding diarrhoea would fo
attention on hepatic amoebiasis, but in *Case* 1
diagnosis was far from clear and suspicion fell
cholecystitis with a calculous basis. In the m
chronic type a preceding history of repeated episo
of upper abdominal pain presenting with signs
peritonitis may give an indication of the diagno
but the complexity of the exercise is evinced by
observation of Vakil, Mehta, and Desai (1970) t
the uncomplicated abscess may still present w
abdominal rigidity, distension, and ileus.

The pitfalls in correct preoperative diagnosis h
been examined by Biggam and Ragab (1931),
(1955), and Singha (1959), with the follow
important observations:—

1. The preceding dysenteric illness is often lacki
as in *Cases* 1, 3, and 4.
2. A history of prolonged ill-health may be missi
especially in non-endemic areas, while in ende
areas the common association of intercurrent dise
would blur the picture.
3. The abdominal pain is not confined strictly
the right hypochondrium prior to rupture (*Case*
and 4).

In general, it would appear that a high index
suspicion, sometimes in spite of atypical features
the most important factor in arriving at a p
operative diagnosis. Laboratory investigations s
as examination of stools for amoebae and a white-
count are unhelpful, but serological tests for amoe
asis may provide confirmatory evidence.

The literature shows no agreement on the choice
the appropriate method of treatment. A few clinici
have favoured surgical intervention (Hulke, 18
Self, 1955; Singha, 1959), but most have prefer
conservative measures, involving repeated aspirat
of the abscess and the soiled abdomen, supported
anti-amoebic and antibiotic chemotherapy (Ludl
1926; Chatterji, 1922a, b; Biggam and Ragab, 19
Chang and Robertson, 1934; Paul, 1959; Thak
1965). With a published mortality of 75 per c
the likelihood of 4 consecutive cases surviv
by chance is 0·3 per cent ($P<0\cdot05$), indicat
the significance of the results which have b
achieved.

The essential details of the method which has b
used in this series have been early operation p
ceded by intensive resuscitation, involving
judicious use of isotonic saline, Rheomacrod
blood, and adequate doses of hydrocortisone a
ampicillin followed later by the amoebicidal dr
metronidazole and emetine hydrochloride (we h
had to give larger doses than the generally accep
400 mg. thrice daily for 7 days). In additi
anaesthesia, whether general or local, has impro
in the past decade, as has to some extent the gene
nutrition of patients in southern Ghana.

The rationale for conservative treatment
discussed by Paul (1959), who observed that
escape of pus from an amoebic abscess cavity
extremely slow and ceased promptly with aspirati
Ludlow's (1926) results show a mortality of 11·1
cent for open operation and 2·3 per cent

conservative treatment. Chatterji (1922a, b) claimed a 1·6 per cent mortality for conservative measures. In these series, however, it is difficult to know whether all the cases had free pus in the peritoneal cavity as the abdomen was not opened. This is important in view of the observation of Vakil and others (1970) that uncomplicated abscesses still present with marked signs of peritoneal irritation. In the average tropical practice with less experience of the varied presentation of hepatic amoebiasis these difficulties of accurate diagnosis adding to the uncertainty of adequate removal by aspiration of thick glairy pus from both peritoneal and abscess cavities far outweigh the dangers of open drainage.

The important lesson from these facts is that the idea that amoebic abscesses should be regarded differently from other hepatic abscesses is perhaps not so tenable, at least when they rupture into the peritoneal cavity, now that surgery is safer and that metronidazole is available as a rapidly acting and non-toxic amoebicide. Restriction to oral administration is a disadvantage in very ill patients on parenteral fluid therapy, but with intensive resuscitation and supplemented by chloroquine during this period it is not a limiting factor. One important cause of failure of surgical treatment in the past has been the use of emetine hydrochloride during the resuscitation period, the myocardial toxicity of the drug prejudicing the chance of recovery from circulatory collapse (Adi, 1966).

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NEW INSTRUMENTS FOR MICROVASCULAR SURGERY

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SUMMARY

Instruments are described which have been developed for use in work on blood-vessels of less than 1 mm. in diameter. They include hand-rests, pedal-operated instruments, vessel clamps, and a counter-pressor.

THE instruments described here were designed on the basis of personal experience in anastomosing vessels of 0·5–0·8 mm. external diameter. In developing a satisfactory technique for such fine work the following obstacles to success were encountered, and steps were taken to overcome them:—

1. Even using an operating microscope it is difficult to visualize very small vessels clearly at a high magnification. Greater clarity can be obtained by the use of simple aids.

2. Tremor and other unwanted movement mask the capacity of the hands for fine manipulation. To overcome this, hand-rests and pedal-operated instruments have been developed.

3. Existing small-vessel clamps are too cumbersome for very fine work. A clamp of suitable dimensions has been developed.

4. It is difficult to hold the vessel edge steady in order to place the suturing needle precisely and to pass it through the vessel wall with the minimum of damage. A counter-pressure device has been developed to overcome this difficulty.

AIDS TO VISUALIZATION

For regular success in anastomosing very small vessels it is necessary to place sutures as close together as 3 or 4 per mm., taking extremely small bites of tissue. The difficulty of doing this accurately with vessel walls which are 6–8 cells thick, colourless, and translucent will be appreciated.

A very bright light is needed when working at the highest magnification of the microscope. A slightly overrun 50-W. bulb is preferable to the 30-W. bulb which is fitted as standard in the Zeiss microscope.

In order to see the faintly opalescent vessel ends clearly it is a great help to have a dark background behind them. A suitable background material can be made using a short length of dental matrix band made of flexible stainless steel, rounded at the corners, and blackened by the process used by instrument makers for aural instruments. Under the microscope this appears dark grey, and black suture material is clearly seen against it.

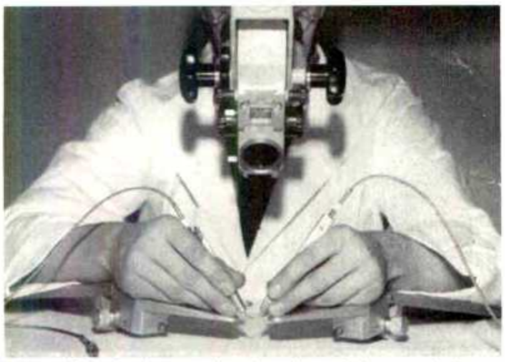

FIG. 1.—The hand-rests, showing the pedal-operated forceps (left hand) and scissors, and the optimal position of the hands.

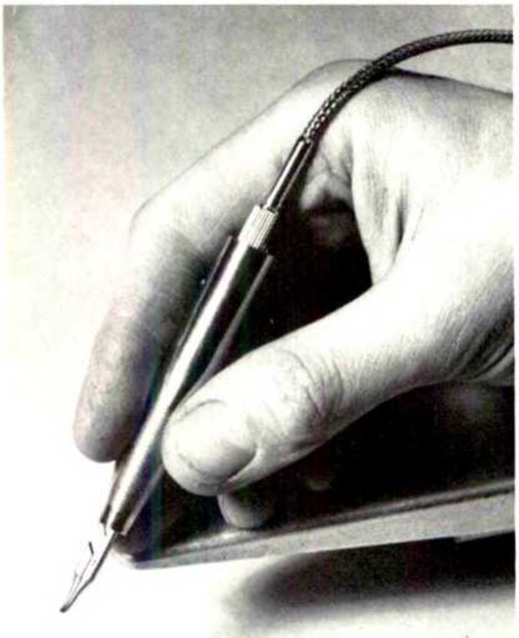

FIG. 3.—The pedal-operated needle-holder. The cable is seen above, right.

HAND-RESTS

The fingers have a remarkable capacity for fine manipulation, but this capacity is entirely masked by tremor unless the hands are resting on a solid supporting surface. The more distally the support extends, the more fully is tremor abolished.

The author's hand-rests (*Fig.* 1) consist of solid duralumin plates, 45 × 6·5 cm., which are hinged at wrist-level. They are used on a solid flat table on which they can be freely moved about. They support the elbows at table-level, slope upwards to support the wrists 5 cm. above the table, and continue beyond the hinge to a blunt point on which the finger-tips are supported 2–8 cm. above the table, this height being adjustable. Using these hand-rests it is possible to do fine work for long periods without fatigue.

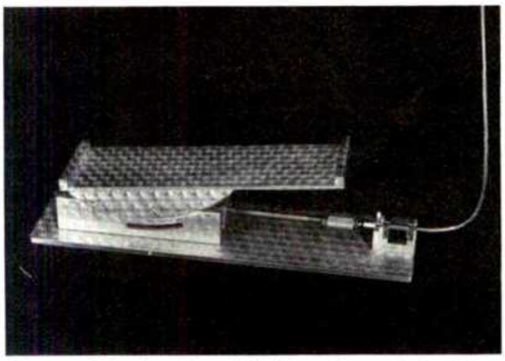

FIG. 2.—Side-view of a pedal, with a cable attached (right).

Work is in progress on a means whereby these hand-rests can be used in clinical procedures.

PEDAL-OPERATED INSTRUMENTS

There is one type of unwanted movement which is not controlled even with the use of hand-rests. When an instrument is opened or closed by reducing or increasing the pressure of the finger-tips upon it, a relatively coarse uncontrolled movement occurs because of imperfect synergism between the opposing fingers. The amplitude of this movement, which is increased by fatigue or anxiety, is commonly of the order of 0·25 mm. This is enough to be highly disturbing in such a delicate task as dissecting the adventitia off a small vein.

To overcome this difficulty a set of three instruments—scissors, forceps, and needle-holder—has been developed. These instruments are held and directed by the hand, but are opened and closed by the remote control of foot-pedals.

Several authors have described pedal-controlled microsurgical instruments, using differing systems of control. Buncke and Schulz (1966) and Acland (1969) used low-pressure hydraulic transmission, Salmon (1968) used compressed air, and the highly sophisticated instruments of Parel, Crock, O'Brien, Henderson, and Galbraith (1970) use electric power.

In the author's present instruments the control movement is transmitted from the pedal to the instrument by flexible lightweight 'Bowden' cables, 2 m. long. The inner moving wire is coated with PTFE, which greatly reduces the friction.

Each cable is attached to a foot-pedal (*Fig.* 2). The pedals do not hinge in the ordinary way but rotate on a curved surface, the centre of which is at an imaginary point corresponding to the position of the user's ankle-joint. This permits precise and variable control both upwards and downwards. The pedals have no spring, the upward movement being made by downward pressure with the heel.

The three present instruments are a modified jeweller's needle-point forceps, a modified Wecker's iris scissors, and a purpose-made needle-holder (*Fig.* 3).

Each instrument, with its attached cable coiled up, can be sterilized without harm in an ordinary autoclave. The instruments have the further advantages of being relatively robust, requiring no adjustment, and being easily assembled for use.

The value of these instruments is that for the beginner they greatly increase the precision and confidence of fine movements. The necessary foot co-ordination is easily acquired. However, it has to be said that with sufficient practice one can learn to do even the finest work without these aids, using such simple instruments as Castroviejo scissors and jeweller's forceps. The place of foot-operated instruments in microsurgery is therefore uncertain.

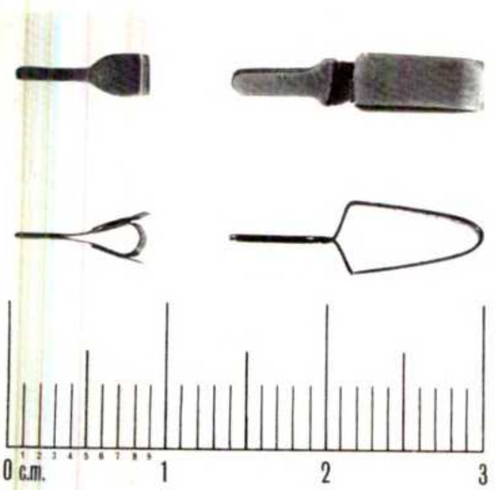

FIG. 4.—The author's artery clamp (left) with a Mayfield clamp (right).

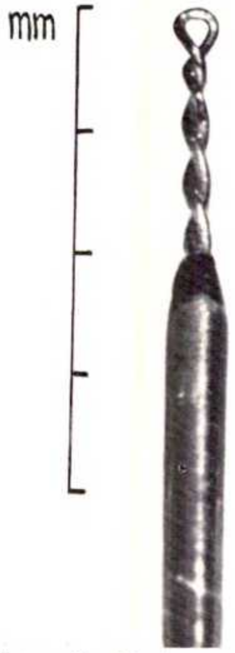

FIG. 5.—The Micro-loop counter-pressor.

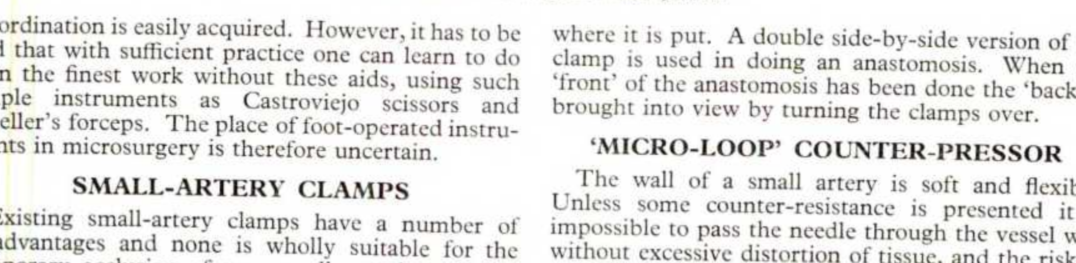

FIG. 6.—Method of using the counter-pressor.

SMALL-ARTERY CLAMPS

Existing small-artery clamps have a number of disadvantages and none is wholly suitable for the temporary occlusion of very small vessels. Clamps such as the Mayfield and Scoville Lewis are bulky and difficult to apply, and have a tendency to fall about in the wound under their own weight, to the detriment of the orderly conduct of the operation. In addition, they exert an unnecessary amount of pressure.

The author's clamp is illustrated in *Fig.* 4. It acts on the principle of the Bulldog type of office paper-clip. The clamp is 8 mm. long and weighs 65 mg. It is easily applied with a pair of slightly modified plain dissecting forceps, and has a strong tendency to stay where it is put. A double side-by-side version of the clamp is used in doing an anastomosis. When the 'front' of the anastomosis has been done the 'back' is brought into view by turning the clamps over.

'MICRO-LOOP' COUNTER-PRESSOR

The wall of a small artery is soft and flexible. Unless some counter-resistance is presented it is impossible to pass the needle through the vessel wall without excessive distortion of tissue, and the risk of tearing out adjoining sutures.

There are three ways of arranging counter-resistance. First, the vessel edges may be picked up with forceps. If this is done just at the point on the edge where the suture is to be, it both weakens the tissue where it needs to be strongest and prevents the taking of the smallest possible bite. If the vessel edge is picked up just to one side of the intended site of the next suture, sideways distortion of tissue occurs and irregular spacing of sutures results.

Secondly, the vessel may be manipulated in a 'no-touch' manner by exerting traction on the ends of the sutures already in place (O'Brien, 1970). This begs the question of how the first sutures are put in. In addition, such a practice is likely to cause enlargement of the needle-holes, which predisposes to thrombus formation.

Thirdly, counter-pressure may be made from within the vessel. A simple and effective counter-pressor (*Fig.* 5) consists of a single circular loop of electro-polished stainless-steel wire. The external diameter of the loop is 0·25 mm. The loop is fixed in the end of a rounded-off fine hypodermic needle which is mounted on a plain handle.

To pass a suture the counter-pressor is placed just inside the vessel (*Fig.* 6A) and the needle is passed through the vessel wall and through the loop. When the needle is a little way through the loop, the loop is withdrawn and placed on the outside of the vessel (*Fig.* 6B) to provide counter-pressure at the point where the needle is brought out.

The advice is often given 'never to touch the intima' on account of the danger of damaging the endothelium and thereby provoking thrombus formation. However this may be, this instrument has been used regularly by the author in anastomosing femoral arteries of rats (diameter 0·6 mm.) without any subsequent thrombus formation attributable to its use.

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WOUND ANTIBIOTICS IN GASTRO-INTESTINAL SURGERY

COMPARISON OF AMPICILLIN WITH PENICILLIN AND SULPHADIAZINE

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Summary

Ampicillin was compared with a penicillin and sulphadiazine combination as a topical wound application in patients undergoing biliary or gastro-intestinal surgery in a controlled study. Eleven of the 53 patients having a topical application of penicillin and sulphadiazine developed wound sepsis (20·8 per cent) compared with 4 of the 59 patients receiving ampicillin (6·8 per cent). This difference is significant ($P < 0·01$).

The incidence of wound sepsis following surgical operations is still regrettably high. Although only rarely associated with mortality, wound infection causes prolongation of convalescence, unpleasant dressings, ugly scars, increased risk of wound breakdown, and the production of a dangerous locus of infection within the surgical ward.

Heavily contaminated wounds and those whose surfaces are soaked by pus during the course of operation are, not surprisingly, associated with a high rate of infection, but numerous reports reveal that sepsis is also particularly common in routine surgical procedures in which the gastro-intestinal and biliary tracts are opened (Committee on Trauma, 1964). Since contamination of the wound at the time of operation is the main cause of suppuration, there has been considerable recent interest in the use of anti-bacterial agents placed in the wound at operation (Nash and Hugh, 1967; Rickett and Jackson, 1969; Mountain and Seal, 1970).

Penicillin and sulphadiazine powder has been used for this purpose for many years, and the present report compares its efficacy with ampicillin powder in patients undergoing gastro-intestinal or biliary-tract surgery.

MATERIALS AND METHODS

Patients undergoing operative procedures in which either the alimentary or biliary tract was to be opened were randomly distributed to receive either Penicillin G (1 MU.) and sulphadiazine (2 g.) powder or ampicillin (1 g.) powder topically into the laparotomy wound after closure of the peritoneum. No powder was given to those patients with a history of sensitivity to any of these compounds. Skin preparation in every case was carried out with iodine in spirit. In those cases requiring a peritoneal drain this was brought out through a separate stab incision. Wounds were assessed on the tenth postoperative day unless there was need for earlier examination because of, for example, pain, fever, or early discharge from hospital.

Wound infection was defined as the presence of pus which discharged spontaneously or needed to be released, according to the criteria of Lundqvist (1964). A swab was taken for bacteriological culture from any wound discharge. Special note was made of any systemic antibiotic therapy used over the operative period, and this comprised in every case a 5–6-day course of ampicillin. Patients undergoing elective colonic surgery received a 5-day course of phthalylsulphathiazole, 2 g. 6-hourly by mouth, supplemented in the last 48 hours by oral neomycin, 0·5 g. 6-hourly. Any special feature relating to the patient or to the operative procedure was also recorded.

Table I.—THE INCIDENCE OF WOUND INFECTION IN RELATION TO THE TYPE OF OPERATIVE PROCEDURE AND THE USE OF A TOPICAL ANTIBIOTIC

TYPE OF OPERATION	AMPICILLIN		PENICILLIN AND SULPHADIAZINE		NO ANTIBIOTIC	
	No. of Patients	No. of Wound Infections	No. of Patients	No. of Wound Infections	No. of Patients	No. of Wound Infections
Appendicectomy	6	2	4	1	0	
Large- or small-bowel surgery	16	1	17	5	2	1
Biliary-tract surgery	18	0	16	3	1	0
Gastroduodenal surgery	19	1	16	2	0	
Total	59	4	53	11	3	1

RESULTS

During the period of study, 121 consecutive patients were subjected to operations involving the opening of the alimentary or biliary tract. Three patients who had had previous reactions to antibiotics received no local therapy. Of the 118 patients receiving topical antibiotics, 6 were subsequently excluded because of death or reoperation during the first 10 postoperative days. Of the 112 patients remaining for study, 15 developed wound infection (14 per cent). Eleven of the 53 patients who had penicillin and sulphadiazine powder in the wound developed infection (20·8 per cent) compared with 4 of the 59 patients who received topical ampicillin (6·8 per cent). This difference is significant ($P < 0{\cdot}01$). One of the 3 patients who had no topical antibiotic because of hypersensitivity became infected.

The incidence of infection considered in relation to the type of operative procedure is set out in *Table I*. It can be seen that the two series of patients are well matched in this respect. Operations on the appendix have the greatest proportion of infections, followed by those on the large and small intestines.

The use of antibiotics systemically and as pre-operative bowel preparation was also reasonably distributed between the two groups. Forty-six patients had had systemic chemotherapy (ampicillin), with 4 postoperative wound infections; 24 had received topical ampicillin, 21 had had penicillin and sulphadiazine, and 1 had not had topical therapy. There were 2 wound infections in the group receiving topical ampicillin and 2 in the group having penicillin and sulphadiazine. Twenty-five patients had received bowel preparation with phthalylsulphathiazole and neomycin, with 3 postoperative wound infections; 11 of these had received topical ampicillin, 13 had had topical penicillin and sulphadiazine, and 1 had received no local therapy. One patient who had had topical ampicillin, 1 receiving penicillin and sulphadiazine, and the 1 patient who had received no topical therapy became infected.

Bacteriology.—Bacteria were cultured from the pus obtained from 11 of the 16 infected wounds, and in every case the infection was due to a Gram-negative organism. The organism in the case which had received no wound antibiotic was sensitive to both ampicillin and sulphonamides and might have been suppressed by either powder. In 4 of the 7 patients in the penicillin and sulphadiazine series the infecting organism was sensitive to ampicillin and resistant to sulphonamides. Two of the three organisms in the ampicillin series were resistant to ampicillin and all were resistant to sulphonamides.

DISCUSSION

In the early days of antibiotics it was hoped that the use of these agents as a prophylactic would abolish sepsis from the surgical wards, but this dream was soon shattered as report after report appeared showing that the use of various antibiotics seemed to have no effect at all on sepsis rates or even potentiated the growth of resistant organisms (Ellis, 1969). Most of these studies can be criticized in that antibiotic therapy was commenced after operation, whereas Linton (1961) has stressed that prophylaxis, if it is to be used, must commence before the operation has begun so that an adequate antibiotic level is present in the tissues at the time that bacterial inoculation takes place. Experimentally, Burke (1961) has demonstrated that systemic antibiotics have no effect on primary staphylococcal wound sepsis if the bacteria producing the infection have been in the tissues for longer than 3 hours before therapy is commenced. Bernard and Cole (1964), in a carefully controlled investigation of patients undergoing gastro-intestinal and biliary-tract surgery, showed that a penicillin, methicillin, and chloramphenicol combination in which the first dose was given 1 or 2 hours preoperatively and the second during operation resulted in a 5 per cent infection rate, compared with a 25 per cent rate in untreated controls. Similar results have been reported using cephaloridine in elective gastro-intestinal operations (Polk and Lopez-Mayor, 1969), and combined carbenicillin and gentamicin begun within 2 hours of surgery (Bloom, 1969).

Most surgeons are averse to the use of systemic antibiotics as a prophylactic measure, but the value of local chemotherapy has aroused considerable interest recently. By this means an extremely high concentration of antibiotic in the wound is achieved at the time when potential bacterial contamination takes place, the concentration of antibiotic being far higher than could be obtained by systemic administration (Ryan, 1967) and yet being without the disadvantages and potential dangers of a full systemic antibiotic course. Matsumoto, Hardaway, Dobek, and Noyes (1967) showed convincingly that a spray of oxytetracycline in heavily contaminated crush wounds in experimental animals had a dramatic effect on mortality: 67 per cent of their control group died compared with only 1 per cent in the treated group. It is interesting that the same dosage of oxytetracycline given systemically reduced the mortality to only 51 per cent.

A number of clinical trials on the use of antibiotics instilled directly into the wound have now been published and their results have been encouraging. Nash and Hugh (1967) used ampicillin powder in the abdominal wound following large-bowel surgery; 3 per cent became infected in the treated group and 41 per cent in the untreated patients. Moylan and Brockenbrough (1968) reduced their rate of wound infection from 19·8 to 9·7 per cent when wounds were irrigated with 1 per cent kanamycin following enterotomies; the control group in this study had the wound irrigated with saline. Bacterial swabs taken at the end of the operation showed a positive culture in all but 1 patient where sepsis later occurred, thus confirming the importance of contamination at the time of surgery. Rickett and Jackson (1969) reported a double-blind trial with the use of topical ampicillin in appendicectomy wounds. There was a 3 per cent infection rate in those patients in whom 500 mg. ampicillin were placed in the wound compared with a 24 per cent infection rate in those receiving lactose powder. This study can be criticized because it may well be that lactose itself encourages wound infection by its presence in the tissues. Mountain and Seal (1970) compared patients undergoing appendicectomy who either received or did not receive topical ampicillin; the sepsis rate in the treated group was 9 per cent compared with 24 per cent in the untreated group.

Sufficient evidence seems to have accumulated which indicates that topical antibiotics can significantly reduce wound infection in alimentary-tract surgery; the problem would now seem to be which is the most effective agent. In this study we have compared penicillin and sulphadiazine powder with ampicillin. Penicillin with a sulphonamide has been a popular topical combination for many years and does indeed provide protection against a wide spectrum of the bowel organisms. However, in modern surgical practice ampicillin has an even wider spectrum of activity with less chance of bacterial resistance to it. Our own findings confirm the greater effectiveness of topical ampicillin in reducing local infection. An incidence of infection of 20·9 per cent was found in patients receiving penicillin and sulphadiazine powder compared with 6·8 per cent in the ampicillin-treated group. Moreover, it is interesting that of the infected wounds in the former group from which bacteria were obtained on culture, 4 out of 7 were ampicillin-sensitive.

Since a number of patients are, or claim to be, sensitive to a variety of antibiotics it is obviously important to determine the efficiency of a variety of agents as topical applicants, and there has been renewed interest in the use of local wound antiseptics (Edlich, Custer, Madden, Dajani, Rogers, and Wangensteen, 1969). Studies of this nature need to determine not only the efficiency of such agents in reducing local infection, but also any effect they might have on wound healing. We have conducted a trial of noxythioline (a chemical compound which undergoes slow decomposition to liberate free formaldehyde) as a topical application in a controlled trial against ampicillin but have found it less effective (Stoker and Ellis, 1971).

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KIDNEY PRESERVATION FOR TRANSPORTATION

EXPERIMENTAL ANALYSIS OF OPTIMAL PERFUSATE COMPOSITION

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SUMMARY

Previous experiments have demonstrated that canine kidneys can be preserved for 24 hours or more following initial perfusion with a solution of intracellular composition (C3) and subsequent ice storage. In the present study the composition of C3 was varied to determine the role of each of the major constituents. The efficacy of the solution was found to depend more on magnesium sulphate than on the potassium content, although potassium assumed a greater importance in perfusates free of magnesium. No variation in composition produced a significant improvement in the results obtained with solution C3 itself.

INITIAL cold perfusion followed by ice storage is, by virtue of simplicity, the method preferred in most transplant centres for the storage of human cadaveric kidneys. Although the success of this technique may be ascribed largely to profound depression of metabolism upon cooling (Levy, 1959), it is clear that perfusate composition is also of considerable importance. One such perfusate, solution C3, formulated to resemble intracellular fluid, would appear to be the best so far developed for both canine and human kidney preservation (Collins, Hartley, and Clunie, 1971a, b; Woods, Holley, and Pheteplace, 1971). The present study was undertaken to define more precisely the role of each of the major constituents of this perfusate.

MATERIALS AND METHODS

The experimental protocol has been described previously (Collins, Shugarman, and Terasaki, 1969). Canine kidneys were stored in iced saline slush after an initial perfusion from a height of 100 cm. with 150 ml. of the cold solution under test, and were reimplanted in the donor 24 hours later, contralateral nephrectomy being carried out at that time. Saline and mannitol diuresis were induced during all operative procedures, and the function of the stored kidneys was assessed by daily measurements of serum creatinine. In the present study serial modifications of solution C3 were tested, varying the composition with respect to sodium, potassium, magnesium, and glucose (*Table I*). The *p*H ranged from 7·05 to 7·15 at 37°C. and the osmolarity from 300 to 330 mosmol per l. In addition to the electrolytes, all the perfusates contained procaine hydrochloride, 0·94 g. per l., glucose,* 23·5 g. per l., and heparin, 5000 U. per l. Statistical analysis of the results was performed using Student's *t*-test.

RESULTS

A total of 64 canine kidney preservation experiments was performed, comparing 9 variations of perfusate composition (*Table I*). The maximum serum creatinine levels reached within the first week after reimplantation of the stored kidneys are recorded in *Tables II* and *III*.

Table I.—COMPOSITION OF PERFUSATES

PERFUSATE	ELECTROLYTE CONTENT (mmol. per l.)						
	Na	K	Mg	SO_4	PO_4	Cl	HCO_3
C3	9	107	28	28	54	14	9
C3 (sucrose)	9	107	28	28	54	14	9
C3 (sodium)	116	—	28	28	54	14	9
C3 (extra magnesium)	3	50	86	86	17	5	3
C3 (no magnesium)	9	107	—	—	54	14	9
Sodium phosphate	128	—	—	—	73	—	—
Sodium phosphate + magnesium	128	—	28	28	73	—	—
Sodium/potassium phosphate + magnesium	64	64	28	28	73	—	—
Potassium phosphate + magnesium	—	128	28	28	73	—	—

In the first group the composition of C3 was modified by either substitution of sucrose for glucose or alteration in the magnesium content. Serum creatinine levels (*Table II*) rose on average to 2·4 ± 0·7 mg. per cent with C3 as the perfusate, and to 2·7 ± 1·2 mg. per cent when sucrose was substituted for glucose, a difference which was not significant ($P > 0{\cdot}05$). Alteration of the magnesium content, however, had a more noticeable effect. When the perfusate contained an increased amount of magnesium sulphate (90 mmol. per l.), with a corresponding reduction in the concentration of the other electrolytes, the average serum creatinine level for the group rose to only 2·2 ± 0·7 mg. per cent, a value which was significantly lower ($P < 0{\cdot}05$) than the mean for the group in which the perfusate was C3 without magnesium, where the maximum serum creatinine was 3·9 ± 2·8 mg. per cent. With sodium phosphate solution (*Table III*) the maximum creatinine was 7·7 ± 5·0 mg. per cent, but the addition of magnesium sulphate (30 mmol. per l.) produced a significant reduction ($P < 0{\cdot}05$) to 2·7 ± 0·9 mg. per cent.

The second series of experiments (*Table III*) was intended to define the importance of the sodium to potassium ratio in the perfusate by substitution of sodium for the potassium in C3, and by utilization of a simplified perfusate containing, in addition to magnesium sulphate, either sodium phosphate, potassium phosphate, or a mixture of the two in equal amounts. In the presence of magnesium sulphate (30 mmol. per l.) alterations in the ratio of sodium to potassium had little effect on the extent of the rise in serum creatinine. The lowest maximum serum creatinine levels were achieved when the perfusate contained both sodium and potassium, as with the C3 solution or the sodium/potassium/phosphate mixture. In these groups the average maximum creatinine levels recorded were 2·4 ± 0·7 mg. per cent in each case. Individually, sodium phosphate or potassium phosphate together with magnesium sulphate resulted in slightly higher maximum creatinine levels of 2·7 ± 0·9 mg. per cent and 3·0 ± 0·5 mg. per cent respectively. These differences, however, were not significant ($P > 0·05$). In the *absence* of magnesium sulphate, on the other hand, a potassium-containing solution appeared to be superior to a purely sodium-containing one. Thus, the average maximum serum creatinine level recorded for the group perfused with sodium phosphate alone was 7·7 ± 5·0 mg. per cent compared with 3·9 ± 2·8 mg. per cent for the group in which C3 without magnesium served as the perfusate. Owing to rather large standard deviations within these groups this difference just failed to reach statistical significance ($P > 0·05$).

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* In solution C3 (sucrose) glucose was replaced iso-osmotically with sucrose (*Table I*).

Table II.—KIDNEY FUNCTION AFTER INITIAL PERFUSION AND ICE STORAGE FOR 24 HOURS

PERFUSATE	MAXIMUM SERUM CREATININE (mg. per cent)			DEATH FROM URAEMIA
	Individual	Mean	S.D.	
C3	1·5, 2·1, 3·8, 2·5, 2·2, 3·3, 1·8, 1·2, 2·8	2·4	0·7	0/9
C3 (sucrose substitution)	1·5, 4·8, 1·6, 4·1, 2·7, 2·1, 2·7, 2·3	2·7	1·2	0/8
C3 (no magnesium)	3·5, 3·2, 9·4,* 1·9, 3·6,† 1·9‡	3·9	2·8	1/6
C3 (extra magnesium)	1·6, 2·0, 3·3, 2·3, 1·5, 1·6, 2·7, 1·5, 2·7, 2·1, 3·2, 1·8§	2·2	0·7	0/12

* Died from uraemia.

† Died from peritonitis.

‡ Died from wound dehiscence.

Died from pneumonia.

DISCUSSION

Undoubtedly the most important single factor contributing to the success of hypothermic kidney storage is the marked reduction in metabolism produced by cooling (Levy, 1959). The efficacy of the method is thus proportional to the reduction in temperature achieved (Stueber, Kovacs, Koletsky, and Persky, 1958). In order to achieve rapid cooling (Markland and Parsons, 1963) it is the normal practice to perfuse the kidney soon after removal with a volume of cold electrolyte solution. This procedure has the added theoretical advantages of the elimination of some antigen in the form of retained blood and providing a basis for assessment of organ viability in terms of the uniformity and quality of perfusion (Belzer and Kountz, 1970). The composition of the perfusate used has usually been based on extracellular fluid, in which the principal cation is sodium, and has frequently contained in addition some colloid in the form of either protein or dextran (Cleveland, Lee, Prout, and Hume, 1964; Dempster, Kountz, and Jovanovic, 1964; Sells and Pena, 1970). Recently, however, we have shown experimentally and in man that a perfusate resembling intracellular fluid, solution C3—4, yields better results (Collins, Shugarman, Terasaki, Braf, Sheil, and Williams, 1970; Collins and others, 1971a, b), and this finding has been amply confirmed by others (Collste, Bjorken, Collste, and Groth, 1970; Liu, Humphries, Stoddard, and Moretz, 1970; Woods and others, 1971). We are unable to explain the failure of certain groups to repeat our experimental results (Kulatilake, O'Donoghue, and Shackman, 1970; Smellie, Marshall, and Hadjiyannakis, 1970), but believe that the proved efficacy of the C3 perfusate when applied to the preservation of human cadaveric kidneys (Collins and others, 1971b) goes some way towards answering the criticism raised by Frost, Ackerman, Finch, and Manlove (1970) that the method would be ineffective after a period of warm ischaemia.

Table III.—KIDNEY FUNCTION AFTER INITIAL PERFUSION AND ICE STORAGE FOR 24 HOURS

PERFUSATE	MAXIMUM SERUM CREATININE (mg. per cent)			DEATH FROM URAEMIA
	Individual	Mean	S.D.	
C3 (sodium)	2·5, 3·0, 3·2, 1·7, 3·0, 2·5	2·7	0·5	0/6
Sodium phosphate	6·6, 7·8,* 16·0,† 4·6, 3·4	7·7	5·0	1/5
Sodium phosphate + magnesium	3·4, 1·3, 3·1,‡ 4·0, 1·8, 2·9, 2·5	2·7	0·9	0/7
Sodium/potassium phosphate + magnesium	3·3, 2·3, 1·5, 2·9, 2·2	2·4	0·7	0/5
Potassium phosphate + magnesium	2·8, 3·3, 3·3, 2·1, 3·6, 2·8	3·0	0·5	0/6

* Died from wound dehiscence.

† Died from uraemia.

‡ Died from ureteric obstruction.

The initial choice of the composition of solution C3, which is rich in potassium and magnesium, as a perfusate for hypothermic kidney storage was based on a number of considerations. A substantial proportion of cellular energy production is utilized by the membrane ionic active-transport mechanisms (Whittam and Ager, 1964). The level of cellular respiration is directly related to the concentration of sodium in the environment (Burck and Petruch, 1966). It would therefore seem logical to endeavour to suppress energy requirements during hypothermic storage by a reduction in the concentration of sodium in the extracellular fluid, using a perfusate rich in potassium and poor in sodium. This type of perfusate would have the added advantage of preventing the loss of intracellular potassium and gain of sodium which are known to occur when active-transport mechanisms are suppressed by cold (Whittam and Davies, 1953; Keeler, Swinney, Taylor, and Uldall, 1966). Similar ionic shifts are known to occur in hibernating animals (Haggag, Raheem, and Khahl, 1965), but are limited by the unusual efficiency of the cell-membrane ionic pumps in these animals at low temperatures (Willis, 1966). A further interesting observation made during hibernation is that the plasma-magnesium levels are increased (Haggag and others, 1965; Pengelley and Chaffee, 1966), and this would tend to support the inclusion of magnesium in a perfusate for hypothermic storage.

In the present study the importance of each of the components of solution C3 was tested by serial modifications of its composition. Substitution of sucrose for glucose in iso-osmolar proportions produced no significant deterioration in the results (*Table II*), implying that exogenous glucose does not provide a useful substrate during hypothermic kidney storage. Alteration of the electrolyte content, on the other hand, seemed to influence the results to a greater extent. Magnesium sulphate was the component of greatest importance. Its inclusion in the C3 perfusate in concentrations above 10 mmol. per l. (Collste and others, 1970) results in consistently good 24-hour kidney preservation. The optimum level would appear to lie in the range of 30–90 mmol. per l. The beneficial effects of magnesium in organ preservation have been described previously (Kamiyama, Webb, and Ecker, 1970), and have been attributed to metabolic inhibition and the ability of magnesium to prevent loss of intracellular potassium. This effect may explain why in the present study the rise in serum creatinine following the use of a perfusate containing magnesium sulphate was low, regardless of the sodium to potassium ratio. When the perfusate contained no magnesium, however, there was a suggestion that the potassium content assumed a greater importance, the maximum creatinine levels in the group perfused with C3 without magnesium being lower than those in the group perfused with sodium phosphate alone. This difference failed to reach statistical significance because of the large standard deviations in the results for both groups. However, taken together with other evidence for the importance of an elevated potassium content in perfusates for organ storage (Keeler and others, 1966; Abouna, 1968; Calman, Bell, MacPherson, Wood, and Quin, 1970), the difference between these two groups may well be meaningful. It is interesting to note that the highest creatinine values followed perfusion with a potassium phosphate/magnesium sulphate solution in which the potassium concentration was 128 mEq./l., and it may be that too high a potassium concentration is deleterious. The lower potassium concentration of 107 mEq./l. in C3 and 64 mEq./l. in the sodium/potassium phosphate mixture may approach more closely the levels of 30–50 mEq./l. which have been found by others to be optimal for continuous perfusion (Abouna, 1968; Calman and others, 1970). *In vitro* studies of canine renal cortical respiration at present in progress in our laboratory tend to support the contention that the potassium concentration should not be too high.

The canine kidney preservation model upon which this and most other studies have been based has been invaluable as a proving ground for storage techniques intended ultimately for clinical use. Unfortunately, the many uncontrollable factors in dog kidney transplantation lead to variability in results, and the resolution of the method is therefore limited to rather broad comparisons between perfusates and storage techniques which differ substantially in their efficacy. Thus, attempts to define more precisely the optimum composition of perfusates with such a method will probably be unrewarding. From the present series of experiments it would appear to be difficult to improve on solution C3, the effect of which seems to be based largely on the magnesium and to a lesser extent the potassium content. However, an increase in the magnesium and a reduction in the potassium concentrations deserve further examination in a more sensitive model. We are currently investigating *in vitro* preservation methods which may provide a better tool for initial assessment of the value of individual constituents of perfusates for hypothermic kidney preservation.

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THE VALUE OF FRUSEMIDE IN 110 CONSECUTIVE PROSTATECTOMIES

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SUMMARY

One hundred and ten patients undergoing open prostatectomy had an induced diuresis using frusemide. The results of this treatment are reviewed. Seventy-one patients (65 per cent) presented as emergencies with acute retention, while the remainder presented with chronic retention or prostatism. The average age was 69 years, and 25 patients (23 per cent) were aged 75 years or more. Only rarely was a patient refused operation because of confinement to bed or failing mental faculties. Blood-loss, fluid and electrolyte balance, and postoperative urinary infection were studied in detail, and the following points are emphasized:—

1. The average postoperative 24-hour urinary output was 4·5 litres, 40 per cent of which was passed in the first 3 hours when the danger of clot retention is greatest.
2. Clot retention was eliminated as a problem, and bladder wash-outs were not necessary.
3. The average blood replacement was 1·05 U., and the average fall in postoperative haemoglobin level was 1·1 g.
4. The postoperative urinary infection rate was low, being 8 per cent at 1 week after operation.
5. A low morbidity was recorded and the mortality was 0·9 per cent.

A vigorous diuresis induced by frusemide after suitable fluid loading is both effective and safe. It is a distinct advance over previous methods used.

THE immediate complication after prostatectomy is haemorrhage, and its possible sequel, clot retention. In general, the threat of this complication is present only in the first few hours after operation. The other important complication, urinary infection, is potentiated by excessive bleeding and poor bladder drainage necessitating interference with the catheter. Any method which ensures a free flow of urine will reduce these hazards. A large urinary secretion will dilute and prevent the clotting of blood that is being shed in the immediate postoperative period. Also, by removing the environment which is favourable to bacterial growth, urinary infection may be prevented.

Osmotic diuretics have been extensively used in prostatic surgery. McKelvie in 1962 and Rickwood and Thorne in 1967 reported good results using intravenous urea. Jameson in 1969 described the use of mannitol and intramuscular frusemide in 80 cases. Recently, Essenhigh and Eustace (1969) have described the use of frusemide administered intravenously in a larger dose in a series of 50 cases.

The use of frusemide, a non-mercurial diuretic of low toxicity, after suitable fluid loading to produce a physiological bladder wash-out would appear to be particularly attractive. Frusemide is a distinct advance over intravenous urea or mannitol because of its ease of administration, its rapid action, and the predictability of its effect. Frusemide acts mainly by reducing sodium reabsorption in the distal tubules and it may also increase the glomerular filtration rate, even when renal function is impaired (Kerr and Robson, 1965). It was decided to carry out a trial of frusemide in patients undergoing prostatectomy.

MATERIALS AND METHODS

During a 9-month period 110 consecutive prostatectomies were carried out; all of the patients were given frusemide. This series of patients was unselected. Very occasionally a patient was refused operation because of either a complete lack of mobility or failing mental faculties. The age range was 50–96 years, the average age being 69 years.

Table I.—ASSOCIATED DISEASE

Associated Disease	*No. of Patients*
Hypertension	46
Chronic bronchitis	14
Coronary thrombosis	5
Cerebrovascular accident	3
Auricular fibrillation	2
Aortic stenosis	1
Congestive cardiac failure	1
Angina pectoris	2
Deep venous thrombosis	1
Severe arteriosclerosis	4
Diabetes mellitus	2

All of these patients were managed in a busy urological unit. Sixty-five per cent presented as emergencies with acute painful retention, 8 per cent had chronic painless retention, and the remaining 27 per cent were admitted for elective surgery because of prostatism. The patients in this study exhibited an impressive array of concomitant 'medical' disease (*Table I*). *Table I* shows that a severe degree of cardiovascular or pulmonary disease, a frequent finding in this age-group, is not in itself a contra-indication to prostatectomy.

Preliminary assessment of the patients included estimation of haemoglobin, blood-urea, and electrolytes, culture of urine, and intravenous pyelography. Blood-urea was normal in 86 per cent, over 50 mg. per 100 ml. in 10 per cent, and over 100 mg. per 100 ml. in 4 per cent. Urinary infection was present in 17 per cent of patients on admission to hospital.

The type of prostatectomy to be performed was decided by cystoscopy and rectal examination. Millin prostatectomy was performed in 79 patients (72 per cent), and transvesical prostatectomy in the minor degree of cellulitis. Two patients developed auricular fibrillation, which was controlled by digoxin. One patient aspirated a small amount of stomach content whilst under anaesthesia and was retained on a positive-pressure respirator for 12 hours postoperatively, recovering without incident thereafter. Vasectomy was not performed, and 3 patients developed a mild epididymo-orchitis after discharge from hospital; all settled rapidly on antibiotics.

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Strictures occurred in 2 patients. One patient had prolonged catheterization and developed a stricture in the penile urethra which was easily dilated. The other patient, who had the prostatic cavity packed at operation for severe haemorrhage, developed a bladder-neck stricture after 6 months which necessitated excision. In 1 patient a bladder stone was missed at cystoscopy, and this precipitated retention 6 months after prostatectomy when it became impacted in the urethra and had to be removed.

There has been no instance of suprapubic fistula formation, and all the patients have satisfactory control of micturition, except for 1 man of 82 years who has stress incontinence; this man had been incontinent for 10 years preoperatively. No patient developed symptoms or signs of either deep venous thrombosis or pulmonary embolism.

Mortality.—No patient died as an immediate result of the operation. One patient, having made an initially satisfactory recovery, died in hospital 3 weeks after operation from acute pancreatitis. The mortality in this series was therefore 0·9 per cent.

There have been 3 late deaths. Two of these patients had carcinoma of the prostate and were aged 81 and 96 years, and the other patient had carcinoma of the bladder and was aged 82 years. These 3 patients died in their own homes approximately 4 months after discharge from hospital, having remained ambulant until shortly before death and free of the burden of an indwelling catheter.

DISCUSSION

The principle of inducing a diuresis after prostatectomy is well known but previous methods using intravenous urea or mannitol have not been entirely satisfactory. The response to intravenous urea and mannitol is not sufficiently predictable: intravenous urea may cause thrombophlebitis and mannitol may cause renal tubular damage or hypokalaemia. The use of frusemide is simple, effective, and would appear to have no contra-indications. Initial fears that frusemide may have some diabetogenic effect have proved unfounded (Schaefer, 1964). Two diabetics in the present series made a smooth postoperative recovery.

The most immediate problem of bleeding in the first few postoperative hours is reduced by an adequate diuresis, and clot retention has not been a problem in this series. Bladder wash-outs have not been necessary. Five patients had small blood-clots aspirated from the catheter with a suction syringe, no foreign substance being introduced into the bladder. This could probably have been avoided if a further dose of frusemide, 40 mg., had been given when the urine became heavily blood-stained. Eight patients were given such an extra dose of frusemide, with rapid clearing of the urine. Rickwood and Thorne (1967), using an intravenous urea technique, found that 45 per cent of their patients needed at least one bladder wash-out at some stage because of catheter blockage.

Blood-loss during and after prostatectomy may be underestimated by the surgeon. Salvaris (1960) estimated a mean overall loss of 1000 ml. in 30 patients. Goldman and Samellas (1961) estimated an average loss of 1050 ml. Over 50 per cent of the total blood-loss occurs in the postoperative period. The presence of a large amount of blood-clot in the bladder appears to encourage prolonged oozing from the prostatic bed, possibly by preventing the prostatic capsule from contracting down. The diuresis, by preventing the accumulation of blood-clot, reduces postoperative oozing, and the urine rapidly becomes clear of any gross blood-staining. In this series blood-loss was estimated by clinical observation and by estimation of the haemoglobin level. The average blood replacement was 1·05 U., and the average postoperative fall in haemoglobin was 1·1 g. Thirty patients did not require blood transfusion.

The incidence of postoperative urinary infection in this series (8 per cent) is low. The rapid clearing of blood from the urine and the elimination of clot retention prevent the formation of a favourable 'culture medium' in the bladder. O'Grady and Cattell (1966) suggest that a high urinary flow rate reduces infection by a mechanical washing-out effect. A minimum of interference with the catheter and early removal of the catheter also reduce the postoperative infection rate. The generally reported incidence of postoperative urinary infection has been between 15 and 100 per cent, including those authors using a no-catheter technique (Spencer, 1967). Salvaris (1960), reviewing a large series of prostatectomies, found that of 40 per cent who had postoperative urine cultures recorded, nearly all had an infection. Allan and Coorey (1966) found urinary-tract infection to be present in almost 100 per cent of their patients following operation, and this had fallen to 8 per cent after 1 year.

Table VI.—MORTALITY OF PROSTATECTOMY

AUTHOR	NO. OF CASES	ACUTE RETENTIONS (per cent)	MORTALITY (per cent)
Salvaris (1960)	1200	25	4·2
Stearns (1961)	500	35	0·66
Allan and Coorey (1966)	1000	69	5·2
Cooper, Ashmalla, and Cobb (1966)	302	22	0·99
Rickwood and Thorne (1967)	132	64	5·0
Spencer (1967)	132	60	6·1
Jameson (1969)	80	25	1·25
Williams (1972)	110	65	0·9

Morbidity from the operation was negligible, and no complications were attributable to the method of fluid loading or to the diuretic agent used. Postoperative mental confusion and chest infection have not been a problem. There has been no instance of deep venous thrombosis or pulmonary embolism. Dehydration is not well tolerated by the elderly and may lead to any of these complications. It is felt that a rapid fluid turnover and the maintenance of a positive fluid and electrolyte balance are important factors in preventing complications.

The mortality of prostatectomy which has been recorded in the literature is shown in *Table VI*, and has ranged from over 6 per cent to 0·6 per cent, which was obtained by Stearns (1961) in a series of rigidly selected cases. The mortality of 0·9 per cent in this series is low and compares favourably with any published series of open prostatectomies or transurethral prostatectomies, for which the accepted mortality is around 1 per cent (Mitchell, 1970).

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THE EFFECT OF ORAL SUPPLEMENTATION OF ZINC SULPHATE ON PRIMARY WOUND HEALING IN RATS

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SUMMARY

The effect of oral supplementation of zinc sulphate on primary wound healing of abdominal wounds was studied in normal rats receiving a standard diet. Daily oral administration of 40 mg. of zinc sulphate ($ZnSO_4.7H_2O$) per rat for 13 days postoperatively resulted in a 35–36 per cent increase in the bursting strength of sutured incision wounds. This increase was statistically significant and corresponded to a gain of about 13 days in healing time. The same daily dose of zinc did not result in a significant increase of wound-bursting strength measured on the sixth day after operation.

IN recent years there has been much interest in the effect of zinc supplementation in the acceleration of wound healing. So far, the effect in man has been demonstrated for secondary healing of open wounds (Pories, Burget, Henzel, Smith, and Strain, 1966; Pories, Henzel, Caris, Rob, and Strain, 1967), leg ulcers (Carruthers, 1969; Husain, 1969; Greaves and Skillen, 1970), leg ulcers in sickle-cell anaemia (Sergeant, Galloway, and Gueri, 1970), and bed-sores (Cohen, 1968). Although the results of zinc supplementation on primary healing of sutured wounds in man have not, to our knowledge, been reported, such a use could also be of importance (Groundwater and Macleod, 1970).

Most of the reported studies on the effect of zinc supplementation in normal animals have been done with rats. Strain, Pories, and Hinshaw (1960), who used zinc methionine, and Pories and others (1966) and Morton and Malone (1969), working with zinc sulphate, demonstrated an acceleration in wound healing of excised skin wounds of rats. On the other hand, O'Riain, Copenhagen, and Calnan (1968), Groundwater and Macleod (1970), and Sandstead, Lanier, Shepard, and Gillespie (1970) found that systematically administered zinc did not affect the strength of sutured incision wounds in rats.

The discrepancy between the reports about the effect of zinc supplementation on the healing of open excision and sutured incision wounds in rats has led to the present study.

MATERIAL AND METHODS

Female Wistar rats, derived from the specific pathogen-free (S.P.F.) colony of TNO, Zeist/Netherlands, were used. The body-weights of the rats ranged from 170 to 200 g. The standard diet contained about 37 mg. of zinc per kg.* The rats underwent operation under aseptic conditions and ether anaesthesia. A standard incision, 5 cm. long, was made in the midline through the skin and linea alba. The wound was closed with six interrupted through-and-through 00 silk sutures.

In a preliminary experiment the rats were killed on the sixth day after operation and the bursting strength of the wound was measured by the method of Prudden, Nishihara, and Batter (1957), using increasing air pressure in a balloon placed inside the abdominal cavity. One group of rats received a daily oral dose of 40 mg. zinc sulphate ($ZnSO_4.7H_2O$) in 2 ml. of water per rat, and another group served as a control.

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* Hope Farms' RMH/TM rat pellets.

In the main series of experiments the rats were killed with ether 13 days after operation and the remaining sutures were removed. The whole of the ventral surface was excised and the bursting strength of the wound was measured, using the principle of Wolarsky and Prudden (1962). The specimen was secured firmly over a trapezoidal hole in a Perspex box so that the box was made air-tight. An air-stream, increasing the pressure by 10 mm. Hg per 5 seconds, was led into the box until wound disruption occurred. The resulting fall in pressure constituted a clear end-point. The maximal pressure attained at the moment of bursting could be read conveniently by means of a float on top of the mercury column in a manometer which was connected with the box. The float was provided with a small steel brush so that it stayed in position after the mercury had fallen, but it could be moved down again with the aid of a magnet at the end of the experiment.

Table I.—BURSTING STRENGTH OF ABDOMINAL WOUNDS IN RATS TREATED WITH ZINC SULPHATE IN AQUEOUS SOLUTION AND IN CONTROL RATS ON THE SIXTH DAY AFTER OPERATION

GROUP	NO. OF ANIMALS	MEAN BURSTING STRENGTH (mm. Hg) ± STANDARD ERROR	PERCENTAGE BURSTING STRENGTH
Control	10	84 ± 5·4	100
Zinc-treated	10	79 ± 13·6	94

The difference between the groups is not statistically significant: $P > 0{\cdot}35$ (method of Welch, 1947).

Table II.—BURSTING STRENGTH OF ABDOMINAL WOUNDS IN RATS TREATED WITH ZINC SULPHATE IN AQUEOUS SOLUTION AND IN CONTROL RATS ON THE THIRTEENTH DAY AFTER OPERATION

GROUP	NO. OF ANIMALS	MEAN BURSTING STRENGTH (mm. Hg) ± STANDARD ERROR	PERCENTAGE BURSTING STRENGTH
Control	13	217 ± 16·7	100
Zinc-treated	13	292 ± 17·5	135

The difference between the groups is statistically significant: $P < 0{\cdot}0025$ (Student's t-test; one-sided tail probability).

Two sets of experiments were arranged. In the first set, consisting of two experiments, the influence of zinc supplementation was investigated. In both experiments the rats were randomly divided into two groups. From the day of operation each rat in the treatment group was given a daily oral dose of 40 mg. zinc sulphate dissolved in water or suspended in 1 per cent amylum. The control animals received a dose of water or 1 per cent amylum only. The experiment with the amylum suspension was carried out as part of an investigation which included other water-insoluble compounds. The results were analysed statistically using Student's t-test (Gosset, 1908) and the method of Welch (1947).

The aim of the second set of experiments was to establish the relation between time and healing of sutured incision wounds in normal untreated rats. Ninety-five rats underwent operation and were assigned randomly to nine groups. A group of rats was killed every 3 days after operation and the tensile strength of the wounds was measured as described. The results were tested statistically for linearity and regression.

RESULTS

1. The daily oral supplementation with 40 mg. zinc sulphate per rat for 6 days did not result in a significant change in the bursting strength of the wounds (*Table I*).

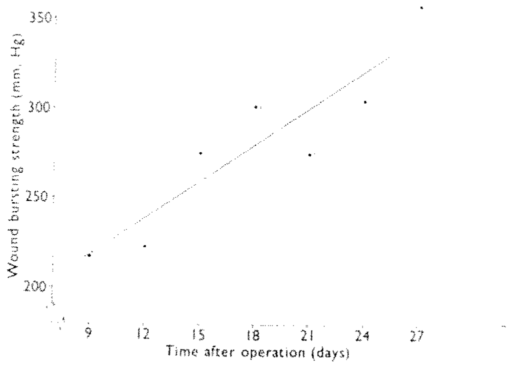

FIG. 1.—Relation between time and bursting strength of sutured abdominal incision wounds in untreated normal rats.

Table III.—BURSTING STRENGTH OF ABDOMINAL WOUNDS IN RATS TREATED WITH ZINC SULPHATE IN A 1 PER CENT AMYLUM SUSPENSION AND IN CONTROL RATS ON THE THIRTEENTH DAY AFTER OPERATION

GROUP	NO. OF ANIMALS	MEAN BURSTING STRENGTH (mm. Hg) ± STANDARD ERROR	PERCENTAGE BURSTING STRENGTH
Control	10	273 ± 20·9	100
Zinc-treated	9	371 ± 8·3	136

The difference between the treated and untreated group is statistically significant: $P < 0{\cdot}0005$ (method of Welch (1947); one-sided tail probability).

Table IV.—BURSTING STRENGTH OF ABDOMINAL WOUNDS IN UNTREATED RATS AT DIFFERENT TIMES AFTER OPERATION

DAY AFTER OPERATION	NO. OF ANIMALS	BURSTING STRENGTH (mm. Hg) ± STANDARD ERROR
3	11	12 ± 5·1
6	11	123 ± 8·7
9	11	217 ± 13·8
12	11	223 ± 24·1
15	11	276 ± 18·1
18	11	302 ± 16·9
21	6	276 ± 31·0
24	11	306 ± 18·1
27	7	359 ± 37·1

2. Forty mg. zinc sulphate, given orally in daily doses for 13 days, resulted in a 35–36 per cent increase in the bursting strength of the sutured abdominal incision wounds. This increase was highly significant (*Tables II, III*).

3. The results of the study of the time–healing relation are given in *Table IV*. The figures for bursting strengths of the wounds indicate three phases of healing: no increase in wound strength during the first 3 days after operation, then a fast increase

during days 3–9, and finally a slow prolonged increase.

By means of a regression analysis of the data on wound strength from the ninth day after operation onwards, it was established that the wound strength showed a significant increase with time which was linear ($F_{\text{regr.}} = 25{\cdot}2$, d.f. 1 and 61; $F_{\text{lin.}} = 0{\cdot}84$, d.f. 5 and 61). This plot is presented in *Fig.* 1. The drawn line represents $\hat{y} = 155{\cdot}41 + 6{\cdot}95x$. This straight line can be used to determine the meaning of the increase in bursting strength in terms of healing time. The treated rats had a wound strength which was 35–36 per cent greater than that of the control animals on day 13; the controls did not reach a comparable level in wound strength until day 25·6. This means that the treated animals had a time-gain in wound healing of 12·6 days in the present experiment. The one-sided lower confidence limit by $\alpha = 0{\cdot}05$ is 6·2 days.

DISCUSSION

The results of our study demonstrate that in addition to a well-established effect on secondary wound healing, zinc supplementation given orally to rats on a normal diet increases the rate of primary wound healing.

Several other workers have failed to demonstrate a beneficial effect of parenteral zinc supplementation on primary wound healing in normally fed rats (O'Riain and others, 1968; Groundwater and Macleod, 1970; Sandstead and others, 1970). Murray and Rosenthal (1968) treated skin wounds in rats locally without favourable results, but they did mention that the suitability of this form of administration may be disputed.

A possible reason why the positive effect of zinc supplementation on primary wound healing has escaped the attention of previous authors seems to be that the duration of the treatment period between operation and testing is an important factor. Most of the previous work, including experiments on the effects of materials other than zinc on primary wound healing (Prudden and others, 1957; Rosenthal, 1968) has been carried out with measurement of wound strength taking place on the sixth or seventh day after operation, apparently since these days lie in the phase of rapid healing. However, Groundwater and Macleod (1970) measured wound strength on days 4, 7, and 10 after operation, and Sandstead and others (1970) did so on day 12. Sandstead and Shepard (1968), using zinc-deficient rats, observed that the tensile strength of wounds in zinc-deficient rats was not lower than that in control rats unless tensiometry was performed on day 12 instead of day 6. In our preliminary experiments we were also unable to demonstrate any effect of zinc supplementation on day 6 after operation. Since we did find a difference on day 13 the effect of zinc on wound strength must have taken place in the intervening period. The conclusion that the slow phase of healing is affected rather than the rapid phase seems obvious, but additional measurements between days 6 and 13 in zinc-treated rats would be necessary to prove this.

It should be noted, however, that there are some differences between the conditions of our experiment and those employed by other authors that may add to the discrepancy in the outcome of zinc supplementation. For example, our oral dose, the equivalent of 9·06 mg. of metallic zinc daily per rat, was larger than the parenteral doses used by Groundwater and Macleod (1970) and by Sandstead and others (1970). The intraperitoneal doses used by O'Riain and others (1968) were even higher, but they reported considerable mortality in all dose groups. A further point of difference is in the surgical technique. Whilst we measured the bursting strength after incisions through the entire abdominal wall, O'Riain and others (1968) and Sandstead and others (1970) made skin incisions only and measured the tensile strength. On the other hand, Groundwater and Macleod (1970) also measured the bursting strength of sutured linea alba wounds. Since in our experiment no increase in wound strength was noted on day 6, we believe the duration of the treatment period to be a very important factor. It is perhaps of interest to note that in a study with excised pilonidal sinus wounds of human patients, Pories and others (1967) also found that oral zinc supplementation only began to accelerate healing significantly after the fifteenth day.

The interpretation of the increase in wound strength in terms of a gain in healing time contributes to the evaluation of the significance of zinc supplementation. Any increase in strength would be of little clinical importance if the untreated patient reached the same stage within a short time.

Acknowledgements.—Thanks are due to Miss A. Blok for technical assistance and to Mr. J. Schuurmans for the statistical analysis.

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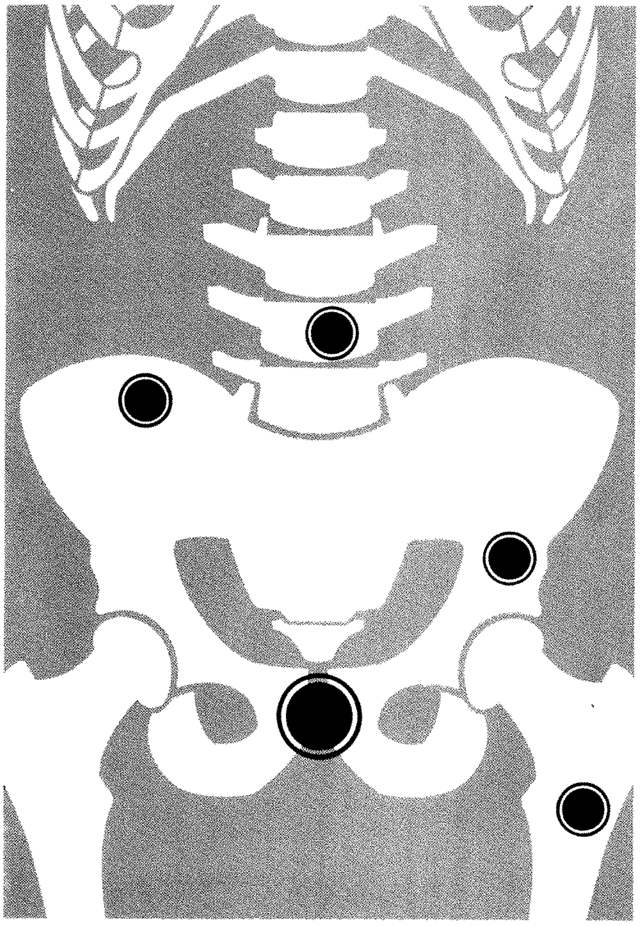

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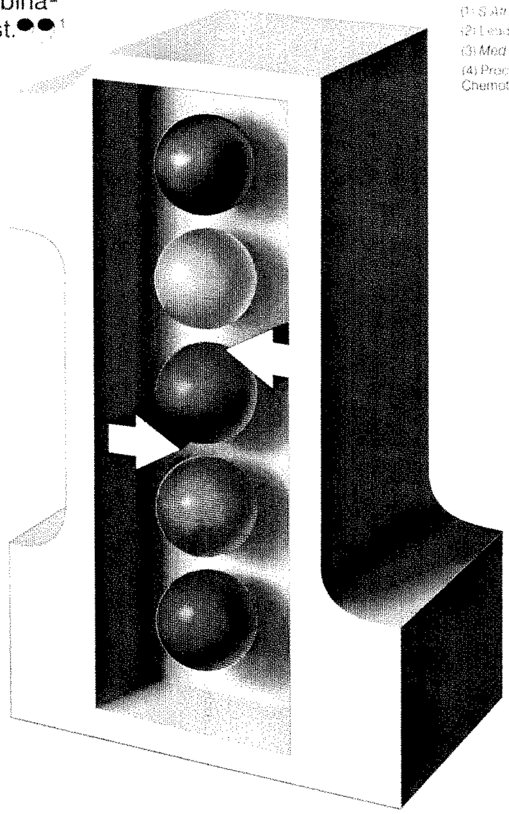

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ACUTE INTRAMURAL ABSCESS OF THE PYLORIC ANTRUM—LOCALIZED PHLEGMON

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SUMMARY

A case of acute 'localized' phlegmonous gastritis is described. The predominant clinical features were persistent abdominal pain and a tender mass in the epigastrium. Complete recovery followed partial gastric resection.

ACUTE phlegmonous gastritis, or 'carbuncle' or 'erysipelas' of the stomach as it was called by early writers, was first described by Cruveilhier in 1820. This rare condition results from bacterial infection of the stomach wall by pathogenic organisms. Until 1947, 355 cases had been described in the world literature (Guzzeta and Southwick, 1947). Starr and Wilson (1957) collected a further 25 cases reported over the next 10 years. Few references to this unusual condition have appeared since then. Acute phlegmonous gastritis may occur in either diffuse or localized form and of the reported cases the diffuse variety is by far the more common. We report here a case of acute localized phlegmonous gastritis which presented some unusual features.

CASE REPORT

A 26-year-old married woman presented to the Casualty Department of Stobhill General Hospital, Glasgow, on 8 Aug., 1970, with epigastric pain of 1 week's duration. The pain had increased in severity and had been unrelenting since onset. There had been no vomiting, bowel upset, or urinary symptoms. The menstrual cycle was normal. In particular, there had been no previous dyspepsia and until the onset of symptoms the patient had been in good health. The only previous admission to hospital was 13 years previously when she had had surgical removal of a swallowed needle from the small bowel.

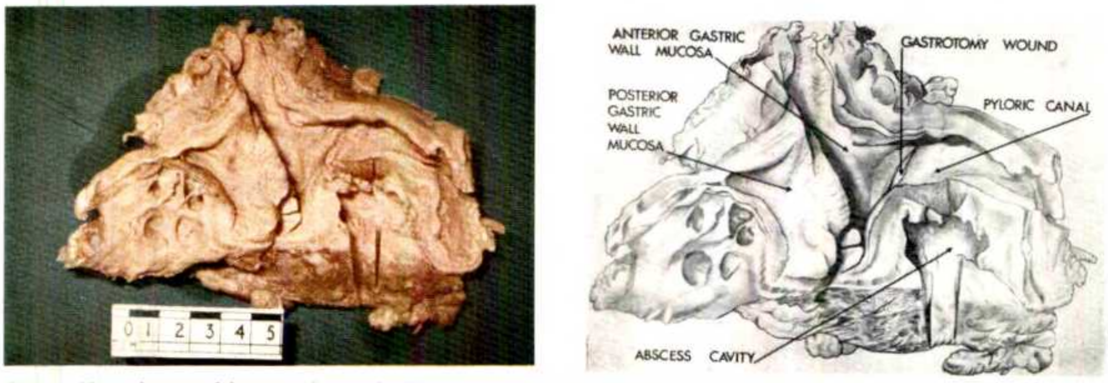

FIG. 2.—Mucosal aspect of the resected stomach. The posterior wall of the stomach has been opened to show the intramuscular multilocular abscess cavity in the antrum producing a narrowing of the pyloric canal. The vertical gastrotomy wound can be seen on the anterior wall.

Examination revealed a distressed, thinly built woman in whom a tender mass was palpable in the epigastrium. The mass was mobile up and down, but not from side to side. She was afebrile. A plain radiograph of the abdomen revealed no abnormality other than a paucity of gas shadows. A chest radiograph was likewise negative. After 24 hours' observation the pain persisted and the tender mass remained.

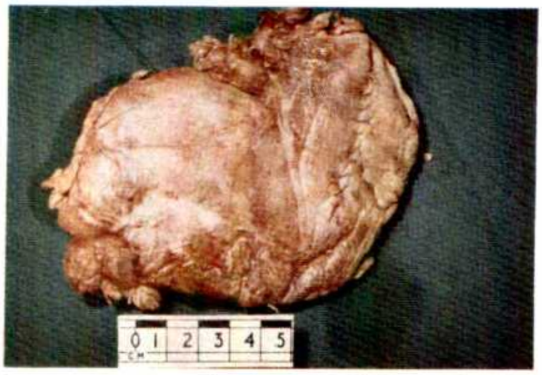

FIG. 1.—Anterior wall of the resected stomach from the serosal aspect. The pylorus is on the left and the body of the stomach with a sutured vertical gastrotomy wound is visible on the right. Note the yellow line of fibrinous exudate along the subpyloric border and the injected appearance of the serosa over the antrum.

At laparotomy on 9 Aug. the pyloric antrum was found to be inflamed on its serosal surface with a thin line of fibrinous exudate extending along the subpyloric border for a distance of approximately 6 cm. (*Fig.* 1). The antrum was mobile and was found to be the seat of an intraluminal tumour measuring approximately 4–5 cm. in diameter. The remainder of the serosal aspect of the stomach appeared normal and there was no other intra-abdominal lesion. A 5-cm. gastrotomy wound was made on the anterior wall of the unaffected body of the stomach to allow inspection of the mucosal aspect. A spherical mass covered by congested but intact mucosa was found occupying the antrum. The mucosa of the body of the stomach appeared normal. A presumptive diagnosis of leiomyoma of the antrum was made and, in view of the sessile nature of the swelling and the grossly narrowed communication remaining as the pyloric canal, a Billroth-I partial gastrectomy was performed.

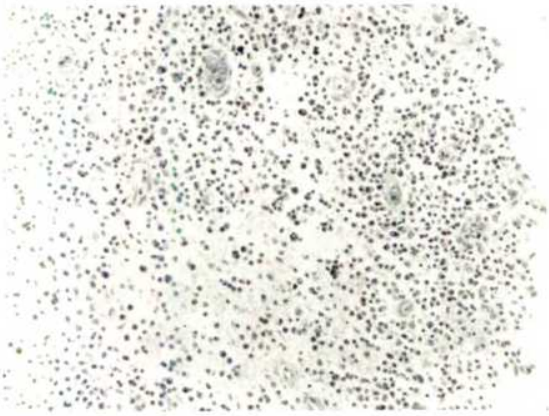

FIG. 3.—Photomicrograph showing pyogenic granulation tissue bordering the abscess cavity on the right. H. and E. (× 160.)

Following operation the patient recovered rapidly and was discharged 12 days after surgery. Further investigations were as follows: Wassermann reaction and Kahn test, negative; postoperative maximal pentagastrin test, peak 30-minute acid output, 1·1 mEq.; plasma proteins, 6·6 g. per cent; haemoglobin, 14·6 g. per cent; white cell count, 6000 per c.mm.; blood-film, normal.

PATHOLOGY.—A partial gastrectomy specimen with a recent gastrotomy incision, 5 cm. long, showed focal haemorrhage and acute inflammatory exudate over the distal third of the serosa (*Fig.* 1). On the cut surface the wall of the stomach enclosed a multilocular abscess, measuring 4–5 cm. in diameter and containing green pus (*Fig.* 2). The abscess projected into the pyloric antrum and resulted in a narrowing of the pyloric canal. The overlying mucosa was congested and stretched. There was no evidence of mucosal ulceration or scar tissue. There were no other pathological lesions present in either the mucosa or the wall of the stomach.

HISTOLOGY.—A multilocular pyogenic abscess was present in the muscle coat of the pyloric antrum. The abscess wall was made up of organizing granulation tissue, and the loculi contained acute inflammatory exudate (*Fig.* 3).

The muscular arteries adjacent to the abscess showed moderately severe endarteritis. The muscle around the abscess was almost completely replaced by fibrous tissue except for a thin layer just below the submucosa where it was infiltrated by chronic inflammatory cells and eosinophils. Apart from a moderate degree of lymphocytic and plasma-cell infiltration of the lamina propria, the mucosa was virtually normal. The serosa over the abscess was thickened owing to fibrosis.

In the multiple sections which were examined there was no evidence of any granulomatous lesion or of active or old healed gastric ulcer. Special stains for fungi and micro-organisms, including acid- and alcohol-fast bacilli, were negative.

DISCUSSION

Acute phlegmonous gastritis occurs in two principal forms: diffuse and localized. In each case the pathological process consists of an exudative fibrinopurulent inflammation of the full thickness of the gastric wall, involving particularly the submucosa and probably commencing there. Microscopy reveals extensive infiltration of all layers of the gastric wall with mixed inflammatory cells. The lesion is produced by a true infection of the stomach wall by pyogenic organisms, usually haemolytic streptococcus but occasionally other organisms. In the commoner diffuse variety of the disease the inflammatory process extends throughout the entire anatomical confines of the stomach, while less commonly focal involvement of the stomach occurs. Predisposing factors to the infection noted in some cases are hypochlorhydria due to alcoholism or chronic gastritis from other causes, and a concurrent infective process elsewhere in the body. The clinical features of phlegmonous gastritis have been reviewed by Starr and Wilson (1957) and by Smith, Garrett, and Herrick (1962) and include epigastric pain, vomiting, high fever, tachycardia, and leucocytosis. Males are affected three times more often than females and 80 per cent of cases occur between 30 and 60 years of age. In the diffuse variety toxaemia and general peritonitis rapidly supervene. Starr and Wilson (1957) classified the disease as chronic if the history revealed a prolonged illness of more than a few weeks' duration and there was an absence of fever or leucocytosis.

Difficulty in making a preoperative diagnosis in this condition and the rapid progress of the disease usually preclude orthodox investigations of the upper alimentary tract. However, it would appear that on some occasions the diagnosis has been made by plain radiographs which may demonstrate submucosal gas (Weens, 1946; Welch and Jones, 1947), and on others by gastroscopy (Mouter, Corent, and Wolfsohn, 1949).

The clinical, operative, and histological findings in the present case suggest that the condition observed was acute localized phlegmonous gastritis with an abscess of the pyloric antrum. The diagnosis was not made before operation and it is of interest that the finding of a persisting tender epigastric mass was the feature which prompted surgery. Unusually, the patient was afebrile and showed none of the features of toxaemia. While nothing is known of her gastric secretory function before surgery, the finding of an acid response to a maximal dose of pentagastrin in the postoperative period confirmed that she was not achlorhydric.

The correct treatment for this condition has been debated over the years. The mortality rate for the disease was reported by Eliason and Murray-Wright (1938) as 84 per cent. These authors suggested treatment by gastrostomy and transmucosal drainage of the abscess. Cutler and Harrison (1940) and Millar and Nushan (1952) recommended a conservative policy. However, Starr and Wilson (1957), reviewing 25 cases reported in the period 1947–57, found a mortality rate of 48 per cent. Ten deaths occurred among 15 patients who were treated conservatively, whereas 6 of 8 patients who had undergone gastric resection survived. More recently, Smith, Garrett, and Herrick (1962) have reported 2 further survivors following partial and total gastric resection, and both remained symptom-free at 5 years after operation. It would appear, therefore, that where the diagnosis is made, resection of the involved area of stomach offers the best choice of therapy for acute phlegmonous gastritis, and that subtotal

MORTALITY IN MISSILE WOUNDS OF THE HEAD

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SUMMARY

In a series of 250 patients with missile wounds of the head treated at the University College Hospital, Ibadan, Nigeria, 35 died after admission, a mortality of 14 per cent. Forty-three per cent of the deaths occurred within a week of wounding and were predominantly due to severe anatomical damage; among the 34 per cent who died at least 4 weeks after wounding there was evidence of intracranial infection. Surgical operation did not improve the outcome in the group with severe anatomical damage. A serious disturbance of the level of consciousness on admission, namely coma, was a bad prognostic sign.

DURING the First and Second World Wars it was estimated that 40–50 per cent of deaths from war wounds were due to missile injuries of the head (Olivecrona, 1940; Campbell, Kuhlenbeck, Cavenaugh, and Nielsen, 1958). In Nigeria between 1964 and 1970, during part of which period a civil war was being fought, 250 patients with missile injuries of the head were admitted to the Neurosurgery Unit of the University College Hospital, Ibadan, Nigeria. Thirty-five of these 250 patients died after arrival at hospital, a mortality of 14 per cent. The purpose of the present paper is to record our observations on the characteristic features of this group of fatal cases and to examine some of the factors noted which could influence the mortality rate in missile wounds of the head.

MATERIALS AND METHODS

The 250 patients included in this series were all Nigerians. Three civilians were admitted before July, 1967, after which period, as a result of the outbreak of civil war, the admissions were mostly soldiers. During the war, 15 other civilians were admitted who either had been injured in combat areas or had accidentally been shot in the head by game guns during hunting.

The soldiers either were referred to University College Hospital, Ibadan, from the military hospitals to which they had first been evacuated from the war front or were admitted directly to University College Hospital from the Army Medical Reception Stations close to the war front. The journey from these stations often spanned several days; rarely it took just over 24 hours on the few occasions when wounded soldiers were air-lifted to Ibadan. Civilians were admitted to hospital much sooner after sustaining an injury than soldiers. Similarly, some civilians were referred from other hospitals, and the rest were admitted directly without passing through a peripheral hospital.

The surgical management of these patients has been outlined elsewhere (Adeloye and Odeku, 1970). The wounds were thoroughly débrided under general anaesthesia. Scalp wounds were excised, and where the missile was lodged in the subgaleal space the skull was usually trephined in search of associated intracranial damage. The dura was opened in all cases of tangential skull injuries, and in all instances where the brain had been penetrated, in-driven bone fragments, haematomata, and accessible missiles and metallic fragments along the wound track were removed. Postoperatively, penicillin, streptomycin, and sulphadiazine were given routinely for about a week; pain was controlled with acetylsalicylic acid; phenytoin sodium and phenobarbitone were administered prophylactically.

Swabs for bacteriological studies were obtained from wounds in which infection was suspected. There was, however, the difficulty of distinguishing with the naked eye between necrosis and infection of the brain. Only 3 of the fatal cases were subjected to necropsy owing to the military regulations which prevailed during the civil war.

CLINICAL FINDINGS

The 35 patients who died were all soldiers. They were all males with ages ranging from 19 to 30 years, except for 1 female of 16 years who was described as a 'soldier in the rebel army'.

The *time interval* between injury and arrival at University College Hospital in the whole series of 250 patients was on average 13 days. For the 35 fatal cases this time interval varied from 1 day to 28 days, with an average duration of 4·7 days. Twenty-four of these fatal cases were admitted within 1 week of sustaining their head injuries, 50 per cent of the 24 arriving 1 day after injury. Five were admitted during the second week, and the rest were admitted to hospital 3–4 weeks after their injuries.

Missile Type.—In the whole group of 250 patients, 140 injuries resulted from bullets, 102 were due to metallic fragments dispersed from bombs, mines, and hand grenades, and in 8 instances the nature of the offending missile was not specified. Twenty-two (15·7 per cent) of the bullet wounds, 10 (9·9 per cent) of the injuries caused by metallic fragments, and 3 wounds in which the missile type was undefined were all fatal.

Type of Head Wounds.—No death was recorded among the patients who sustained scalp injuries alone. On the other hand, the mortality was greatest among the patients with through-and-through brain wounds in which the brain damage was maximal. The tangential skull wounds were slightly more lethal than the penetrating brain wounds (*Table I*). It is pertinent to observe that most of the tangential wounds were inflicted by bullets, which caused more fatality than metallic fragments in this series.

Anatomical Loci of the Wounds.—Head wounds in which relatively large areas of the brain suffered damage were the most lethal. These included the through-and-through brain wounds especially, and the extensive tangential and penetrating wounds which involved more than one anatomical region of the head. It would appear from *Table II* that isolated wounds of the front of the head—the frontal and the orbitocranial wounds—carried the least mortality.

Table I.—TYPE OF HEAD WOUNDS

TYPE OF WOUND	TOTAL NO. OF CASES	MISSILE TYPE		NO. OF DEATHS			MORTALITY (per cent)
		Bullets	Metallic Fragments	Operation performed	No Operation	Total	
Scalp wounds alone	25	14	11	—	—	—	0
Tangential skull wounds	92	70	22	11	2	13	14·1
Penetrating brain wounds	104	46	59	10	3	13	12·5
Through-and-through brain wounds	15	10	5	3	2	5	33·3
Unspecified	14	—	5	2	2	4	28·5
Total	250	140	102	26	9	35	14

Table II.—ANATOMICAL LOCATIONS OF HEAD WOUNDS

LOCATION OF WOUND	TOTAL NO. OF CASES	NO. OF DEATHS	MORTALITY (per cent)
Frontal	61	4	6·6
Parietal	74	13	17·6
Vertex	8	1	12·5
Temporal	24	3	12·5
Temporoparietal	3	1	33·3
Orbitocranial	10	1	10
Temporofrontal	8	3	37·5
Temporoparietofrontal	2	2	100
Frontoparietal	8	1	12·5
Parieto-occipital	15	4	26·7
Occipitofrontal	2	1	50
Fronto-occipital	1	1	100

Table III.—GENERAL CONDITION OF PATIENTS ON ADMISSION

Features noted	*Frequency*
Dehydration	6
Respiratory distress	5
Grunting respiration	
Stertorous breathing	
Cheyne-Stokes respiration	
Fever	5
Pneumonia	3
Generalized convulsions	3
Pallor	2
Bilateral conjunctivitis	2
Chemosis	1
Foul-smell	1
Bleeding mouth	1

General Condition of the 35 Fatal Cases on Admission.—The general physical signs exhibited by these patients on admission are shown in *Table III.* The starvation and the relatively immobile decubitus of the patients during the several days intervening between injury and arrival at University College Hospital would account for the respiratory manifestations which were commonly encountered. The respiratory distress consisted of grunting or stertorous respiration, and in 1 instance, Cheyne–Stokes respiration was observed. Two of the 3 patients with convulsions were admitted the day after injury; 1 of them died in status epilepticus a few hours after admission.

None of the patients had peripheral circulatory failure, the blood-pressures ranging from 110/70 to 160/110 mm Hg.

Level of Consciousness of the 35 Fatal Cases on Admission.—The patients were allocated into one of five categories of level of consciousness, ranging from the comatose to the fully conscious, depending on their response to verbal call or command and to the application of painful stimuli.

The patient was *comatose* when there was no response at all to any form of stimulation; *stuporose* when he responded to painful stimulation but only in an inappropriate manner; *drowsy* when he responded correctly to painful stimulation by withdrawing the appropriate part of the body which was stimulated, and, where the language barrier could be broken, he responded to a call or a command. The drowsy patient lapsed into somnolence on cessation of these stimuli. The *confused* patient was abusive or wanted to be left alone during the course of physical examination. He was intermittently restless and disorientated.

On admission, 14 patients were comatose, 5 were stuporose, 6 were drowsy, and 6 were confused. The remaining 4 patients, who were fully conscious on admission and were thus able to relate their own stories, gave a history of post-traumatic amnesia varying from 3 hours to 4 days.

Those patients with severe disturbance of consciousness were admitted sooner than the rest. Thus, the patients admitted in coma or in stupor were all admitted within 1 week of sustaining their head injuries: 12 were admitted 1 day after injury, 3 were admitted on the second day, and 1 each arrived on the third, fourth, and sixth days respectively after sustaining their head wounds. The only exception was a comatose patient who arrived 8 days after injury.

Neurological deficits were described in 24 of these patients. These consisted of hemiparesis or hemiplegia (18) with facial palsy of an upper motor neuron type (6), paraplegia with bilateral extensor plantar response (4), and paraplegia with paresis of one arm (2).

Neck stiffness was elicited in 11 patients.

Associated Wounds.—In the entire series of 250 patients, missile wounds in other parts of the body besides those of the head were encountered in 53 patients, an incidence of 21 per cent. Among the 35 fatal cases only 3 (8·6 per cent) had associated wounds, none of which was serious enough to threaten life. These comprised a penetrating wound of the hand with fractured metacarpals, facial lacerations, and a right clavicular fracture.

EFFECTS OF SURGICAL TREATMENT ON SURVIVAL

Nine of the 35 fatal cases died before any operative treatment was undertaken. The rest had neurosurgical débridement of their wounds at University College Hospital. In 5 of the latter group some inadequate surgical procedures had been carried out by doctors at the war front who had sutured the scalp wounds in every patient except 1, who, in addition, had had a limited débridement of his intracranial wound at a military hospital before referral to University College Hospital.

Time of Operation at University College Hospital.—Fifteen of the fatal cases had their operation within 1 week of injury, 4 were operated on in the second week, 4 in the third week, 2 in the fourth week, and 1 in the fifth week.

Table IV.—Time of Death after Operation

Time of Death after Operation	*No. of Patients*
Within 1 week	12
1–2 weeks	1
2–3 weeks	—
3–4 weeks	5
After 4 weeks	8
Total	26

Time of Death after Operation.—In the entire series, 192 patients were treated neurosurgically. Of these, 26 died, an operative mortality of 13·5 per cent. Twelve (46 per cent) of those who had an operation survived for 3 hours to 7 days (*Table IV*). All these had severe *anatomical damage*, and none had established overt intracranial infection. However, in 1 patient from whom an intracerebellar bullet was removed 10 days after sustaining a penetrating brain wound, a pocket of pus was encountered around the bullet. In another who was admitted 3 days after his injury, maggots were found at the bottom of his wound. Three of the 12 patients had generalized convulsions before operation. These fits occurred 24 hours, 2 days, and 3 days respectively after injury. In none of the 12 patients was there any improvement in the level of consciousness after operation.

Among those who survived for more than 3 weeks, *infection* was the main cause of death. In the 5 patients who survived for 3–4 weeks after operation there was heavy infection of the wounds, which suppurated and yielded a mixed bacteriological growth. After the third postoperative week, the longer the survival, the more extensive was the infection, which could involve every compartment of the intracranial chamber as well as the subgaleal space extracranially. The organisms obtained on bacteriological studies were *Pseudomonas pyocyaneus*, *Staphylococcus pyogenes*, and *Proteus vulgaris* (each occurred three times), and infection with coliforms was encountered on two occasions. In the patients with intracranial infection the tendency was for the level of consciousness to improve postoperatively, and when these patients developed convulsions, they occurred late.

TIME INTERVAL BETWEEN INJURY AND DEATH

Most of the deaths (43 per cent) occurred during the first week after injury. Another peak incidence of mortality (34 per cent) was recorded 4 weeks after sustaining head injury (*Table V*). The deaths in the first week were due to neuronal (anatomical) damage, and those occurring later were predominantly due to overwhelming intracranial suppuration. Between these two peak periods, death resulted from a combination of anatomical damage and intracranial infection.

Table V.—Interval between Injury and Death

Time of Death after Injury	No Operation	Operation performed	Total No. of Deaths	Incidence (per cent)
Within 1 week	8	7	15	43
1–2 weeks	1	4	5	14
2–3 weeks	—	1	1	3
3–4 weeks	—	2	2	6
After 4 weeks	—	12	12	34
Total	9	26	35	100

Nine patients died without operation. All of them were admitted to hospital either in coma or in stupor, and died within 1 week of injury, except for 1 patient who arrived 6 days after sustaining his head wound and died 3 days after admission. There was no evidence of overt infection in these patients, and severe anatomical damage seemed the probable cause of death. This was confirmed at autopsy in 2 patients.

One unique cause of death was severe erythema multiforme (Stevens–Johnson's syndrome) which occurred in 1 patient who died 47 days after sustaining his head injury and 38 days after operation. This patient had a course of penicillin, streptomycin, and sulphadiazine for a week immediately after his operation, and he also had phenytoin sodium and phenobarbitone continuously postoperatively. The patient was only on these anticonvulsants when he developed his fatal erythema multiforme.

All the deaths occurred during the first admissions of the patients, except in 2 patients who died of brain abscesses. These 2 patients were readmitted 4 and 6 weeks after they had left hospital respectively; both were in stupor, with nuchal rigidity, fever, and Jacksonian epileptic fits. Intracranial suppuration was suspected clinically and they both died shortly after admission. Autopsy confirmed the presence of intracerebral abscesses.

DISCUSSION

The reported mortality in battle casualties from head wounds has varied according to the type of case studied. Acutin (1940), from examinations of the dead, estimated that 30–40 per cent of men with head wounds in the Finnish campaign died on the battlefield, and among those evacuated the mortality was 27 per cent. On the other hand, fatality rates for cases who reached base or forward hospitals have been much less and have variously been reported at 10·9 per cent (Gaynor and Gruwitz, 1945), 13·2 per cent (Jefferson, 1919), 13·9 per cent (Pilcher and Angelucci, 1942), 15·9 per cent (Terian, 1943), and 17 per cent (Munslow, 1946). The variability in mortality figures is hardly surprising since it reflects the type of cases selected for referral to these hospitals, the timing and type of the initial and the definitive surgical treament, and the nature of the aftercare of the wounds.

In general, certain factors, a number of which have been exemplified by this series, have a bearing on the survival of patients with missile wounds of the head. Rifle bullets were more deadly than bullets from civilian game guns and small metallic fragments dispersed from grenades, bombs, and mines. These rifle bullets travel at a greater velocity than both shrapnel and the relatively low-velocity missiles encountered in civilian practice, and thus cause more extensive tissue damage (Raimondi and Samuelson, 1970). The surprisingly low figure recorded by Wolf (1940) of 10 deaths out of 343 craniocerebral wounds subjected to surgery during the First World War was probably because 80 per cent of these wounds were caused by splinters from grenades, bombs, and mines, and only 20 per cent were due to rifle bullets.

Frontal wounds seemed to be less dangerous than wounds in other parts of the cranium. Cushing (1918) observed that occipital cases tended to do less well after operation than frontal ones. Despite the mental disturbance which he noted in patients with frontal wounds, as far as survival was conerned, 'they have usually done well'. Among the casualties with penetrating brain wounds sustained during the bombing of Hawaii in 1941, Cloward (1942) described patients with large gaping frontal wounds oozing brain matter who were found to be conscious, rational, and co-operative. Schorstein (1944) reported only 1 death out of 8 patients with orbitofrontal gunshot wounds who were treated with débridement and in 3 cases with fascia lata graft of the dura.

The freedom of simple scalp wounds from fatality is generally and universally recognized (Cushing, 1918; Horrax, 1919; Jefferson, 1919). In the other categories of head wounds there is a progressive increase in the mortality-rates with increase in the extent and severity of the brain damage sustained. Horrax (1919) reported the lowest mortality of 5·8 per cent among patients with tangential skull injury without dural laceration, and the highest mortality of 80 per cent in through-and-through brain wounds in which large areas of the brain had suffered damage. In tangential skull wounds with lacerated dura the shattered bone fragments are driven intracranially, lacerating blood-vessels and brain tissue over a much wider area than the size of the gutter of the scalp wound would lead one to suspect. In this respect, tangential skull wounds are more dangerous than the penetrating brain wounds in which the missile carves out a neater and narrower path in the brain before coming to rest. Jefferson (1919) reported a mortality of 41·1 per cent in tangential skull wounds with in-driven bone fragments, and 34·8 per cent in penetrating brain wounds; in the latter category when the ventricle was penetrated the mortality rose to 75 per cent, the same incidence as Jefferson (1919) reported for through-and-through brain wounds. These various observations were confirmed in our series.

Missile wounds occurring elsewhere in the body in association with head injuries and other concomitant diseases such as pneumonia or gas gangrene were found to be contributory to death in most series (Cushing, 1918; Horrax, 1919; Gaynor and Gruwitz, 1945; Ascroft, 1947). Indeed, Ascroft (1947) recorded associated wounds in 33 per cent of fatal cases as opposed to the 20 per cent incidence in survivors. On the other hand, in our series, as in that of Jefferson (1919), no death was attributable to severe associated missile wounds.

Two clinical physical signs of grave prognostic significance which have been noted in patients with missile wounds of the head are rise in temperature and coma on admission. Pilcher and Angelucci (1942) found that a rise of temperature above 103° F. (39° C.) was an ominous sign. Cushing (1918) observed during the First World War that 5 out of every 6 patients admitted in coma or stupor died, whereas only 1 out of every 21 patients who were conscious on admission and capable of giving a history died. The importance of coma as a grave prognostic sign was again emphasized during the Second World War by Miller (1942) and Eden (1943) in connexion with high mortality from missile wounds of the head during the North African campaign.

There is hardly any controversy about the role of anatomical or neuronal damage and of intracranial infection and haemorrhage in the causation of death in missile wounds of the head. Prior (1944), a pathologist working in a hospital near the front line, performed post-mortem examinations on soldiers who had died on the battlefield. He found that the injury was usually gross in cases who had died from skull wounds; where the injury was of lesser degree, death was from intracranial suppuration or intracranial haemorrhage. As to the temporal relationship of these factors, neuronal damage and intracranial haemorrhage were the main causes of mortality in the first few days, with haemorrhage being particularly important in the first 24 hours. After 5 days, sepsis began to become important, with progressive increase in incidence with the passage of days. Where the period of time between injury and admission to hospital was long, infection was more prevalent than the other causes of death (Jefferson, 1919). In a series of fatal head wounds described by Ascroft (1947) the causes of death were neuronal damage (41 per cent), intracranial sepsis (40 per cent), intracranial haematoma (13 per cent), and others (6 per cent).

One of the problems of attributing the cause of death to intracranial haematoma is that of defining what constitutes significant haematoma. Small and Turner (1947) noted that a small haematoma was such a common finding along the missile track that one would expect it in penetrating wounds. Similarly, Gillingham (1947) observed that it was rare to find any large intracranial clot either at operation or at autopsy. Schorstein (1947), in the North African and Italian campaigns, found that only 83 of 2000 patients (4·2 per cent) had intracranial haematoma. At the other extreme, Lewin and Gibson (1956) reported the unusually high incidence of 46 per cent for intracranial haematoma among British casualties in the Korean war. Where it was found, the incidence of intracranial haematoma increased with earlier hospital care (Barnett and Meirowsky, 1955). The fact that we did not find intracranial haemorrhage to be an important cause of death in the present series was presumably because such patients died almost immediately after injury and failed to reach hospital, and also because of the incomplete autopsy examination of those who died after admission.

It is important to know what role surgical treatment can play in reducing mortality in missile injuries of the head. Although early surgery is desirable in these patients (Guleke, 1941), it has been shown that the time interval between injury and surgical treatment is less important to ultimate survival than meticulous specialized care in the investigation, operation, and after-treatment of the patients (Cairns, 1940; Terian, 1943). Since these patients travel well prior to surgery (Ascroft, 1943; Money and Nelson, 1943; Gaynor and Gruwitz, 1945), in the absence of adequate surgical facilities, further evacuation is preferable to incomplete 'débridement' (Campbell, 1945). When a large number of these patients have to be dealt with there may be difficulty in selecting those who would benefit most from the available surgical care. Miller (1942) and Eden (1943), realizing that coma was a bad prognostic sign, preferred to leave aside the deeply unconscious patient and they operated on the more promising ones in whom it was important to prevent the development of intracranial infection, the other important cause of mortality besides severe anatomical damage. Pilcher and Angelucci (1942) found that in 61·5 per cent of the fatal cases in their series, death occurred within 24 hours of injury, and they thought it unlikely that the lives of these patients could have been saved by any therapeutic procedure. At University College Hospital, Ibadan, where we operated on all those who could stand the procedure, patients with severe brain damage who came in comatose or stuporose did not benefit from débridement, on the whole. Yet despite these observations, in peace or in war it is never absolutely right to abandon comatose patients with head wounds to their fate, for it is known that the poorest cases on admission sometimes do surprisingly well later. In addition, Campbell and others (1958), who set out in a study of 24 fatal missile wounds of the head to establish the clinical criteria of mortal brain wounds, were unable to indicate which wounds were apt to be definitely fatal and therefore better left alone.

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COMPARATIVE EVALUATION OF PREOPERATIVE AND OPERATIVE RADIOLOGY IN BILIARY-TRACT DISEASE

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SUMMARY

In 100 consecutive patients with an abnormal cholecystogram a study was carried out to compare the value of the 4-day Telepaque test, intravenous cholangiography, and operative cholangiography. Of the 100 patients, 87 were shown at operation to have stones in the gall-bladder and 22 to have stones in the common bile-duct. In 4 of the latter patients, stones were absent from the gall-bladder.

Operative cholangiography was the most accurate investigation in the diagnosis of a stone in the common duct; the operative cholangiogram gave definite evidence of stones in the duct in 20 of the patients, and was abnormal in some respect in all of the patients with a stone in the common duct. It is concluded that this investigation should be performed on all patients undergoing cholecystectomy.

The 4-day Telepaque test demonstrated stones in the gall-bladder in 30 per cent of the patients with a non-functioning gall-bladder on oral cholecystography, thus materially improving the diagnosis of gall-bladder stones preoperatively. Of duct stones, however, only 32 per cent were shown by the 4-day Telepaque test, and 59 per cent were demonstrated by intravenous cholangiography. In view of the risk associated with Biligrafin, and to a lesser extent with large doses of Telepaque, it is concluded that neither of these tests is desirable prior to cholecystectomy in

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the good-risk patient, provided that a satisfactory technique of operative cholangiography is used. They should be reserved for the poor-risk patient, when the presence or absence of duct stones may influence the decision to operate.

THE importance of radiological assessment of the bile-ducts as well as the gall-bladder prior to cholecystectomy is well recognized. In recent years interest has been centred on methods of decreasing the percentage of residual stones and on avoiding unnecessary exploration of the common bile-duct. The incidence of residual stones in the bile-duct after cholecystectomy without operative cholangiography varies in different series, from 2 per cent (Colcock and Liddle, 1958) to 20 per cent (Hicken, McAllister, and Call, 1954). The average incidence is probably 5 per cent (Le Quesne, 1960). Operative cholangiography diminishes the residual stone rate from 5 to 0·4 per cent (Ferguson and Estes, 1967), whilst providing criteria for exploration of the common bile-duct.

Two methods of demonstrating stones in the bile-ducts preoperatively were developed in the 1950's, namely, intravenous cholangiography using Biligrafin (Frommhold, 1953), and the 4-day Telepaque test, as described by Salzman and Warden (1958) and Salzman, Spurck, Kier, and Watkins (1959).

The present paper describes a prospective study which was undertaken in order to evaluate each of these techniques, individually and together, in the diagnosis of stones in the gall-bladder and bile-ducts.

MATERIALS AND METHODS

The study was performed on 100 consecutive patients with an abnormal cholecystogram demonstrated in the course of investigation for suspected gall-stones. A cholecystectomy was performed in all of these patients. No patient was jaundiced at the time of operation. There were 28 males and 72 females in the series, with ages ranging from 23 to 81 years, and with an average age of 52 years. Stones were present in the gall-bladder and/or the common bile-duct in 91 per cent.

The cholecystogram was considered to be abnormal if it fell into one of the following categories:—

1. Unequivocal evidence of stones in the gall-bladder.
2. A 'non-functioning' gall-bladder, i.e., no opacification on an examination which was repeated on the following day.
3. A 'poorly functioning' gall-bladder, i.e., poor opacification on an examination repeated on the following day.

After the initial cholecystographic examination the following investigations were performed on all the patients: a 4-day Telepaque test, an intravenous cholangiogram with tomography, and an operative cholangiogram.

Cholecystogram.—A standard technique was employed, using 3 g. of Telepaque (iopanoic acid). In the absence of adequate opacification the examination was repeated the following day after a second dose of Telepaque.

4-Day Telepaque Test.—Telepaque (1 g.) was given three times a day for 4 days, during which time the patient took a relatively fat-free diet. On the morning of the fifth day a film was taken of the gall-bladder area, the patient having fasted overnight.

Intravenous Cholangiogram.—A film was taken 20 minutes after an intravenous injection of 20 ml. of Biligrafin forte (iodipamide methylglucamine), and tomograms were obtained 30 minutes to 1 hour after injection, when optimal filling of the ducts was to be expected.

Operative Cholangiogram.—The patient, on an Eric Samuel tunnel, was tilted 15° to the right to deflect the image of the common bile-duct from that of the vertebral column. After careful digital and visual examination of the biliary tract, the cystic duct was cannulated using a transparent polythene catheter (size PE 205) filled with saline and connected to a syringe by a pyelostomy nozzle with a tap. Introduction of air-bubbles was prevented by initial aspiration of bile into the syringe. Three successive films were taken using the pull-through technique described by Samuel (1959) after the injection of water-soluble contrast medium (45 per cent Hypaque or 60 per cent Urografin). The first injection was of small volume in order to demonstrate the normally narrow terminal segment of the common bile-duct and to avoid obscuring stones in this region by intraduodenal contrast. The gall-bladder was removed whilst the films were being developed. The latter were studied by the surgeon, the criteria for exploration of the common bile-duct being as follows:—

1. Filling defects in the ducts.
2. Dilatation of the common bile-duct (diameter greater than 11 mm.).
3. Failure of contrast to flow into the duodenum on the second film.

Postoperative T-tube Cholangiogram.—A T-tube was inserted after exploration of the common bile-duct, and a cholangiogram was carried out through this on the tenth to twelfth postoperative days.

RESULTS

Operation showed that of the entire 100 patients, stones were found in the gall-bladder in 87. Stones were removed from the common bile-duct in 22; in 4 of these patients stones were absent from the gall-bladder. We have no reason to believe that any patient has developed residual stones.

Cholecystography demonstrated unequivocal evidence of stones in the gall-bladder in 50 patients (group A), a 'non-functioning' gall-bladder in 45 (group B), and a 'poorly functioning' gall-bladder in 5 (group C).

The 4-day Telepaque test confirmed the presence of stones in the gall-bladder in all 50 patients in group A, and in addition showed unequivocal evidence of stones in the gall-bladder in 15 of the 50 patients in groups B and C, including all 5 patients in group C; i.e., the test increased the positive diagnosis of stones in the gall-bladder by 30 per cent. In addition, in the whole series the Telepaque test demonstrated stones in the common bile-duct in 7 patients (*Fig.* 1).

The results of intravenous cholangiography are shown in *Table I*. The value of intravenous cholangiography in the diagnosis of stones in the gall-bladder could not be estimated as this investigation often immediately followed the 4-day Telepaque test, but there is no evidence that it was more effective than the 4-day Telepaque test alone. Stones were demonstrated in the common bile-duct in 14 patients, including all 7 who had been shown to have stones by the 4-day Telepaque test. These findings were verified at operation in 13 patients. Failure of Biligrafin to concentrate was noted in 2 patients: 1 patient who had recently been jaundiced and another who had a cholecystocolic fistula but with no history of ascending cholangitis. There was one major reaction to Biligrafin (immediate hypotension) and the number of unsatisfactory examinations was 7, including 2 patients who were subsequently found to have a stone in the duct.

Table I.—RESULTS OF INTRAVENOUS CHOLANGIOGRAPHY

Result	*No. of Cases*
Stones demonstrated in common bile-duct	14
Normal common bile-duct demonstrated	79
Major reaction to Biligrafin	1
Failure of Biligrafin to concentrate	2
Total No. of unsatisfactory Biligrafin examinations	7

Table II.—FINDINGS ON OPERATIVE CHOLANGIOGRAPHY

Finding	*No. of Cases*	
'Definite' stones in common bile-duct	22	(Stone found in 20)
Suggestion of stones in common bile-duct	4	Stone found in 2 Stenosis of ampulla in 1 No abnormality in 1
Dilated duct but no filling defect	4	Stenosis of ampulla in 1 No abnormality in 1 Duct not explored in 2
Unsatisfactory films	2	
Normal films	68	

Table III.—SUMMARY OF OPERATIVE FINDINGS

	PRESENT SERIES	LE QUESNE (1960)
No. of common bile-ducts explored	32 out of 100 (32 per cent)	34 out of 109 (31 per cent)
No. of common bile-ducts explored in which stones found	22 out of 32 (68 per cent)	21 out of 34 (62 per cent)

The operative cholangiogram was considered to show definite evidence of stones, i.e., a filling defect, often with other abnormalities, in 22 patients, including the 13 referred to above. Stones were found and removed in 20. In a further 8 patients the operative cholangiogram was considered abnormal—although showing no filling defect—and stones were found in 2 cases. The findings in these 8 patients are shown in *Table II*. Stones in the duct were palpated in 13 of the 22 patients who showed evidence of stones, and in 6 of the remaining 9 the operative cholangiogram demonstrated stones which had been unsuspected on either preoperative assessment or operative palpation. Flow of contrast into the duodenum on the first or second film was observed in 84 patients; stones were present in 15 of these. In the remaining 16 patients, in whom duodenal flow was not seen or was present only on the third film, stones were shown in 7. *Table III* shows that the percentage of bile-ducts explored (32) and the percentage with stones (22) were very similar to those of Le Quesne (1960). Of the 10 patients in whom stones were not found, 4 had a dilated common bile-duct, 2 had ampullary stenosis, 1 had gritty debris in the bile and a history of jaundice, and 1 had a thickened bile-duct. The operative cholangiogram erroneously suggested duct stones in the remaining 2 patients.

Postoperative T-tube Cholangiogram.—This did not reveal any residual stones, and no patient has subsequently been seen with a stone over periods ranging from 2 to 8 years.

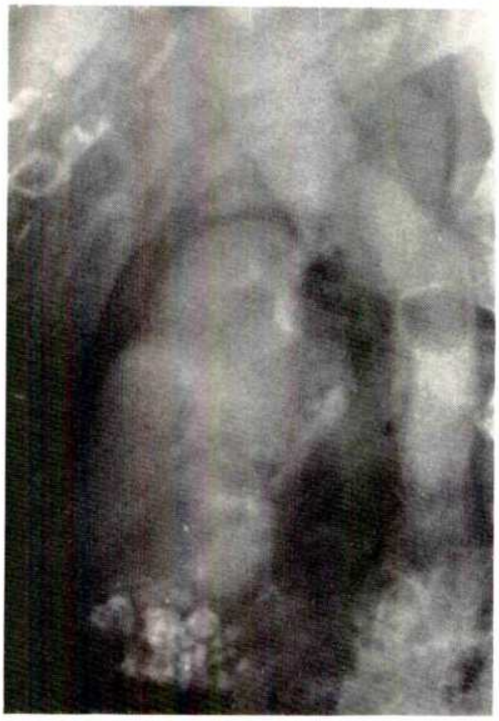

FIG. 1.—The 4-day Telepaque test, showing radiolucent and radio-opaque stones in the gall-bladder, and radiolucent stones rimmed by contrast in a dilated common bile-duct. The cholecystogram merely demonstrated the radio-opaque stones and a 'non-functioning' gall-bladder.

Deaths.—There were 2 deaths in the series. One was an 81-year-old woman who had had many stones removed from the common bile-duct and who died 8 days postoperatively with a diagnosis of cerebrovascular accident. The other was a 68-year-old woman who died suddenly 15 days postoperatively with a diagnosis of pulmonary embolism, autopsy being refused.

DISCUSSION

The original work on excretion cholecystography was done by Graham and Cole in 1924. Telepaque was introduced in 1951 by Dunne, Jensen, and Hughes, and Biligrafin in 1953 by Frommhold. Operative cholangiography was described in 1931 by Mirizzi, but our technique and interpretation are based on the work of Le Quesne (1960).

Cholecystography is widely accepted as a safe and accurate investigation in the diagnosis of stones in the gall-bladder. This is borne out by the present series. There was positive evidence of stones in 50 patients. In the remainder of the patients the diagnosis was based on an inability to demonstrate contrast medium in the gall-bladder. This study confirms that the repeated failure to demonstrate the gall-bladder on cholecystography is reliable evidence of the presence of gall-bladder pathology, but it also shows that in many such patients definite positive evidence of stones is provided by a 4-day Telepaque test. In this study the latter test was the most successful in providing conclusive evidence of stones in the gall-bladder. If definite evidence of the presence of stones is required before advising cholecystectomy, the 4-day Telepaque test will give such information in some 30 per cent of patients with a so-called 'non-functioning' gall-bladder. The test is safe, provided that there is no serious impairment of hepatic function (Teplick, Myerson, and Sanen, 1965). However, Canales, Smith, Robinson, Remmers, and Sarles (1969) have since described 4 cases of renal failure due to large doses of Telepaque in patients with no clinical or laboratory evidence of hepatic dysfunction. Telepaque causes nausea in 14–18 per cent of patients, and diarrhoea, usually mild, in 38 per cent (Healey and Grainger, 1965). We did not find these reactions a serious problem.

Turning to the diagnosis of stones in the common bile-duct, the 4-day Telepaque test was disappointing in that it only demonstrated stones in 7 (32 per cent) out of 22 patients with such stones, and, furthermore, in all these 7 patients the stones were demonstrated by intravenous cholangiography. From the literature (Salzman and others, 1959) and the present series it is clear that occasionally the 4-day Telepaque test will outline a common-duct stone in a patient in whom it either cannot be demonstrated by intravenous cholangiography or in whom it is less well shown by this means.

Intravenous cholangiography demonstrated stones in the common bile-duct in slightly over half (59 per cent) of the patients in whom they were present, but major reactions with hypotension and renal failure have been described in patients with diminished hepatic function (Craft and Swales, 1967), and Ansell (1970) has quoted a mortality of 1 in 5000. The investigation is time-consuming for the radiography department, and if tomography is performed it involves a considerable number of films, but its usefulness is apparent in the elderly or poor-risk patients when the presence or absence of stones may influence the decision to operate. There is little point in performing an intravenous cholangiogram if this decision has already been taken.

In view of the evidence which has since come to light concerning the toxicity of Biligrafin and Telepaque, it follows that the combined techique of a 4-day Telepaque test followed by an intravenous cholangiogram would not be recommended in any patient in the future.

It is clear from the present study, as shown by other workers previously (Le Quesne, 1960; Ferguson and Estes, 1967), that operative cholangiography is undoubtedly the best method of demonstrating stones in the common bile-duct. In our series the operative cholangiogram was interpreted as showing stones in 22 patients, and stones were removed in 20, which represents an accuracy rate of 92 per cent. It is, of course, possible that stones were present in the duct of some of the patients in whom the cholangiogram was considered to be normal. This is unlikely, as the criteria of normality of the operative cholangiogram were essentially the same as those of Chapman, Curry, and Le Quesne (1964), who showed that a normal operative cholangiogram can be relied on with confidence as indicating a stone-free duct. In our opinion this examination should be used routinely, for not only does this make for speed and efficiency in the procedure but it may reveal totally unexpected stones. It is a completely safe examination, but does require the services of a radiographer in theatre for about half an hour. We did not perform post-exploratory cholangiography, partly because of the difficulty in excluding air-bubbles. Elimination of this procedure seems justified by the absence of residual stones on subsequent T-tube cholangiograms.

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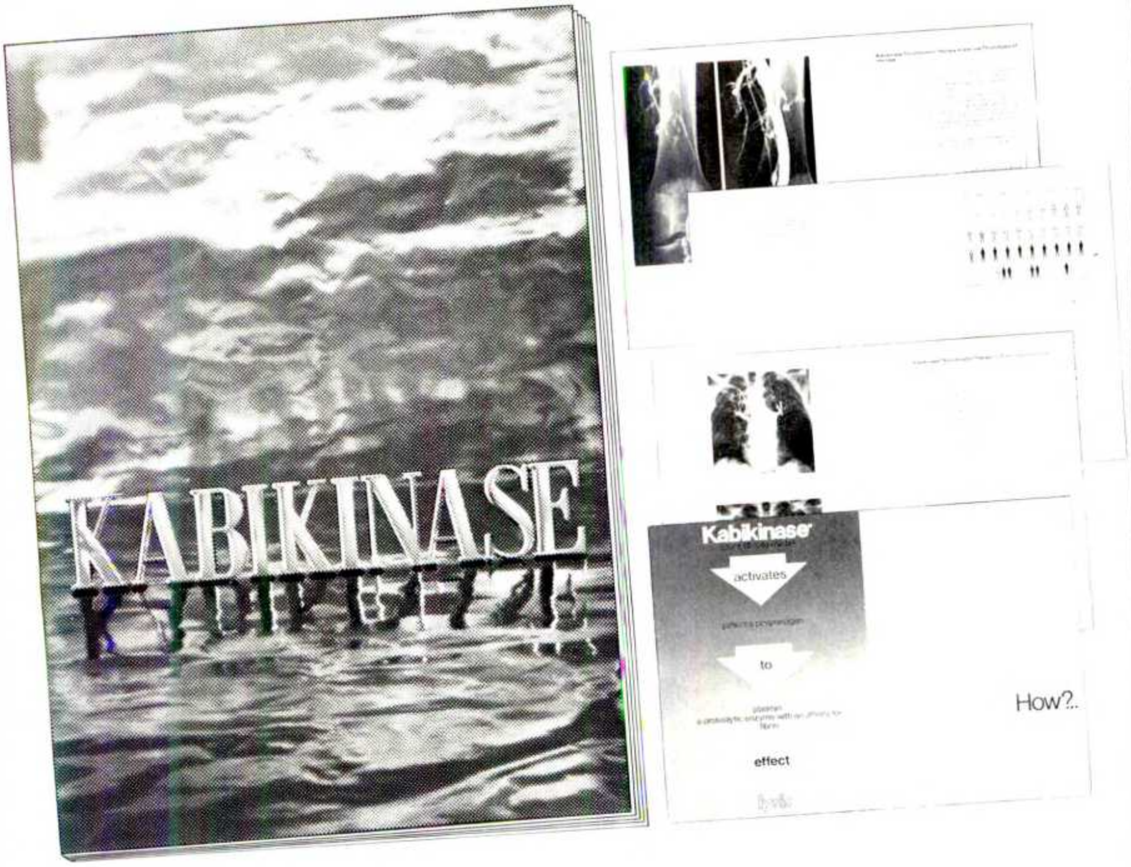

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MEDIASTINOSCOPY

AN ANALYSIS OF 320 CONSECUTIVE CASES

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SUMMARY

Three hundred and twenty consecutive cases of mediastinoscopy are analysed.

1. Mediastinoscopy is a safe procedure and causes little disturbance to the patient.
2. The preoperative assessment of patients with presumably resectable bronchial carcinoma was the main indication for mediastinoscopy, and its use was associated with a fall in the non-resectability rate at thoracotomy from 28 to 15 per cent over two 3-year periods.
3. The policy of exclusion from exploratory thoracotomy of patients with bronchial carcinoma and mediastinal lymph-node metastases is discussed in relation to the histological nature of the lesion and the site and extent of the mediastinal node involvement.
4. It is concluded that there is a case for offering resection to selected patients with limited mediastinal node invasion from bronchial carcinoma.
5. The value of mediastinoscopy as a diagnostic procedure for mediastinal and pulmonary hilar masses and for undiagnosed pulmonary opacities is shown.

MEDIASTINAL lymph-node metastases and invasive growth of the mediastinum are the commonest causes of failure to carry out resection at thoracotomy for bronchial carcinoma (Reynders, 1964). Daniels (1949) had introduced routine scalene-node biopsy in the preoperative investigation of bronchogenic carcinoma in order to spare some patients the risk and discomfort of an exploratory thoracotomy. Harken, Black, Clauss, and Farrand (1954) extended the scope of the investigation by unilateral exploration of the superior mediastinum through a supraclavicular incision. Radner (1955) suggested a method of digital exploration of both sides of the upper mediastinum through a suprasternal incision, the same incision through which Carlens (1959) explored the superior mediastinum in immediate relationship to the front and sides of the trachea and proximal main bronchi, introducing the mediastinoscope (*Fig.* 1) which permitted specimens of the mediastinal tissues to be obtained under direct vision.

TECHNIQUE

The investigation is carried out under general anaesthesia with endotracheal intubation. The patient is supine with a pillow under the shoulders to extend the neck. Slight elevation of the upper half of the body relieves venous congestion. A 4-cm. transverse incision is made half-way between the laryngeal prominence and the upper border of the manubrium. The sternohyoid and sternothyroid muscles are separated in the midline, and the pretracheal fascia below the thyroid gland is incised to expose the trachea. With the finger the loose space between the pretracheal fascia and the front and sides of the trachea is opened up and the mediastinal structures are palpated; abnormal glands are assessed for hardness and mobility. Thereafter the Carlens mediastinoscope is introduced (*Fig.* 2), and with the aid of a suction dissector the subcarinal, the tracheobronchial, and the right and left paratracheal lymph-nodes, if present, are dissected and specimens are removed under direct vision. Bleeding is controlled by diathermy coagulation.

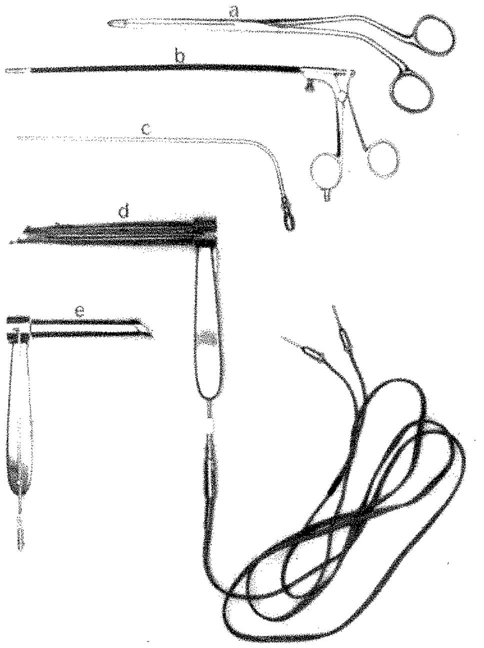

FIG. 1.—The Carlens mediastinoscope. a, Dissector. b, Biopsy forceps. c, Suction dissector. d, e, Adult and child mediastinoscopes.

INDICATIONS FOR MEDIASTINOSCOPY

Although mediastinoscopy was initially introduced as a means of detecting superior mediastinal node metastases of bronchial carcinoma, the indications for the procedure now fall into two main groups:—

1. Bronchogenic carcinoma: Mediastinoscopy is used for (*a*) the preoperative assessment of patients with presumably resectable carcinoma, and (*b*) the histological diagnosis of carcinoma in patients believed to have non-resectable tumours.

2. Intrathoracic disease other than bronchial carcinoma: Mediastinoscopy is used for the histological diagnosis of (*a*) mediastinal and pulmonary hilar masses, and (*b*) pulmonary lesions of unknown aetiology.

MATERIAL

During the 3-year-period 1968–70, 545 patients with bronchogenic carcinoma were seen at the Cardiothoracic Unit, Royal Infirmary, Edinburgh. One hundred and seventy-seven (32 per cent) of them were found to have presumably resectable tumours and they were all submitted to mediastinoscopy. The remaining 368 patients had accepted contra-indications to resection, such as positive scalene nodes, cerebral metastases, hepatic metastases, poor respiratory function, phrenic nerve paralysis, or vocal cord paralysis. Most patients over the age of 70 years with bronchial carcinoma have been considered unsuitable for resection even in the absence of a specific contra-indication. One hundred and three of the patients who were not considered for resection had mediastinoscopy in order to obtain histological confirmation of the diagnosis. The remaining patients were not subjected to mediastinoscopy because the histological diagnosis had been obtained by other means or because they were too ill for operative investigation.

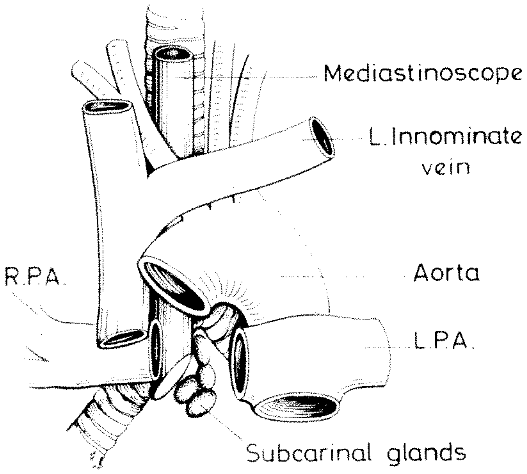

FIG. 2.—The mediastinoscope in position.

Forty-two patients with mediastinal masses or pulmonary lesions of unknown aetiology were investigated by mediastinoscopy.

RESULTS OF 320 CONSECUTIVE MEDIASTINOSCOPIES

Preoperative Assessment of Patients with Presumably Resectable Bronchial Carcinoma.—One hundred and seventy-seven patients fell into this group and 43 (24 per cent) of them were found to have mediastinal lymph-node metastases. *Fig.* 3 shows the distribution of glandular metastases for left- and right-sided lesions respectively.

Fourteen of the 82 patients with left-sided bronchial carcinoma had metastases in the mediastinal nodes. One patient with a lower lobe squamous carcinoma and metastases limited to the subcarinal lymph-nodes underwent exploratory thoracotomy, but the tumour was not resectable because of invasion of the descending thoracic aorta. The other 13 patients with positive mediastinal nodes were not submitted to thoracotomy. The 68 patients without mediastinal lymph-node metastases had exploratory thoracotomy. Resection was carried out in 59, and in 2 of these, subcarinal lymph-node metastases were found which might have been detected at mediastinoscopy. Nine patients had exploratory thoracotomy without resection. The reasons for not undertaking resection are shown in *Table I*.

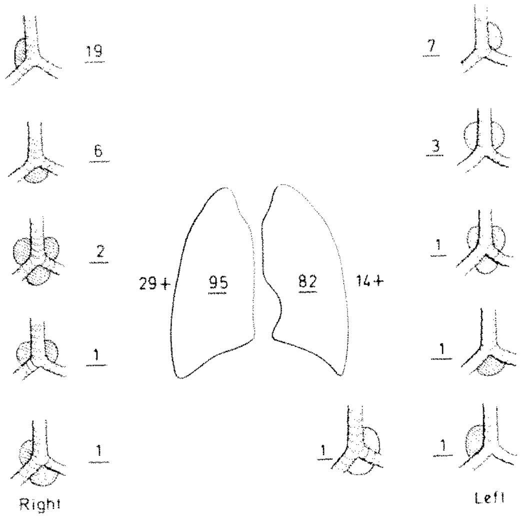

FIG. 3.—The distribution of mediastinal lymph-node metastases in 177 cases of presumably resectable bronchial carcinoma.

Table I.—CONTRA-INDICATIONS TO RESECTION IN BRONCHIAL CARCINOMA WITH NEGATIVE MEDIASTINOSCOPY

CONTRA-INDICATION	NO. OF CASES	
	Right Pulmonary Tumour	Left Pulmonary Tumour
Mediastinal lymph-node metastases	4	1
Pericardial invasion	3	3
Pleural metastases	1	2
Chest-wall invasion	1	—
Superior caval invasion	1	—
Respiratory function sufficient for lobectomy which had been planned, but too low to permit pneumonectomy which was necessary	—	2
Invasion of descending thoracic aorta	—	1
Total	10	9

Twenty-nine of the 95 patients with right-sided tumours were shown to have mediastinal lymph-node metastases. Two patients with well-differentiated squamous carcinoma in the right upper lobe and metastases only in the right paratracheal lymph-nodes were submitted to pneumonectomy, with clearance of all visible tumour. The remaining 27 patients with positive nodes did not have thoracotomy. The 66 patients without mediastinal node involvement underwent thoracotomy, and the tumour was resected in 56, 1 of whom was shown to have subcarinal node metastases. The reasons for not carrying out resection in 10 patients are shown in *Table I*.

The total number of thoracotomies carried out was 137 and resection was undertaken in all but 20 (15 per cent).

The Histological Diagnosis of Carcinoma in Patients believed to have Non-resectable Tumours.—Mediastinoscopy was carried out in 103 such patients and provided the only proof of the diagnosis in 33 (32 per cent).

Intrathoracic Disease other than Bronchial Carcinoma.—This group of patients had mediastinal masses of unknown aetiology or undiagnosed pulmonary opacities. A histological diagnosis was obtained in 20 of the 42 patients. The findings are summarized in *Table II*.

Table II.—HISTOLOGICAL DIAGNOSIS OF LESIONS OTHER THAN BRONCHIAL CARCINOMA

Diagnosis	*No. of Patients*
Mediastinal and hilar masses	
Sarcoidosis	8
Reticulosis	4
Neurofibroma of vagus nerve	1
Secondary testicular tumour	1
Total	14
Pulmonary lesions	
Tuberculosis	3
Alveolar cell carcinoma	1
Sarcoma	2
Non-specific inflammation	22
Total	28

COMPLICATIONS OF MEDIASTINOSCOPY

The incidence of complications was low: a total of 8 complications occurred in the 320 patients. One required thoracotomy to control bleeding from a tear in the left innominate vein. In another patient removal of tissue from a tumour mass in the right paratracheal region caused brisk haemorrhage from the superior vena cava. A blood-loss of 900 ml. occurred before the bleeding was controlled with a gauze pack in the mediastinum for 30 minutes. Minor pneumothorax was caused on two occasions when tissue was taken from the anthracotic right lung instead of the right paratracheal lymph-nodes. Left recurrent nerve palsy occurred on three occasions. Twice this was due to the diathermy which was used to control bleeding which followed dissection in the left paratracheal region, and on the third occasion a patient who developed vocal cord paralysis shortly after mediastinoscopy was shown at thoracotomy to have invasion of the lymph-nodes in relation to the left recurrent nerve at the aortic arch. There was one instance of tumour invasion of the suprasternal wound 3 months after mediastinoscopy in a patient with extensive neoplastic involvement of the mediastinum.

DISCUSSION

Mediastinoscopy is a safe procedure. Only two serious complications occurred in 320 consecutive investigations, although they were carried out by a number of clinicians of varying experience. A study of the 137 patients who underwent thoracotomy showed that involved glands were missed in 8 patients, in 5 of whom the glandular metastases precluded resection. In 2 of these 5 patients the glandular metastases were situated in front of the great vessels —an area not accessible at mediastinoscopy.

Table III.—COMPARISON OF THE MANAGEMENT OF PATIENTS WITH BRONCHIAL CARCINOMA SEEN AT THE CARDIOTHORACIC UNIT, ROYAL INFIRMARY, EDINBURGH, OVER TWO 3-YEAR PERIODS

	3-YEAR PERIOD 1964–6	3-YEAR PERIOD 1968–70
Total No. of patients with bronchial carcinoma	652	545
No. of patients with presumably resectable lesions	291 (44 per cent)	177 (32 per cent)
No. of patients excluded from thoracotomy because of positive mediastinoscopy	—	40
No. of patients undergoing resection	210	117
No. of patients undergoing only exploratory thoractomy	81	20
Non-resectability rate as a percentage of total thoracotomies	28	15
No. of resections frustrated because of mediastinal glandular metastases	30	5

The investigation is carried out under general anaesthesia immediately after bronchoscopy; the general disturbance is small and many patients have been discharged home the day afterwards with no untoward results. Use of frozen-section histology has permitted a decision on management to be made within a few hours of mediastinoscopy. Thoracotomy has usually been carried out within 48 hours, but on the occasions when operation was delayed for administrative or other reasons, oedema and hyperaemia of the mediastinal and hilar structures caused minor inconvenience.

The presence of mediastinal node metastases indicates a poor prognosis in patients with bronchial carcinoma and most authors regard it as a contra-indication to exploratory thoracotomy. Accepting this, with 3 exceptions which are discussed later, our own non-resectability rate at thoracotomy dropped from 28 per cent in the 3 years 1964–6 to 15 per cent in the years under review (*Table III*). A greater reduction in the non-resectability rate has been recorded by others: from 40 to 10 per cent (Reynders, 1964), and from 23 to 6 per cent (Pearson, 1968). An examination of the causes of failure to resect the tumour at thoracotomy showed that the presence of mediastinal glandular metastases was the main reason in 30 (37 per cent) out of 81 patients in the 3-year period 1964–6, in comparison with 5 (25 per cent) out of 20 patients in the 3 years 1968–70. Prior to 1968 mediastinal glandular invasion was not considered a contra-indication to resection if the involved glands could be removed. The findings of invaded glands at mediastinoscopy does not mean that they cannot be removed, and Konrad and Schulte (1969) were able to resect the tumour and the invaded mediastinal glands in 50 per cent of patients in whom invaded glands had been detected by mediastinoscopy. Konrad and Schulte, however, made the point that they did not know what the chances of prolonged survival were in these patients.

There is considerable variation in the survival rates reported after resection for bronchial carcinoma in the presence of mediastinal glandular metastases, as shown by the following: 4-year survival rates of 8 per cent (Bergh and Schersten, 1965) and 9 per cent (Nohl, 1962); 5-year survival rates of 16 per cent (Belcher and Anderson, 1965) and 17 per cent (Collier, Blakemore, Kyle, Enterline, Kriley, and Johnson, 1957). This makes it difficult to evaluate the importance of mediastinal lymph-node metastases.

The extent and distribution of lymph-node metastases in our series of patients were shown to be different for the two sides. A higher proportion of positive nodes was detected in right-sided bronchial carcinoma than in the left-sided lesions (*Fig.* 3). The difference between the two sides is accounted for by the frequency of right paratracheal node metastases in comparison with left paratracheal node involvement. The right paratracheal nodes are commonly the first extrapulmonary nodes to be involved from carcinoma of the right upper lobe (Nohl, 1956), whereas left upper lobe tumours reach the left paratracheal nodes only after passage through the left tracheobronchial nodes under the arch of the aorta. This region is not easily accessible to mediastinoscopy. The subcarinal nodes may become involved early from left or right lower lobe tumours.

A study of the relation of the cellular nature of the tumour to the survival rate after resection in the presence of mediastinal glandular metastases shows that resection for squamous carcinoma with mediastinal metastases may offer a chance of prolonged survival. Le Roux (1968), recording the experience of this unit, reported a 14 per cent 3-year survival rate after resection for squamous carcinoma with mediastinal glandular metastases, but he does not mention the extent or site of the involved mediastinal lymph-nodes. Three of our 43 patients with positive mediastinal nodes as the only contra-indication to thoracotomy had well-differentiated squamous carcinoma. Resection was successfully undertaken in 2 of these patients who had right upper lobe tumours and only right paratracheal node metastases. Local invasion of the aorta prevented resection in a third patient with well-differentiated squamous carcinoma in the left lower lobe and metastases limited to the subcarinal lymph-nodes. During the 3-year period under review, patients with poorly differentiated squamous carcinoma in the mediastinal lymph-nodes were not considered for thoracotomy. Megavoltage X-ray treatment for inoperable squamous carcinoma of the bronchus confined to the chest resulted in a 3-year survival rate of 7 per cent if the mediastinum was involved (Deeley and Singh, 1967), which is half of the survival rate recorded by Le Roux (1968) after resection for squamous carcinoma with mediastinal metastases.

The 3-year survival rate after radiotherapy for anaplastic carcinoma (including oat-cell carcinoma) with mediastinal metastases was 2 per cent (Deeley and Singh, 1967). Le Roux (1968) reported a 10 per cent 3-year survival rate after pneumonectomy for similar tumours with mediastinal glandular metastases. These figures suggest that resection offers a better chance of survival than radiotherapy even if the mediastinum is involved, but a further survey of the literature reveals conflicting results due mainly to difficulties in histological classification. Those authors who have regarded anaplastic carcinoma as an entity distinct from oat-cell carcinoma have reported 5-year survival rates after resection varying from 0 per cent (Paulson, 1957; Barrett, Day, O'Rourke, Chapman, Sadeghi, Perry, and Tuttle, 1963) to 25 per cent (Kirklin, McDonald, Clagett, Moersch, and Gage, 1955) and 27 per cent (Clagett, 1960). In view of this confusion we would suggest that resection should be attempted in some patients with anaplastic carcinoma even in the presence of mediastinal node metastases, since radiotherapy appears to be of limited value.

Oat-cell carcinoma responds as well to radiotherapy as to surgery (Miller, Fox, and Tall, 1969). There is little to be gained by resection of oat-cell carcinoma if the mediastinal glands are involved.

The position with regard to adenocarcinoma is confused. In this series 13 patients had adenocarcinoma of the lung. There were no mediastinal metastases in 12 of these, and they all underwent resection. Only 1 patient was not offered thoracotomy, as mediastinoscopy had revealed extensive mediastinal metastases. Barrett and others (1963) reported a 5-year survival rate of 40·7 per cent after pneumonectomy for adenocarcinoma, but Le Roux (1968) recorded that all but 2 of 35 patients with adenocarcinoma which was managed by pneumonectomy died within 5 years whether or not glands were invaded at the time of thoracotomy. In a small number of patients Deeley and Singh (1967) had an 11 per cent 5-year survival rate for inoperable adenocarcinoma which was treated by radiotherapy. Since pneumonectomy for adenocarcinoma appears to give a poorer chance of prolonged survival than radiotherapy it is debatable whether resection should be undertaken if positive mediastinal nodes are found.

With three exceptions, positive mediastinal nodes in 43 patients were regarded as a contra-indication to surgery. For the past 6 years the operative mortality for exploratory thoracotomy without resection in this unit has been 3 per cent. This is not regarded as a prohibitive figure and therefore to deny thoracotomy to patients with squamous or anaplastic carcinomas because they have mediastinal node metastases irrespective of the site and extent of the mediastinal involvement possibly impairs the chance of survival for an undue number of patients. It is suggested that patients with only right paratracheal node metastases from a right carcinoma (squamous or anaplastic) or with subcarinal node metastases from a right or left carcinoma should be considered for surgery.

Those with contralateral or left paratracheal node metastases should not be offered resection. No additional patients with left-sided tumours would have been offered resection if such a policy had existed in the past 3 years (*Fig.* 3). Twenty-six patients with right-sided lesions had only right paratracheal and/or subcarinal node metastases. Six of them had oat-cell carcinoma, which is probably not worth resecting in the presence of mediastinal node invasion, leaving 20 patients with squamous or anaplastic carcinoma who might have been offered resection; in fact 2 of them underwent pneumonectomy. Thus, 18 patients, nearly half of the total number of 40 patients who were not considered for resection because of positive findings at mediastinoscopy, were possibly denied curative resections.

Mediastinoscopy provided a histological diagnosis in all 14 patients with mediastinal or pulmonary hilar masses. The investigation is of particular value in the diagnosis of sarcoidosis, and Hristov (1969) reported that the investigation gave histological confirmation of the diagnosis in 96 per cent of cases, whereas other biopsy techniques were effective in only 15–26 per cent. A positive histological diagnosis was obtained in 6 out of 28 patients with atypical pulmonary opacities. We do not think that a negative finding at mediastinoscopy is of value in excluding malignancy as a cause of an undiagnosed pulmonary opacity, as was suggested by Sarin and Nohl-Oser (1969).

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ARGENTAFFIN-CELL TUMOUR OF MECKEL'S DIVERTICULUM

A REPORT OF 2 CASES AND REVIEW OF THE LITERATURE

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SUMMARY

Two patients with argentaffin carcinoma (carcinoid tumour) of Meckel's diverticulum are described and the literature is reviewed. Only 45 previous cases have been reported.

In both patients the primary tumour had metastasized by the time the diagnosis was made. The first patient developed the carcinoid syndrome 3 months after removal of the tumour but he is alive and well over 5 years later.

The findings in these 2 patients add further support to the view that a carcinoid in a Meckel's diverticulum behaves like that in the small bowel rather than that in the appendix, with an appreciable (21 per cent) incidence of metastasis. The recommended treatment, therefore, should be similar to that of small intestinal carcinoid, namely, wide excision of intestine with a wedge of mesentery. Furthermore, prophylactic resection of Meckel's diverticulum is recommended whenever possible to eliminate the possibility of subsequent development of this tumour.

CARCINOID tumour (argentaffin carcinoma) occurring in a Meckel's diverticulum is rare. Since Oberndorfer's report in 1907 of 2 carcinoid tumours in the tip of a Meckel's diverticulum of a 68-year-old man, 45 additional cases have been reported. The literature has recently been reviewed by Weitzner (1969).

This report is of 2 patients who developed carcinoid tumours of Meckel's diverticulum, 1 of whom subsequently developed the carcinoid syndrome and is alive and well 5 years after the primary tumour was removed. This case appears to be the first reported example of the carcinoid syndrome resulting from a primary Meckelian carcinoid tumour in a male.

CASE REPORTS

Case 1.—A 69-year-old man presented with 1-year history of diarrhoea, becoming worse in the last 4 months with the passage of approximately six stools per day. The stools were unusually pale but occasional blood-streaking was observed. There were no other gastro-intestinal symptoms and no weight-loss. The blood-pressure was 130/80 mm. Hg, and no abnormal signs were detected on examination of all systems.

INVESTIGATIONS.—The haemoglobin was 16·2 g. per 100 ml. (109 per cent), the white blood-count was 8100 cells per $mm.^3$, and the differential count was normal. The erythrocyte sedimentation rate was 4 mm. per hour. Barium radiographic examination of the large bowel showed the presence of diverticula in the sigmoid and descending colon, and a barium follow-through examination of the small bowel showed a coarsening of the mucosal pattern of the mid-portion of the small bowel, giving a fixed distorted area close to the ascending colon.

The radiological picture was interpreted as being consistent with lymphosarcoma, Crohn's disease, or carcinoid.

LAPAROTOMY.—An indurated mass of ileum was found matted to the ascending colon. Fixity to the posterior abdominal wall made removal difficult and one fixed node was left behind where it was densely adherent to the superior mesenteric vessels and the third part of the duodenum.

A hemicolectomy and distal ileostomy were performed, from which the patient made an uncomplicated recovery.

PATHOLOGY.—The specimen consisted of caecum and ascending colon, 15 cm. in length, with 89 cm. of terminal ileum. A complex Meckel's diverticulum was located 35 cm. from the ileocaecal valve. A greyish-white tumour mass, 1·5 cm. in diameter, involved the neck and wall of the diverticulum (*Fig.* 1). The mesenteric tissues close to the diverticulum were indurated and infiltrated by deposits of greyish-white tumour, drawing together several loops of small intestine.

Histologically, the tumour consisted of cords and solid clumps of small uniform cells (*Fig.* 2) with occasional acinar or 'pseudo-rosette' formations. The nuclei were round or oval with prominent nucleoli and infrequent mitotic figures. The cytoplasm was eosinophilic and

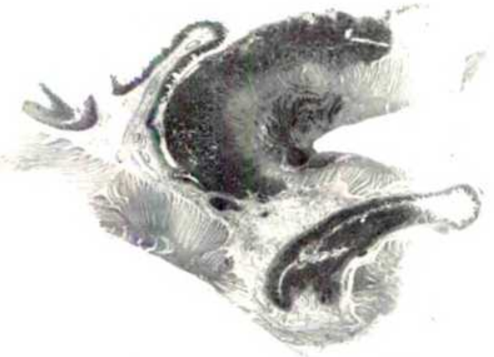

FIG. 1.—Section through Meckel's diverticulum showing tumour mass involving the neck and wall of the diverticulum. H. and E. (× 2.)

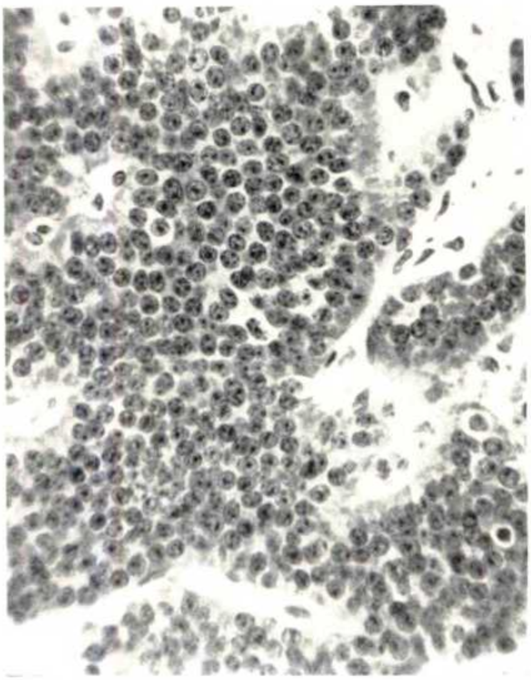

FIG. 2.—Solid clumps of uniform oval cells with occasional acinar differentiation (top left). H. and E. (× 450.)

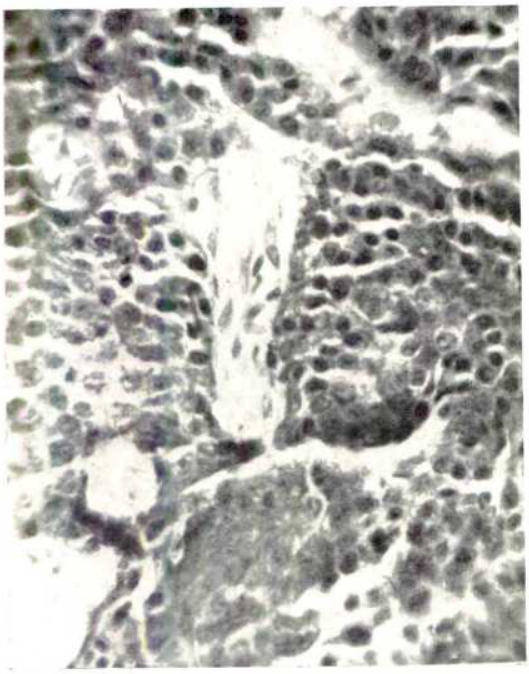

FIG. 3.—Cytoplasm of tumour cells showing dark granules. Diazo. (× 450.)

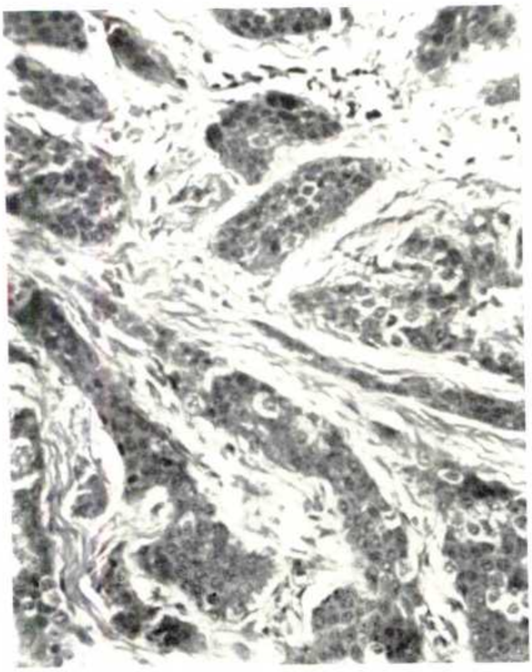

FIG. 4.—Small cords of tumour cells separated by dense fibrous trabeculae. Haematoxylin and van Gieson's. (× 250.)

finely granular. The tumour widely infiltrated the submucosa, muscularis externa, and serosa. Histochemical staining techniques for argentaffin granules demonstrated positive black granules in Masson-Fontana and brown granules in diazo-stained sections (*Fig.* 3). Metastatic deposits involved the adjacent mesentery and mesenteric lymph-nodes. The deposits in the mesentery were surrounded by dense fibrous trabeculae (*Fig.* 4).

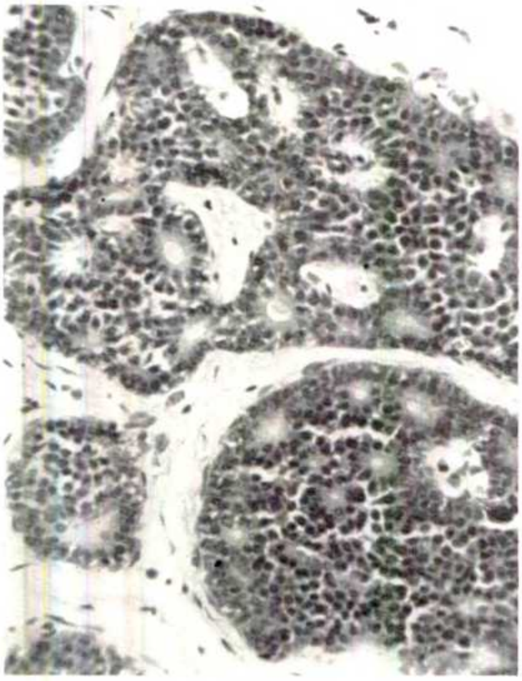

FIG. 5.—Omental metastasis of argentaffin carcinoma showing a well-developed 'pseudorosette' formation. H. and E. (× 250.)

A diagnosis of a moderately well-differentiated argentaffin carcinoma of Meckel's diverticulum was made.

POSTOPERATIVE COURSE.—After recovery a 24-hour collection of urine was found to contain less than 8 mg. of 5-hydroxyindole-acetic acid (HIAA).

FOLLOW-UP EXAMINATION.—Three months later there was evidence of 'flushing' after meals and the patient continued to pass three or four loose stools per day; these features were suggestive of the carcinoid syndrome. Serum estimation of 5-hydroxytryptamine (HT) was 372 ng. per ml. and the platelet HT was 2278 ng. per 10^9 platelets.

Over the following 5 years these symptoms have not worsened. Five years later the patient was readmitted to hospital with acute retention of urine, and a retropubic prostatectomy for benign prostatic hypertrophy was performed.

INVESTIGATIONS.—On the second admission the haemoglobin was 14·6 g. per 100 ml. (100 per cent), E.S.R. was 10 mm. per hour, and W.B.C. was 10,000 per mm.^3 Urine HIAA was 73 mg. per 24 hours.

OPERATION.—A laparotomy was performed and some of the multiple peritoneal nodules were removed for biopsy. Assessment of the liver was not possible because of dense omental adhesions.

HISTOLOGY.—The omental biopsy specimen was infiltrated by trabecular and acinar deposits of argentaffin carcinoma showing well-developed tubules (*Fig.* 5) and acinar differentiation. Argentaffin granules were seen in Masson-Fontana stained sections. Deparaffinized unstained sections mounted in a fluorescent-free medium were examined for autofluorescence with a Reichert Zetopan microscope fitted with Fluorlux ultra-violet illumination equipment. All the tumour cells showed a vivid, golden-yellow, granular fluorescence of the cytoplasm (*Fig.* 6) which is characteristic of HT.

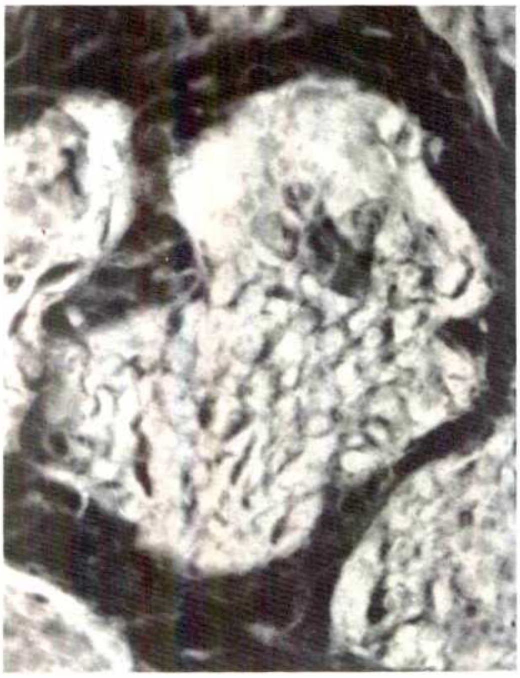

FIG. 6.—Clumps of tumour cells showing (golden-yellow) autofluorescence in ultra-violet light. Unstained. (× 790.)

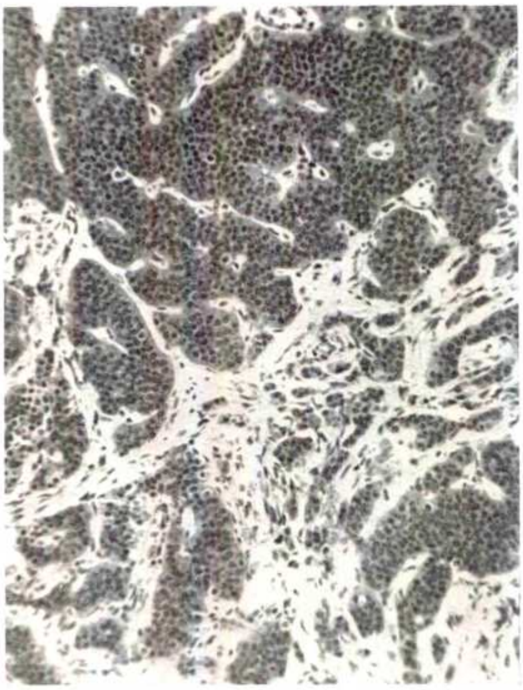

FIG. 7.—Omentum infiltrated by trabecular 'scirrhous' type of argentaffin carcinoma. H. and E. (× 150.)

FOLLOW-UP EXAMINATION.—The patient made a good recovery from the prostatectomy, and on examination 6 months later was well, in spite of flushing and six or seven daily bowel actions.

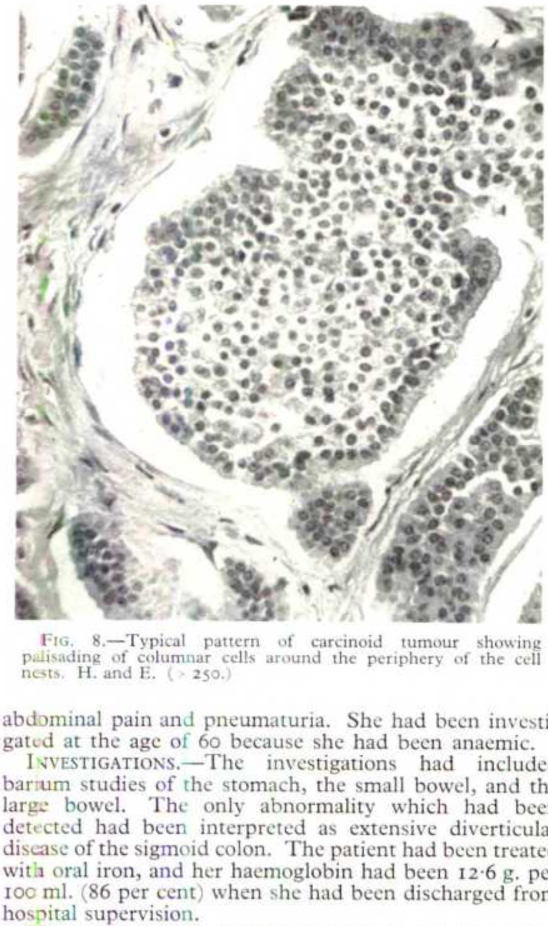

FIG. 8.—Typical pattern of carcinoid tumour showing palisading of columnar cells around the periphery of the cell nests. H. and E. (× 250.)

Case 2.—A 64-year-old woman presented with a 3-month history of intermittent diarrhoea and colicky lower abdominal pain and pneumaturia. She had been investigated at the age of 60 because she had been anaemic.

INVESTIGATIONS.—The investigations had included barium studies of the stomach, the small bowel, and the large bowel. The only abnormality which had been detected had been interpreted as extensive diverticular disease of the sigmoid colon. The patient had been treated with oral iron, and her haemoglobin had been 12·6 g. per 100 ml. (86 per cent) when she had been discharged from hospital supervision.

When the patient presented again as an emergency admission 3 years later her haemoglobin was 12·8 g. per 100 ml. (88 per cent), W.B.C. was 12,000 per mm.^{3}, and E.S.R. was 29 mm. per hour. A plain radiograph of the abdomen showed that gas was present in the urinary bladder, and a pyelogram showed caliceal hydronephrosis on the right with a normal left kidney. Cystoscopy supported the suspicion of a vesicocolic fistula. Barium examination of the rectum demonstrated a stricture of the sigmoid colon through which barium would not pass; a connexion was demonstrated between the stricture site and the bladder. The blood-urea was 46 per 100 ml., and urine culture grew a heavy growth of monilia and *Staphylococcus aureus*. The blood-pressure was 230/110 mm. Hg.

LAPAROTOMY.—Laparotomy revealed a mass in the sigmoid colon and nodules in the omentum. The small intestine was interpreted as being normal. A diverting transverse colostomy and omental biopsy were performed.

HISTOLOGY.—The omental biopsy specimen was infiltrated by a trabecular 'scirrhous' type of argentaffin-cell carcinoma (*Fig.* 7).

POSTOPERATIVE INVESTIGATIONS.—Assessment of HIAA showed excretion of 14·7 and 26 mg. on two separate 24-hour specimens.

A presumptive diagnosis of carcinoid tumour of the colon was made, and 6 weeks later a planned resection of the sigmoid colon was attempted despite technical difficulty due to fixity of the sigmoid colon. An estimated blood-loss of 2 litres during the operation was replaced, but her blood-pressure fell to 120 mm. Hg systolic and could not be restored, despite further rapid transfusion and the maintenance of the central venous pressure at 16 cm. of saline. The patient died within 12 hours of the operation.

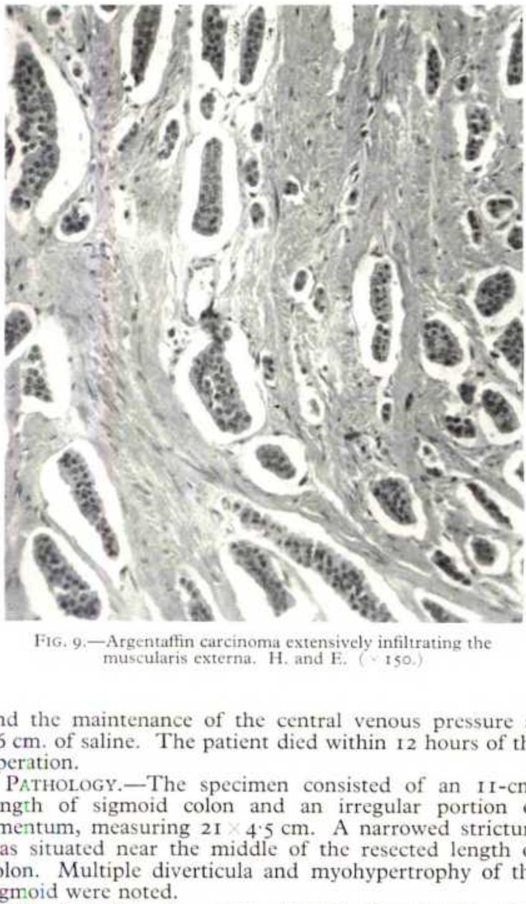

FIG. 9.—Argentaffin carcinoma extensively infiltrating the muscularis externa. H. and E. (× 150.)

PATHOLOGY.—The specimen consisted of an 11-cm. length of sigmoid colon and an irregular portion of omentum, measuring 21 × 4·5 cm. A narrowed stricture was situated near the middle of the resected length of colon. Multiple diverticula and myohypertrophy of the sigmoid were noted.

Histologically, the colon showed diverticulitis with secondary deposits of argentaffin carcinoma in the serosa. The omentum was infiltrated by multiple deposits of argentaffin carcinoma.

NECROPSY.—The peritoneal cavity contained 1500 ml. of blood and serous fluid. A nodule of yellowish-white tumour tissue, 2 cm. in diameter, was situated at the orifice of a Meckel's diverticulum at a level approximately 75 cm. from the ileocaecal valve. Metastatic deposits of greyish-white tumour tissue were found in the pelvic lymph-nodes and measured up to 1 cm. in diameter.

The liver (weight, 1090 g.) did not contain secondary deposits, but multiple tumour nodules up to 1·5 cm. wide were found on the right diaphragm.

HISTOLOGY.—The plaque-like tumour situated at the mouth of the Meckel's diverticulum consisted of solid nests and cords of round, uniform cells, showing a tendency to columnar palisading at the periphery of the nests (*Fig.* 8). The cytoplasm was eosinophilic and granular. Positive argentaffin granules were seen in sections stained by the Masson-Fontana and diazo methods.

The tumour was penetrating all layers of the wall and was diffusely infiltrating the muscularis externa (*Fig.* 9).

A diagnosis of a well-differentiated argentaffin carcinoma in Meckel's diverticulum was made.

DISCUSSION

Argentaffin carcinoma of the ileum is a rare tumour. MacDonald (1956) found only 74 examples out of 26,401 necropsies and 418,166 surgical specimens.

More recently, Brookes, Waterhouse, and Powell (1968) described 168 cases of malignant disease of the small intestine reported to the Birmingham Regional Cancer Registry in a 10-year survey (1950–9). The types of tumours found in the Birmingham Regional Cancer Registry series included 55 adenocarcinomas (32 per cent), 56 sarcomas (33 per cent), 32 carcinoid tumours (19 per cent), and in 25 cases (15 per cent) there was no definite histological diagnosis. Of the 32 carcinoid tumours, 28 were situated in the ileum, 2 in the jejunum, and 2 in the duodenum.

Table I.—CLINICAL FEATURES OF 45 PATIENTS WITH CARCINOID TUMOUR OF MECKEL'S DIVERTICULUM

AUTHOR	AGE AND SEX		SIZE (cm.)	METASTASES	CARCINOID SYNDROME	PRESENTATION
Oberndorfer (1907)	68 yr.	M.	½ pea	No	No	Necropsy
Kaspar (1914)	13 yr.	M.	Walnut	No	No	Surgery
Hicks and Kadinsky (1922)	12 yr.	M.	Walnut	No	No	Surgery
Schaetz (1925)	69 yr.	M.	Walnut	No	No	Surgery
Stewart and Taylor (1926)	54 yr.	M.	Pea	No	No	Necropsy
Hertzog and Carlson (1935)	54 yr.	M.	0·4	No	No	Necropsy
Hertzog and Carlson (1935)	58 yr.	M.	0·3	No	No	Necropsy
Price (1935)	54 yr.	F.	3 × 3 × 2	No	No	Surgery
Cagnetto (1938)	14 mth.	M.	—	—	—	—
Collins, Collins, and Andrews (1938)	56 yr.	M.	0·6	No	No	Surgery
Ashworth and Wallace (1941)	46 yr.	M.	0·8	No	No	Necropsy
Pautler and Scotti (1951)	68 yr.	M.	0·6	No	No	Necropsy
Mrazek, Goodwin, and Mohardt (1953)	37 yr.	M.	—	No	No	Surgery
Mrazek and others (1953)	54 yr.	M.	0·3	No	No	Necropsy
Stoll (1953)	58 yr.	M.	0·5	Liver	No	Necropsy
Fox (1954)	58 yr.	M.	0·5	Liver	No	Necropsy
Grimes and Crane (1955)	59 yr.	F.	1·5	Liver	No	Surgery
Pierce (1955)	47 yr.	M.	—	No	No	Surgery
Snow, Lennard-Jones, Curzon, and Stacey (1955)	58 yr.	F.	1·0	Liver, mesenteric lymph-nodes	Yes	Necropsy
Eldred (1956)	50 yr.	F.	—	Liver	No	Surgery
Parnassa, Friedman, and Cincotti (1956)	56 yr.	M.	0·5	No	No	Surgery
Baird, Anderson, and Mills (1958)	42 yr.	M.	0·4	No	No	Surgery
Rintala (1958)	25 yr.	M.	0·3	No	No	Surgery
Becker (1960)	51 yr.	M.	0·6	No	No	Surgery
Camp and Hays (1960)	50 yr.	M.	0·8	No	No	Surgery
Drickman and Hodges (1960)	71 yr.	M.	0·8	Mesenteric lymph-nodes	No	Necropsy
Ciampa (1961)	40 yr.	F.	1·0	No	No	Surgery
Classen, Wiederanders, and Symbas (1961)	64 yr.	M.	1·0	No	No	Surgery
Lykke and de La Lande (1961)	60 yr.	F.	—	Liver, lung, mesenteric lymph-nodes	Yes	Necropsy
Kinley and Penner (1962)	70 yr.	M.	—	No	No	Surgery
Kravetz, Balsam, and Jiminez (1962)	61 yr.	M.	1·0	No	No	Necropsy
Kravetz and others (1962)	55 yr.	M.	5 × 3	Liver, vertebrae, mesenteric lymph-nodes	No	Necropsy
Lechner and Chamblin (1962)	52 yr.	M.	0·6	No	No	Surgery
Blomquist (1963)	64 yr.	F.	—	No	No	Surgery
Southam (1963)	58 yr.	F.	1·0	Liver, ileum	Yes	Necropsy
Herena and Schraft (1964)	55 yr.	M.	1·5	No	No	Necropsy
Roselli and Paulino (1964)	80 yr.	M.	0·3	No	No	Surgery
Dencker and Norberg (1965)	72 yr.	M.	—	No	No	Surgery
Johnston, Hall, and Erickson (1965)	73 yr.	M.	—	No	No	Surgery
Doyle and Severance (1966)	55 yr.	M.	—	No	No	Surgery
Figueroa and Tedeschi (1967)	61 yr.	F.	0·9	No	No	Necropsy
Schlicke and Johnstone (1968)	76 yr.	M.	1·0	No	No	Surgery
Traill (1968)	61 yr.	M.	0·7, 0·2	No	No	Necropsy
Weitzner (1969)	68 yr.	M.	0·6	No	No	Necropsy
Shaw (1969)	70 yr.	M.	—	No	No	Surgery

During the period 1958–67, 78 further carcinoid tumours of the small intestine have been reported to the same registry. Sixty-three of these 78 tumours were situated in the jejunum and ileum, 2 of which were in a Meckel's diverticulum.

The occurrence of an argentaffin-cell tumour in a Meckel's diverticulum is very rare, and to date there are only 45 other documented cases reported in the literature (*Table I*), although Anthony and Drury (1970) refer to 1 other example which was seen among 100 cases of argentaffin carcinoma of all sites found during a 12-year-period from 1956 to 1968 from the files of the Central Middlesex Hospital, Bland-Sutton Institute of Pathology, Middlesex, and St. Mark's Hospital, London.

Most carcinoids occurring in Meckel's diverticulum are unsuspected incidental findings at necropsy (19 out of 45,) or operation (25 out of 45). Nine (20 per cent) have shown invasion of the intestinal wall (Sanders and Axtell, 1964). Nine out of 44 (21 per cent) have shown metastases, the liver being involved in 8, mesenteric lymph-nodes in 4, lungs in 1, vertebrae in 1, and ileum in 1.

Three of the 8 patients with hepatic metastases developed the carcinoid syndrome; all were females, the majority (5 out of 9) of patients with disseminated tumour being women. This is unusual in view of the very low incidence to date of carcinoid in Meckel's diverticula in women and the apparent fairly equal occurrence of metastasizing carcinoids of the small intestine in both sexes. Thus, 36 of the patients were men and 9 were women. The fact that carcinoid of Meckel's diverticulum has been encountered four times as often in males than in females probably reflects the twofold (Wansbrough, Thomson, and Leckey, 1967) to threefold (Seagram, Louch, Stevens, and Wentworth, 1968) greater incidence of Meckel's diverticulum in males.

The size of the tumour was recorded in 32 cases and varied from 0·3 to 5·3 cm. The youngest case was a 14-month-old child and the oldest an 80-year-old man. Thirty-six patients were aged 50 or over. The average age was 55 years. Special stains for argentaffin granules in the tumour were positive in 21 of 23 cases in which they were performed. The carcinoid was ulcerated and was the source of the gastro-intestinal haemorrhage in 2 patients. Six of the diverticula showed diverticulitis. A double carcinoid was present in 2 of the diverticula (Oberndorfer, 1907; Traill, 1968).

Thirty-four (75 per cent) of the cases of carcinoid tumour in Meckel's diverticulum have been reported since 1950. Although this may suggest that the lesion is more prevalent than previously was suspected, it most probably reflects the more common practice of resecting normal diverticula found incidentally at surgery (Weitzner, 1969). Prophylactic resection of Meckel's diverticulum is recommended whenever possible in order to eliminate the potential site of this rare tumour.

Rigidity and collagenous fibrosis of the mesentery are frequently present in association with carcinoid tumour of the small intestine and cause obstruction by retraction and kinking, a complication known to surgeons for many years (Cooke, 1931; Grimes and Bell, 1949; Moertel, Sauer, Dockerty, and Baggenstoss, 1961). In both of the present cases there was extensive fibrosis and induration of the mesentery with indrawing of the coils of small intestine. Moertel and others (1961) and later Dockerty (1963) reviewed the same series of 209 cases seen at the Mayo Clinic over a period of 50 years. They noted that in only 1 out of 56 cases who presented with symptoms was the correct diagnosis made preoperatively. The commonest form of presentation was small intestinal obstruction in 49 cases, which was due to mesenteric fibrosis in 33 (67 per cent).

Metastases occurred in 21 per cent of Meckelian carcinoids, compared with 30 per cent of carcinoids of the small intestine (Moertel and others, 1961).

Although there are too few cases to draw valid conclusions, carcinoids in Meckel's diverticulum tend to behave more like small intestinal than appendiceal carcinoids. For this reason the recommended treatment of carcinoids in this area is the same as that for similar tumours of the small intestine, namely, wide excision of the intestine with a wedge of mesentery.

In the report of Brookes and others (1968) 31 cases of small intestinal carcinoid tumour were followed up, with a 5-year survival rate of 41·9 per cent, and of 16 cases receiving radical surgery, 56 per cent survived 5 years. A similar 5-year survival of 52 per cent was found by Pagtalunan, Mayo, and Dockerty (1964). During the period reviewed by Brookes and others (1968) there were 47 cases of carcinoid tumour of the appendix reported to the same registry, and the 5-year survival rate was 91·5 per cent (43 cases).

In the literature on carcinoid tumours arising in Meckel's diverticulum very few of the cases have been reported some time after the diagnosis was made. Two of the women with disseminated carcinoid were alive for 10 and 24 months following surgery and cytotoxic therapy. None of the other patients has been known to develop metastases, although only 2 had been followed up for more than 5 years.

The findings in the present 2 cases are summarized in *Table II.* Both cases showed dissemination to the peritoneum and the mesenteric nodes. In *Case* 1 the symptoms of the carcinoid syndrome developed 3 months after the removal of the primary tumour. Despite this the man is alive and well 5 years later. A further operation for prostatic enlargement 5 years later revealed extensive omental secondaries, containing large quantities of HT, the presence of which was by confirmed histochemical staining reactions and positive autofluorescence in ultra-violet light. We believe this to be the first report of the carcinoid syndrome from a primary argentaffin carcinoma in a Meckel's diverticulum in a man. It is clear from the clinical progress in this case that the natural history of this tumour closely mimics the now well-recognized apparently slow growth-rate and good survival which are associated with other gastro-intestinal carcinoids despite early local invasion and metastases.

Table II.—CLINICAL FEATURES OF 2 PATIENTS WITH CARCINOID OF MECKEL'S DIVERTICULUM

CASE	AGE (years) AND SEX	SIZE (cm.)	SPECIMEN	METASTASES	COMMENT
1. J. T.	69 M.	1·5	Surgery	Mesentery, mesenteric lymph-nodes	Argentaffin reaction. Carcinoid syndrome present. Alive and well 5 years later.
2. G. A.	64 F.	2·0	Necropsy	Mesentery, mesenteric lymph-nodes, colonic serosa, diaphragm	Argentaffin reaction. Died following operation for sigmoid diverticulitis

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THE EFFECTS OF INTERMITTENTLY APPLIED EXTERNAL PRESSURE ON THE HAEMODYNAMICS OF THE HIND-LIMB IN GREYHOUND DOGS

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SUMMARY

The application of intermittent compression of 30 mm. Hg to the hind-limb of a greyhound results in an increase of about 400 per cent in the pulsatility of femoral vein flow and of 250 per cent in the peak femoral vein flow. This effect may result in adequate filling and emptying of the deep venous channels and sinuses of the lower limb of man, thereby preventing stasis in them. Intermittent compression of the calf seems, therefore, to have an obvious place in the prophylaxis of deep-vein thrombosis.

During exercise the skeletal muscle of the calf interacts with the valved veins of the lower limb to produce a mechanical blood pump. Exercise results in intermittent compression of the deep veins of the calf and thigh which displaces and maintains venous blood-flow towards the heart (Waterfield, 1931; Clark, Cotton, and Zarek, 1965). During the subsequent muscle relaxation, reflux of blood is prevented by the 'non-return' action of the venous valves. Thus, calf-muscle contraction is followed by a considerable drop in venous pressure at the ankle (Pollack and Wood, 1949; Henry and Gauer, 1950; Højensgard and Sturup, 1952). It has been suggested that the action of the muscle pump on the venous pressure and flow in the lower limb may be simulated by using rhythmical external compression of the calf, e.g., by applying pneumatic cuffs (Henry, Slaughter, and Greiner, 1955; Allwood, 1957; Loane, 1959). The resultant 'milking' of the venous channels reduces the venous pressure, thereby increasing the arteriovenous pressure gradients in the lower limb, which in turn promote the blood-flow (Henry and others, 1955; Allwood, 1957).

MATERIALS AND METHODS

Eight greyhound dogs, weighing 25–30 kg., were anaesthetized with intravenous Nembutal in a dose of 30 mm. per kg. body-weight and maintained with additional small doses as required. Both femoral veins were exposed and all their tributaries were ligated. Intermittent external pressure was applied to one limb using a standard half-leg inflatable plastic splint (Parke-Davis & Co.), while the other leg acted as control.

The first group of 5 dogs was used to investigate the effects of varying the interval between each successive compression on the haemodynamics of the hind-limb. Intermittent compression was achieved by connecting the splint to a Beaver respirator and the resultant variation in splint pressure was monitored with a Bell and Howell L221 transducer (*Fig.* 1). Blood-flows in the femoral veins were measured using a Nycotron 372 electromagnetic flow-meter and cuff flow-probes type PS. Following placement of the probes, a period of time was allowed for the flows to stabilize and then a train of equispaced compressive impulses, having a maximum value of 30 mm. Hg, was applied to the leg. The compression was then stopped, the pressure in the splint was reduced to zero, and the flows were allowed to restabilize. The whole procedure was then repeated for a further six settings of the respirator speed control. In this way the interval between successive compressions in each train was varied over the range of 1·45–4·15 seconds. Continuous recordings of blood-flow and splint pressure were traced by an ultra-violet recorder, and the mean, minimum, and peak femoral vein flows were calculated from the traces.

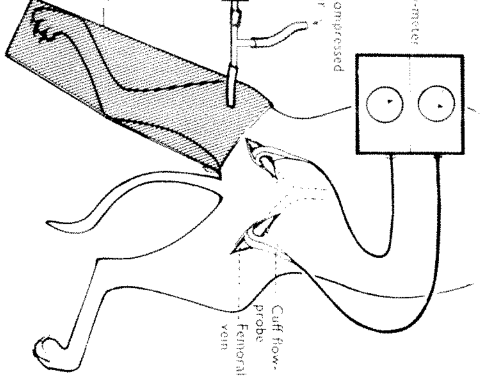

FIG. 1.—Experiment to determine the effects of intermittent compression of the leg on femoral vein flow in greyhounds. Compressed air is supplied from a Beaver respirator.

The second group of 3 dogs was used to investigate the effects of applying, for 60 minutes, a compressive impulse of 30 mm. Hg every 4 seconds. Continuous recordings of both the mean and pulsatile femoral vein blood-flows were made throughout the 60-minute period. Changes in both the mean and pulsatile femoral vein blood-flows were then taken from the traces at 5-minute intervals.

RESULTS

Table I shows the effects of varying the interval (T) between successive compressions of 30 mm. Hg on the mean [Q(mean)], peak [Q(max)], and minimum [Q(min)] femoral vein blood-flows in the experimental

Table I.—EFFECT OF VARYING THE INTERVAL (T) BETWEEN SUCCESSIVE APPLICATIONS OF AN EXTERNAL PRESSURE OF 30 mm. Hg. ON THE MEAN VOLUME FLOW RATE [Q(mean)] IN THE CONTROL (UNCOMPRESSED) LEG AND IN THE COMPRESSED LEG. ALSO GIVEN ARE THE MAXIMUM [Q(max)] AND MINIMUM [Q(min)] FLOWS IN THE COMPRESSED LEG

SETTING	DOG 1					DOG 2					DOG 3					DOG 4					DOG 5				
		Compressed Leg			T (sec.)		*Compressed Leg*			T (sec.)		*Compressed Leg*			T (sec.)		*Compressed Leg*			T (sec.)		*Compressed Leg*			T (sec.)
	Control Leg Q(mean) (ml. per min.)	Q(mean) (ml. per min.)	Q(max) (ml. per min.)	Q(min) (ml. per min.)		*Control Leg* Q(mean) (ml. per min.)	Q(mean) (ml. per min.)	Q(max) (ml. per min.)	Q(min) (ml. per min.)		*Control Leg* Q(mean) (ml. per min.)	Q(mean) (ml. per min.)	Q(max) (ml. per min.)	Q(min) (ml. per min.)		*Control Leg* Q(mean) (ml. per min.)	Q(mean) (ml. per min.)	Q(max) (ml. per min.)	Q(min) (ml. per min.)		*Control Leg* Q(mean) (ml. per min.)	Q(mean) (ml. per min.)	Q(max) (ml. per min.)	Q(min) (ml. per min.)	
0	336	320	352	240		160	168	272	116		150	132	224	128		224	208	224	112		228	200	208	144	
1	312	288	640	32	3·9	176	208	656	0	3·9	160	192	420	20	4·0	218	232	536	32	3·6	188	156	400	0	4·15
0	332	296	336	240		160	176	256	128		154	164	224	136		200	200	272	64		204	176	184	128	
2	316	288	672	32	3·4	172	192	560	0	3·1	152	184	440	40	3·3	200	218	512	16	3·35	208	176	400	16	3·35
0	312	272	304	208		184	200	288	128		146	152	216	104		190	192	240	64		200	160	176	128	
3	332	296	608	32	2·45	176	200	608	0	2·4	142	176	368	64	2·55	196	208	464	80	2·5	192	160	288	64	2·4
0	320	272	304	208		168	176	264	120		152	160	216	120		192	200	224	96		198	172	192	144	
4	328	296	560	80	2·05	176	192	520	0	2·0	158	184	368	72	2·15	196	224	448	0	2·05	200	176	320	64	2·0
0	336	288	320	224		176	192	272	128		160	172	240	144		182	192	208	72		200	160	176	128	
5	324	304	528	120	1·75	168	184	448	0	1·75	144	180	336	56	1·8	188	216	400	32	1·8	200	164	288	64	1·7
0	332	288	320	224		176	192	272	128		144	172	228	128		180	184	208	80		292	176	192	120	
6	320	304	512	128	1·55	168	184	448	0	1·6	146	184	352	56	1·6	184	208	400	16	1·55	288	200	288	144	1·6
0	320	288	320	208		172	192	288	136		160	172	240	144		176	184	208	88		268	188	200	144	
7	324	304	496	96	1·45	180	200	448	0	1·45	138	188	368	64	1·45	178	208	368	80	1·45	260	192	288	96	1·45

(compressed) limb. Also given is the mean flow [Q (mean)] in the control (uncompressed) limb. Intermittent compression produced small but haphazard changes in the mean femoral vein flow which were probably not significant. The results obtained from *Table I* are plotted in *Figs.* 2 and 3. The changes in pulsatility were calculated from the difference between the maximum and minimum femoral vein blood-flows [Q(max)] – [Q(min)]. It can be seen from *Figs.* 2 and 3 that the greater the interval between successive compression, the greater was the increase in both the pulsatility and in the peak femoral vein blood-flow. The best result in the experimental range occurred when a compression was applied once every 4 seconds, although mathematical analysis of the results shows that the effect should be maximal when a compression is applied about once every 45 seconds. Applying a compression every 4 seconds increased the pulsatility by about 400 per cent (*Fig.* 2) and the peak femoral vein flow by 250 per cent (*Fig.* 3).

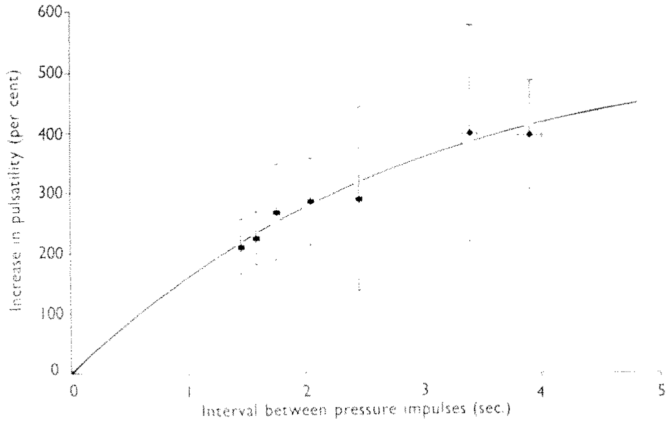

FIG. 2.—Graph showing how the increase in pulsatility of the venous flow varies with the interval between each compressive impulse (The vertical and horizontal bars represent ± 1 S.D. about the mean value.)

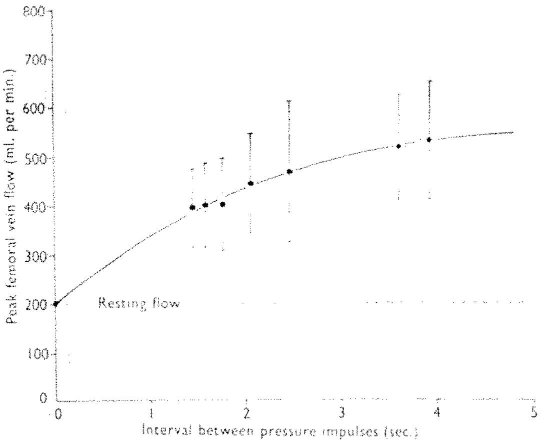

FIG. 3.—Graph showing the relationship between the peak femoral vein flow and the interval between the compressive impulses. Also shown is the resting flow. (The vertical and horizontal bars represent ± 1 S.D. about the mean value.)

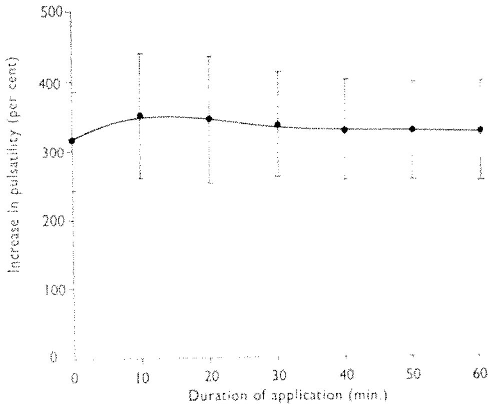

FIG. 4.—Graph showing how the effects of intermittent compression on the pulsatility of the venous flow are maintained over a period of 1 hour. (The vertical and horizontal bars represent ± 1 S.D. about the mean value.)

Table II shows the effects of applying, for a period of 60 minutes, a compression pressure of 30 mm. Hg once every 4 seconds. The results obtained from *Table II* were applied in *Fig.* 4, which demonstrates that the increase in pulsatility is maintained throughout the entire 60-minute period.

DISCUSSION

Venous stasis in the lower limb of resting recumbent patients (McLachlin, McLachlin, Jorg, and Rawlings, 1960; Cotton and Clark, 1965) is thought to be an important cause of thrombosis in the deep veins of the calf (Hadfield, 1950). Radiographic and anatomical studies have shown that venous blood stagnates in the thin-walled soleal sinuses which have been shown to be functionally isolated in the recumbent state (Gibbs, 1957; Sevitt and Gallagher, 1961; Cotton and Clark, 1965). Induction of anaesthesia and the associated inactivity of the calf muscles during operation aggravate remarkably the stagnation in these sinuses (Cotton and Clark, 1965; Clark and Cotton, 1968).

Arteriophlebographic studies have revealed that static compression of the lower limb results in an increase in the flow-rate in the deep veins of the leg but does not result in any filling of the soleal sinuses

Table II.—EFFECT OF APPLYING SUCCESSIVE COMPRESSIVE IMPULSES TO THE HIND-LEG OF A DOG OVER A PERIOD OF 1 HOUR*

DURATION OF APPLICATION (min.)	DOG 1				DOG 2				DOG 3			
	Control Leg	*Compressed Leg*			*Control Leg*	*Compressed Leg*			*Control Leg*	*Compressed Leg*		
	Q(mean) (ml. per min.)	Q(mean) (ml. per min.)	Q(max) (ml. per min.)	Q(min) (ml. per min.)	Q(mean) (ml. per min.)	Q(mean) (ml. per min.)	Q(max) (ml. per min.)	Q(min) (ml. per min.)	Q(mean) (ml. per min.)	Q(mean) (ml. per min.)	Q(max) (ml. per min.)	Q(min) (ml. per min.)
Base-line	140	124	224	96	192	232	304	176	324	280	320	208
0	140	128	420	−20	192	232	624	0	328	304	592	128
10	152	144	420	−20	176	200	608	−32	332	328	608	48
20	150	152	420	−20	176	200	624	−32	344	336	608	64
30	130	160	440	−16	172	192	608	−40	316	312	608	112
40	140	172	440	−16	168	192	592	−48	328	320	592	112
50	140	176	440	−20	168	176	592	−48	300	304	560	80
60	126	160	440	−16	164	160	592	−48	308	304	560	80

* The compressive impulses were applied at the rate of 15 per minute with a maximum pressure of 30 mm. Hg. For each dog mean volume flow-rate [Q(mean)] in the control leg and in the compressed leg is given at 5-minute intervals. Also given are the maximum [Q(max)] and Q(min)] flows.

(Clark and others, 1965). The combination of electrical stimulation and external compression of the calf, however, results in a rapid filling of both the deep veins and the soleal sinuses (Cotton and Clark, 1965). It is therefore suggested that the increased pulsatility of venous blood-flow which is obtained by the combination of electrical stimulation and compression of the calf is a reflection of the degree to which the venous system of the calf is being emptied and refilled, and is thus a measure of the degree of stasis present.

Applying an intermittent compression of 30 mm. Hg 15 times per minute results in an increase of about 400 per cent in the pulsatility of the femoral venous flow. Furthermore, the results of this investigation have indicated that there is no concomitant increase in the mean femoral vein blood-flow of any significance, a finding which does not agree with that of Henry and others (1955), Allwood (1957), and Loane (1959), who showed that intermittent compression of the calf will increase the arteriovenous gradients and therefore increase the blood-flow in the limb.

The study of the effects of intermittent compression provides a useful method of investigating the haemodynamic causes of postoperative deep-vein thrombosis. For example, if a clinical trial designed to study the efficacy of this method were to indicate that peroperative intermittent compression of the leg was effective in preventing postoperative deep-vein thrombosis, then one could conclude that in all probability the damping of the flow pulsatility caused by induction of anaesthesia (Clark and Cotton, 1968) is the most important factor in the initiation of the thrombus in the deep veins of the leg.

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THE EFFECT OF INTERMITTENTLY APPLIED EXTERNAL PRESSURE ON THE HAEMODYNAMICS OF THE LOWER LIMB IN MAN

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SUMMARY

The effects of intermittently applied external pressure on blood-volume flow-rate in the femoral vein have been investigated in a series of 6 patients undergoing surgery for bilateral varicose veins. During the investigation, pressure was applied to the legs with the aid of an inflatable plastic splint, while blood-flow in the femoral veins was measured with an electromagnetic blood flow-meter.

The investigation has shown that intermittently applied pressure increases the pulsatility of the venous flow-wave while leaving its mean level largely unaltered. It has been shown that the increase in peak flow is directly proportional to the rate of pressure application, being maximal at about 10 mm. Hg per second. It has further been shown that the increase in both the pulsatility and the peak flow reaches a maximum when the interval between successive pressure applications is 1 minute.

IN the search for effective measures to prevent post-operative deep-vein thrombosis the use of statically applied external pressure has not been successful (Rosengarten, Laird, Jeyasingh, and Martin, 1970). The reason for this probably lies in the failure of external pressure, unless precisely controlled, to alter significantly the haemodynamics of the situation (Spiro, Roberts, and Richards, 1970; Sabri, Roberts, and Cotton, 1971a). More recently it has been suggested that the haemodynamics might be changed to more advantage by the use of intermittently applied external pressures (Sabri, Roberts, and Cotton, 1972). During this latter investigation it was shown in greyhounds that intermittently applied external pressure can significantly increase both the peak femoral vein flow and its pulsatility while leaving its mean level largely unaltered. These increases have been shown to vary with the interval between the compressive impulses, the effect being theoretically maximal when a pulse is applied every 45 seconds.

Other work on the effects of externally applied pressure has shown that the volume of blood ejected from the calf of supine subjects varies with the magnitude of the applied pressure, tending to a maximal value when the pressure is 40 mm. Hg (Roberts, 1971). Since this ejected volume must be constant for any given patient, the peak achieved by applying a pressure will depend on the speed with which the pressure is applied. This present investigation was therefore divided into two parts. In the first part the effect on the peak femoral vein flow of varying rates of pressure application was investigated, and in the second part the effects of varying the interval between successive compressive impulses on the peak flow were studied.

MATERIALS AND METHODS

Six patients undergoing surgery for bilateral varicose veins were asked for their informed consent and co-operation. General anaesthesia was induced and maintained with spontaneous respiration. Blood-flows in the femoral veins were measured with a Nycotron 372 electromagnetic flow-meter and Nycotron cuff flow-probes type PS, using a standard procedure reported previously (Spiro and others, 1970).

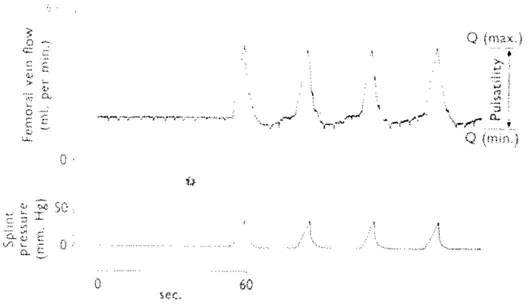

FIG. 1.—Two typical flow and pressure traces obtained during the investigation. The traces show that as pressure is applied to the leg the flow rises and then as the pressure is released falls to below its resting level. The flow then gradually rises to its previous resting level.

The patients were divided into two groups of 3. In the first group blood-flow was measured in one leg only while the leg was subjected to controlled compression with the aid of an inflatable, plastic, below-knee splint (Parke-Davis & Co.). Following placement of the flow-probe, a period was allowed for the flow to stabilize and pressure was then applied at a controlled rate until it had reached 50 mm. Hg. The pressure was released when the flow had fallen to its original resting level, and a period of time was then allowed for the flow to restabilize. This procedure was then repeated for several different rates of pressure application over the range 0·89 to 9·40 mm. Hg per second (i.e. the time taken for the pressure in the splint to reach 50 mm. Hg took between 56 and 5·3 seconds from the time that filling commenced, the higher filling rates producing the lower filling times).

In the second group of 3 patients blood-flows were measured in both the femoral veins. Following placement of the probes, a period of time was allowed for the flows to stabilize and then a train of equi-spaced compressive impulses was applied to the leg by means of an inflatable splint (*Fig.* 1). These were stopped, the flows were allowed to restabilize, and the procedure was repeated three times. The interval between successive compressions in each train was controlled, in four discrete steps over the range

18·0–55·7 seconds, by means of a modified Therepac pneumatic controller (Epac Ltd.). The compression rate was fixed at 6 mm. Hg per second and the pressure was released when it reached 30 mm. Hg. Thus, each compression lasted for approximately 5 seconds.

RESULTS

The results of the first part of the investigation are shown in *Table I*. For each subject the resting flow prior to compression [Q^R(mean)] is tabulated against the peak flow [Q(max)] achieved at each rate of pressure application (dP/dt). Also shown is the time taken for the flow to return to its resting level following release of the compression (T^R). The results from these 3 patients are summarized in *Fig.* 2, which shows the increase in peak flow as a function of the rate of pressure application.

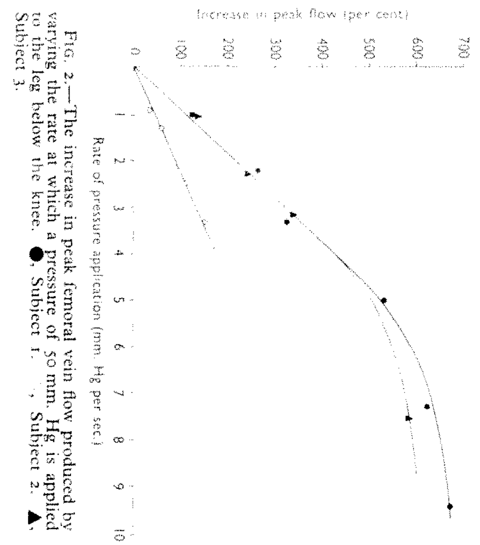

FIG. 2.—The increase in peak femoral vein flow produced by varying the rate at which a pressure of 50 mm. Hg is applied to the leg below the knee. ●, Subject 1. ○, Subject 2. ▲, Subject 3.

Table I.—EFFECT OF VARYING RATES OF APPLICATION OF PRESSURE (dP/dt) ON PEAK FEMORAL VEIN FLOW [Q(max)] AND ON TIME TAKEN (T^R) FOR FLOW TO RETURN TO ITS RESTING LEVEL [Q^R(mean)] ON RELEASING THE PRESSURE

SUBJECT	Q^R(mean) (ml. per min.)	Q(max) (ml. per min.)	dP/dt (mm. Hg per sec.)	T^R (sec.)
1	116	260	1·00	73
	92	352	2·22	58
	96	408	3·33	65
	84	608	7·30	59
	88	680	9·40	71
	84	532	5·07	59
2	288	384	0·89	54
	272	432	1·29	54
	280	528	2·16	60
	280	592	2·50	60
	272	680	3·35	60
3	264	624	1·05	44
	200	680	2·33	48
	192	840	3·16	60
	176	1248	7·55	54

The data obtained during the second part of the investigation are shown in *Table II*. At each setting of the Therepac controller the mean flow [Q(mean)] in

Table II.—EFFECT OF VARYING THE REST PERIOD (T) BETWEEN PRESSURE APPLICATIONS ON MEAN FLOW IN THE CONTROL LEG [Q(mean)] AND MEAN [Q(mean)], MAXIMUM [Q(max)], AND MINIMUM [Q(min)] FLOWS IN THE COMPRESSED LEG

SETTING	SUBJECT 4					SUBJECT 5					SUBJECT 6				
	Control Leg	*Compressed Leg*				*Control Leg*	*Compressed Leg*				*Control Leg*	*Compressed Leg*			
	Q(mean) (ml. per min.)	Q(mean) (ml. per min.)	Q(max) (ml. per min.)	Q(min) (ml. per min.)	T (sec.)	Q(mean) (ml. per min.)	Q(mean) (ml. per min.)	Q(max) (ml. per min.)	Q(min) (ml. per min.)	T (sec.)	Q(mean) (ml. per min.)	Q(mean) (ml. per min.)	Q(max) (ml. per min.)	Q(min) (ml. per min.)	T (sec.)
0	240	224	232	216	—	—	120	152	−16	—	152	116	114	96	—
1	240	219	416	160	19·8	—	130	520	−64	15·7	148	119	509	24	18·0
0	240	200	208	192	—	—	128	152	0	—	148	120	152	104	—
2	240	214	448	144	23·3	—	149	560	−56	25·0	148	126	542	24	21·9
0	238	200	208	192	—	—	128	152	0	—	144	128	160	112	—
3	240	209	480	152	31·8	—	159	600	−80	28·4	144	126	566	−8	26·4
0	240	208	216	200	—	—	136	160	−16	—	128	128	168	88	—
4	240	227	592	144	55·7	—	146	672	−112	51·8	126	131	609	−16	52·5

both the control and compressed legs are given, as well as the maximum [Q(max)] and minimum [Q(min)] flows in the compressed limb. The period between successive compressions in each train (T) is also given.

Fig. 1 shows a typical pressure recording obtained during this investigation. The recording commences with a rest period during which no pressure is applied to the leg. The venous flow trace during this period is only very slightly pulsatile, a small dip occurring in synchronism with respiration. Following this rest period, a train of compressive impulses is applied to one leg and the pulsatility of the flow wave-form increases markedly. The pulsatility is defined as being the difference between the maximum [Q(max)] and minimum [Q(min)] flows, and in *Fig.* 3 the increase in pulsatility is shown as a function of the interval between the compressive impulses.

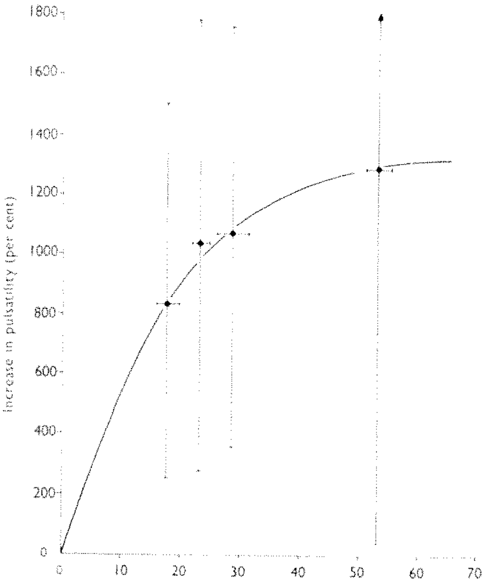

FIG. 3.—Graph showing the increase in pulsatility of the femoral vein flow-wave as a function of the interval between successive pressure impulses. (The vertical and horizontal bars represent ±1 S.D. about the mean value.)

In *Fig.* 4 the peak femoral vein flow achieved by intermittent compression is shown as a function of the interval between the pressure impulses (T).

DISCUSSION

In attempts to prevent postoperative deep-vein thrombosis, considerable attention has been focused on the role played by stasis of blood in the veins of the leg. Attempts at preventing this stasis by bandaging have, however, produced inconclusive and often conflicting results. More recently, the peroperative use of passive calf exercise, which increases both the mean level and the pulsatility of the venous flow (Roberts, Sabri, Pietroni, Gurewich, and Cotton, 1971), has been shown to reduce significantly the incidence of postoperative deep-vein thrombosis (Sabri, Roberts, and Cotton, 1971b). However, this work still leaves several questions unanswered, the chief of which concerns the role of flow pulsatility in the development of deep-vein thrombosis.

An investigation conducted in greyhounds into the effects of intermittently applied external pressure revealed that both the peak value and the pulsatility of the femoral vein flow could be increased, while the mean level was unchanged (Sabri and others, 1972). Furthermore, theoretical analysis of the results indicated that the maximum effect would be produced when the compressive impulses were applied every 45 seconds.

In the present investigation the original animal study has been extended to cover human subjects and the results obtained are very similar in many respects. It has been shown that the peak femoral vein flow can be increased sixfold and its pulsatility increased almost thirtyfold. These maximal values occur when the interval between successive compressions is about 60 seconds, a finding which appears to be related to the time required for the venous system to refill following release of leg compression, for as *Table I* shows it takes an average of 58·6 seconds for the flow to return to its normal level after the compression has been released. Furthermore, the increase in the peak flow is linearly related to the rate of pressure application up to a value of 4 mm. Hg per second. Thereafter the effect tails off as the resistance to the ejected blood builds up to reach a maximum when the pressure is applied at about 10 mm. Hg per second.

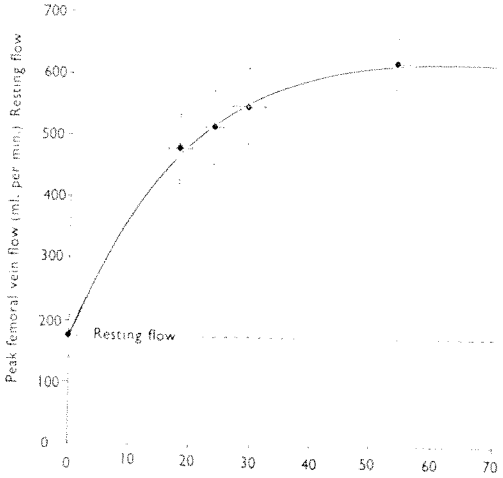

FIG. 4.—Graph showing the peak femoral vein flow achieved by intermittent compression as a function of the interval between the pressure impulses. The level of the resting flow is also shown. (The vertical and horizontal bars represent ±1 S.D. about the mean value.)

The mean level of the femoral vein flow is, however, largely unaltered, a small but haphazard increase being produced which is relatively insignificant. Similar findings have been obtained in the field of pressure-assisted circulations where the mean flow is rarely, if ever, increased by the effects of intermittent compression (Hahnloser, Gallo, and Schenk, 1966; Mullens, Sugg, Kennelly, Jones, and Mitchell, 1971).

A technique has been developed by which the relatively steady venous flow in the leg may be made pulsatile without at the same time producing any overall increase in the limb perfusion. A clinical trial has been initiated to investigate the efficacy of this technique as a prophylactic measure against post-operative deep-vein thrombosis, and it is hoped that the results obtained will lead to a greater understanding of the role of haemodynamics in the initiation of deep-vein thrombosis.

Acknowledgements.—The authors are indebted to the Wates' and British Heart Foundations, without whose generous support this work would not have been possible. We would also thank Epac Ltd. for kindly loaning the Therepac controller used in this investigation.

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A NEW NON-INVASIVE TECHNIQUE FOR ASSESSMENT OF SUPERFICIAL FEMORAL ARTERY OBSTRUCTION

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SUMMARY

A transcutaneous technique is described utilizing two ultrasonic Doppler-shift flow-velocity meters simultaneously at sites down the arterial system of the leg in patients with superficial femoral disease. The change in shape of the blood-velocity/time wave-form over the cardiac cycle and the pulse propagation time between the two sites are measured. The transit time and change in pulse shape are used to assess limb viability. This method is compared with two other non-invasive techniques: whole-limb flow measured by a strain-gauge plethysmograph and with the systolic pressure difference between the arm and the calf. It is shown that as the pulse propagation time and the degree of damping of the blood-velocity/time wave-form increase, then limb perfusion decreases, and a nomogram is presented relating these parameters.

IN assessing patients for reconstructive vascular surgery to circumvent a femoral artery block, it is important to have some estimate of the dynamic capability of the collateral around the block and of the distal circulation in the whole limb. Current pre-operative techniques rest mainly on angiography, plethysmography, and brachial/calf pressure differences. Whilst angiography outlines the vessels and is probably essential if surgery is decided upon, it does involve some risk and discomfort as well as hospitalization. These factors mitigate against the procedure as a routine *initial* screening test. Plethysmography is essentially a whole-limb measurement and lacks vessel-specific information. Pressure-gradients down a particular vessel, as inferred from measurements with a thigh or calf cuff, can be misleading (Allen and Terry, 1969).

The transcutaneous Doppler-shift blood-velocity meter has made it possible to measure the velocity of blood-flow in almost any particular vessel atraumatically (Rushmer, Baker, and Stegall, 1966; Strandness, Schultz, Sumner, and Rushmer, 1967). The instrument and associated tape-recorder are portable and easily used, if necessary in the ward or office. The signals may be processed elsewhere to obtain a record of the arterial blood-velocity variation with time through each cardiac cycle (Gosling, King, Newman, and Woodcock, 1969). We have shown (Woodcock, 1970; FitzGerald, Gosling, and Woodcock, 1971a, b; Gosling, Dunbar, King, Newman, Side, Woodcock, FitzGerald, Keates, and MacMillan, 1971) that by measuring the damping of such an arterial velocity/time wave-form, together with the time of pulse propagation, along any section of an artery it is possible to produce a system of grading the dynamic capability of any collateral circulation present, and also to give a description of the vessel capability in cases of arterial disease in which there are no complete blocks.

The purpose of this paper is to present, in cases of superficial femoral artery obstruction, a comparison of the use of regional arterial blood-velocity/time wave-forms obtained transcutaneously by the ultrasound Doppler-shift technique with the assessment of limb viability given by occlusive strain-gauge plethysmography (hyperaemic flow) and that obtained by measuring the systolic pressure difference between the calf and the right arm. These techniques are all non-invasive. However, the information from the ultrasonic technique also compares favourably with that obtained from arteriograms (Woodcock, 1970).

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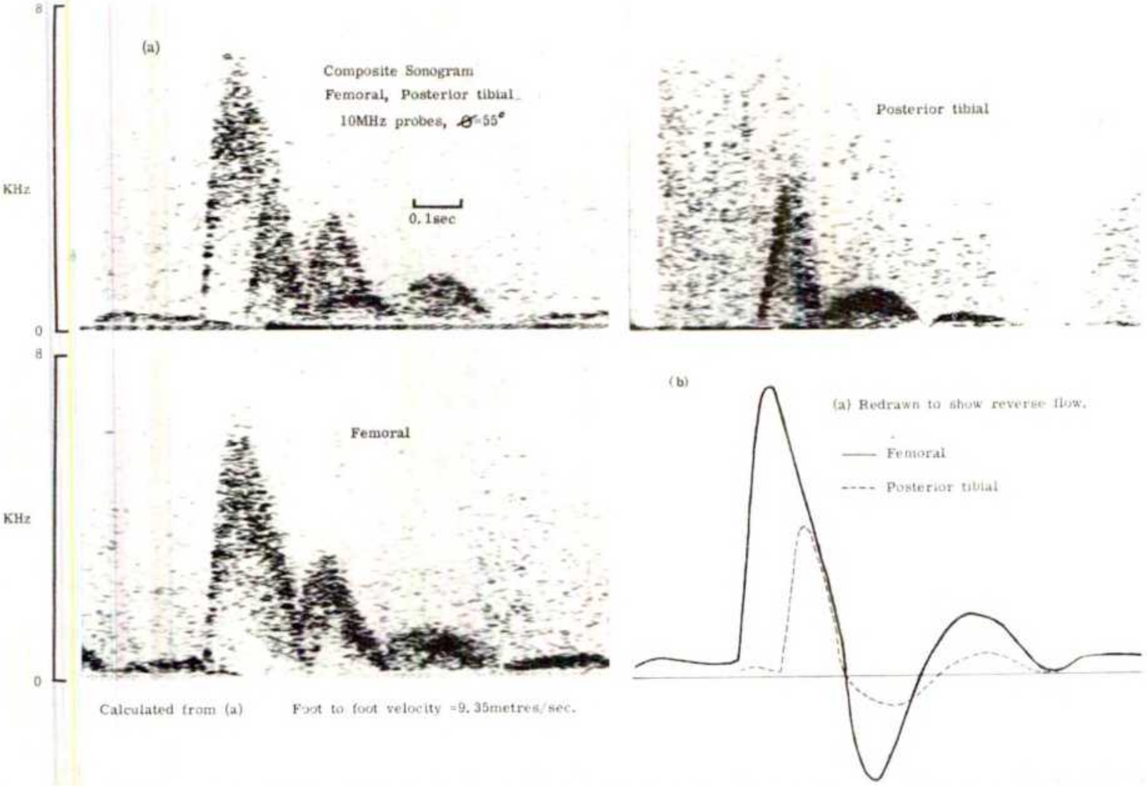

FIG. 1.—Sonograms displaying the frequencies present in the input signal (range 0–8 kHz) against time, with the trace blackening proportional to the amplitude. a, Measurement of 'foot-to-foot' propagation velocity between the femoral and posterior tibial arteries of a normal subject (aged 22 years). b, Arterial wave-forms redrawn from the sonograms to display reverse flow.

MATERIALS AND METHODS

Two Doppler-shift flow-velocity meters[*] are used simultaneously and successively at the following sites down the leg: the common femoral and popliteal arteries; the common femoral and posterior tibial arteries. Each instrument generates ultrasound at 5 MHz in a hand-held probe consisting essentially of two small $2{\cdot}5 \times 6{\cdot}0$-mm. piezo-electric crystals (PZT 5H), mounted coplanarly, acting as a transmitter and a receiver. The probe is placed lightly on the skin and the ultrasonic beam is coupled into the tissue via a suitable jelly. Ultrasound is then scattered by the moving blood-cells in any underlying vessel that the beam traverses. The radiation that is back-scattered towards the probe emerges through the skin and is detected by the receiver crystal. This back-scattered ultrasound is shifted in frequency by the velocity of the blood-cells according to the Doppler effect.[†] The frequency shift is in the audio-range for physiological blood velocities, e.g., 0–6 kHz for a velocity from 0 to 100 cm. per sec. with a beam inclined at about 30° to the vessel axis. Thus, an audio-frequency signal is generated which is proportional to the velocity of each scattering blood-cell within the incident beam.

Signals from any two arterial sites, generated as described above, are continuously recorded on a two-channel Revox 77K stereo tape-recorder and the frequency spectrum—corresponding to all the velocities present in the vessel—is displayed as a sonogram (*Fig.* 1) using a Kay Sonagraph.[‡] We have shown (Gosling and others, 1969) that the maximum frequency envelope of such a sonogram is closely similar in shape to the instantaneous average velocity/time wave-form as generated by an electromagnetic flowmeter, over a wide range of conditions, whereas this is not true of the output of any electronic averaging device, e.g., a zero-crossing frequency meter. Therefore, in all that follows we have used the maximum frequency envelope of the sonogram to represent the blood-velocity wave-form over the cardiac cycle. The transit time of the pulse wave between any two sites is simply measured by displaying the two signals simultaneously on a single sonogram. *Fig.* 1 shows such a sonogram obtained from the Doppler-shift signals from the common femoral and posterior tibial arteries in a normal healthy subject. This figure also illustrates the construction of the blood-velocity wave-form shape and the measurement of pulse propagation time.

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[*] Model 803 Parks Laboratory, Beavertron, Portland, Ogaren, U.S.A.

[†] $\Delta f = 2fv\cos\phi/c$, where Δf is the Doppler shift, f the frequency of the ultrasonic beam at angle ϕ to the axis of the vessel, v the velocity of the blood-cell (assumed parallel to the axis), and c the velocity of ultrasound propagation in tissue.

[‡] Model 6061B Kay Electric Co., Pine Brooks, New Jersey, U.S.A.

In order to compare the blood-velocity wave-forms obtained at different sites on the same patient, or from different patients, it is necessary to eliminate the unknown calibration factor—converting Doppler-shift frequency to blood-velocity—operating on the ordinate of each sonogram, i.e., some form of normalization is required. We have suggested (Gosling and others, 1971) that the shape of the blood-velocity/time wave-form over the whole of one cardiac cycle may be characterized by the pulsatility index (P.I.), which we have defined as the sum of the maximum oscillatory energy of the Fourier harmonics of the wave-form divided by the energy of mean forward flow (*see* Appendix). To obtain the Fourier harmonics the blood-velocity/time wave-form recorded at each site is digitized (in x and y) using a d-Mac electromagnetic pencil follower interfaced to an IBM 029 card punch which automatically assembles the data in a convenient format for computation. These data are then Fourier analysed

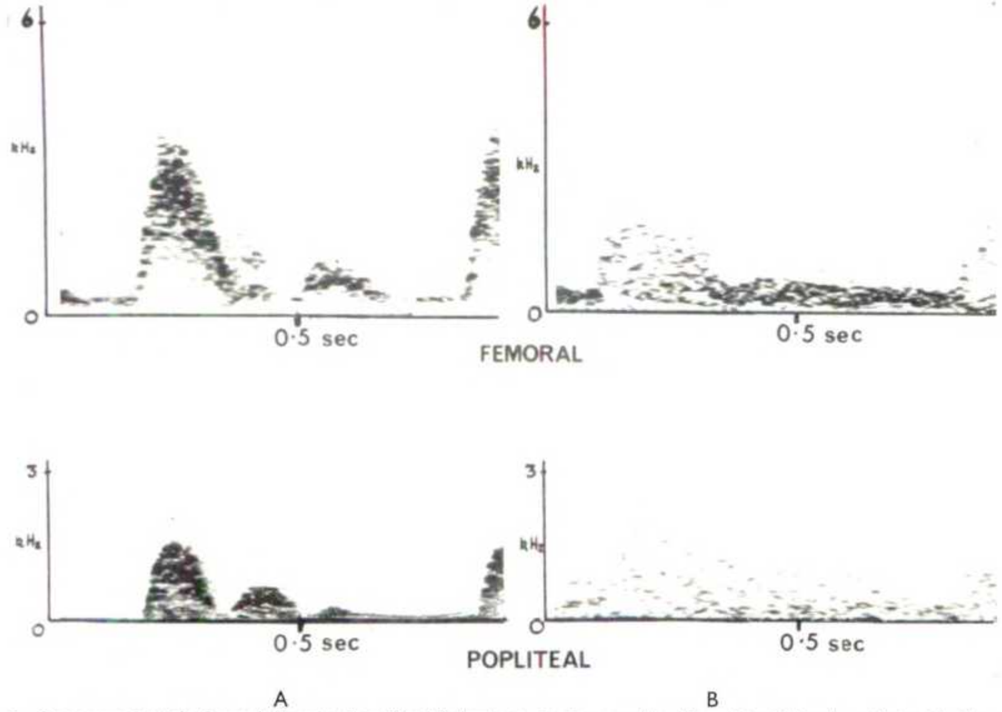

FIG. 2.—Sonograms from the femoral (above) and popliteal (below) arteries of a normal healthy subject (A) and a patient with atheromatous involvement of the iliac artery and a superficial femoral block (B). The P.I. values of these waveforms are: Normal: femoral P.I. = 7·0; popliteal P.I. = 7·5; hence Δ = 0·9. Abnormal: femoral P.I. = 1·6; popliteal P.I. = 0·6; hence Δ = 2·7.

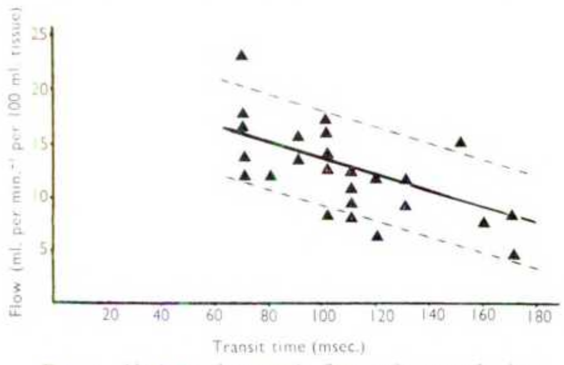

FIG. 3.—Maximum hyperaemic flow against transit time. The regression line is shown with dashed lines representing ± 1 standard deviations of the mean. The correlation coefficient, $r_s = 0·57$ and the level of probability $P_s \leqslant 0·01$.

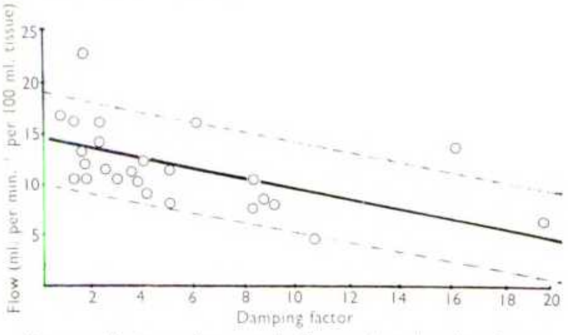

FIG. 4.—Maximum hyperaemic flow against damping factor, $r = 0·76$ and $P \leqslant 0·01$.

by an IBM 360 computer using a program written by Gosling and Goldring (1967–8).

Damping of the blood-velocity/time wave-form is quantified by the damping factor (Δ), which is defined as the P.I. value of the proximal velocity/time wave-form divided by the P.I. value of that at the distal site. In this way a single number specifies the degree of damping introduced by a section of the arterial system. The extent of the damping in an obstructed leg (abnormal) may be compared with the wave-forms from a normal, healthy subject in *Fig.* 2. In the diseased leg the input wave-form at the femoral artery is less pulsatile, i.e., more damped, than in the normal leg. This indicates atheromatous involvement proximal to the measuring site, i.e., in the aorto-iliac segment. The wave-form at the popliteal artery is hardly pulsatile at all in the diseased leg, i.e., it is considerably more damped than the femoral pulse in this leg. This damping, in addition to the longer than normal transit time between the two sites, indicates a complete block of the superficial femoral artery. This was confirmed by arteriography.

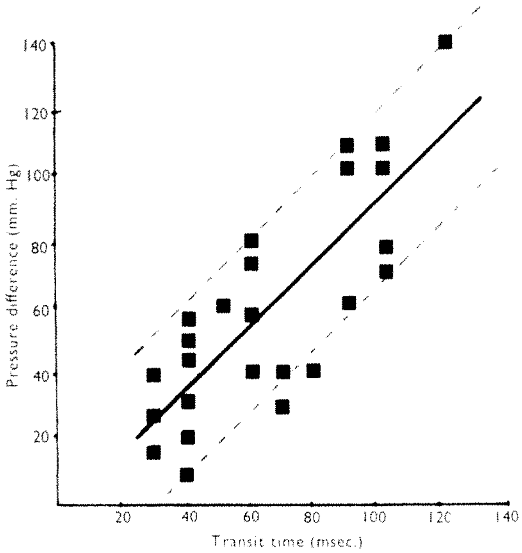

FIG. 5.—Pressure difference against transit time; $r = 0{\cdot}76$ and $P \leqslant 0{\cdot}01$.

Whole-limb perfusion was measured directly with a strain-gauge plethysmograph placed in the mid-calf position and a thigh occlusion cuff. Maximum flow was recorded under conditions of reactive hyperaemia produced by 200 mm. Hg occlusion pressure in the thigh cuff for 5 minutes while the patient exercised. As an indirect method of assessing limb perfusion the systolic pressures in both the calf and the right arm were also measured. The sphygmomanometer cuff was placed just below the knee and the posterior tibial pulse was detected by means of the Doppler-shift velocity meter. The cuff was inflated until the signal disappeared and deflated until the first flow signal was heard. This pressure is then taken as the systolic pressure in the calf. Similarly, for the arm pressure the flow signal is detected at the brachial artery. It is interesting to note that this method gives values consistently higher by about 10 mm. Hg than those obtained by listening for Korotkoff sounds.

RESULTS

Measurements were made on 25 subjects with occlusive disease of the superficial femoral artery. *Fig.* 3 shows the maximum flow in reactive hyperaemia plotted against the pulse transit time measured in conditions of normal resting flow with a supine patient. The regression line and correlation coefficient were calculated and it was found that the flow (F) in ml. per min. per 100 ml. tissue is related to the transit time (T) by the following relationship:—

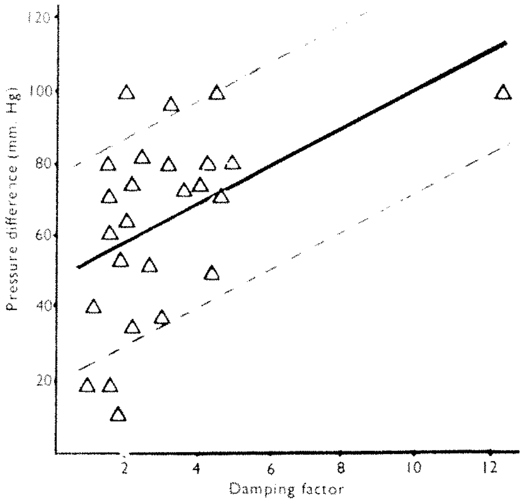

FIG. 6.—Pressure difference against damping factor; $r = 0{\cdot}4$ and $P \leqslant 0{\cdot}01$.

$$F = -0{\cdot}08T + 20{\cdot}4.$$

The results are significant to a level of probability of $P \leqslant 0{\cdot}01$.

Fig. 4 shows the maximum flow plotted against the damping factor. The regression line and the correlation coefficient were calculated and the flow is related to the damping factor by

$$F = -0{\cdot}4\Delta + 14,$$

with a level of probability of $P \leqslant 0{\cdot}01$.

In *Figs.* 3 and 4 the transit times and damping factors were measured between the common femoral and posterior tibial arteries, whilst the 'maximum flow' was measured with a strain-gauge in the mid-calf position. If the limb has additional occlusions distal to the gauge, then a longer transit time and a greater damping factor will be introduced and may therefore account for the spread of the data.

The difference, P_s, between the systolic blood-pressure measured in the arm and the systolic blood-pressure measured in the calf distal to the arterial occlusion is related to the transit time and damping in *Figs.* 5 and 6. The regression lines and correlation coefficients were calculated in both cases, giving

$$P_s = 0{\cdot}96T - 4 \quad \text{and} \quad P_s = 5{\cdot}4\Delta + 48.$$

Both sets of results are significant to a level of probability of $P \leqslant 0{\cdot}01$. These results show that as the pressure drop across the collateral increases the transit time and damping factor also increase.

DISCUSSION

The results shown here indicate a good correlation between the ultrasonic technique and the two other non-invasive methods which are frequently used to estimate the extent of peripheral arterial disease. In addition, the linear relationship found between Δ and *T* derived from the ultrasound measurements and the flow indicated by plethysmography demonstrates that it is possible to use Δ and *T* to grade limbs to levels of hyperaemic flow between 10 and 15 ml. per min. per 100 ml. tissue and to below 10 ml. per min. per 100 ml. tissue. FitzGerald, Keates, and MacMillan (1971) have shown that the maximum blood-flows in conditions of reactive hyperaemia can be divided arbitrarily into two categories which separate the more severely affected limbs, namely, flows above and below 10 ml. per min. per 100 ml. tissue. Flows above 10 ml. per min. per 100 ml. tissue are indicative of an exercise tolerance of about 250 m. or more, and flow rates below this level indicate exercising tolerance of about 50 m.

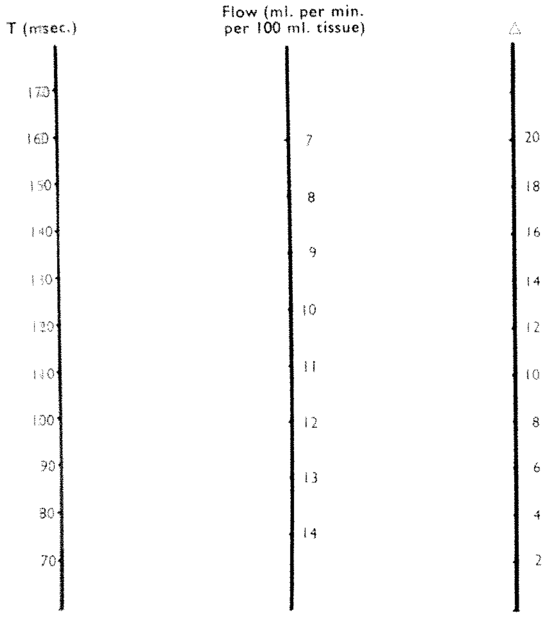

FIG. 7.—Nomogram relating the transit time and damping factor between the common femoral and posterior tibial arteries with the maximum hyperaemic flow measured in the mid-calf.

A nomogram has been constructed using the regression lines obtained for flow *F* plotted against *T*, and *F* against Δ. Thus, if the damping factor and transit time over the common femoral and posterior tibial section are measured in a patient with disease of the superficial femoral artery the flow-rate in the mid-calf region can be inferred (*Fig.* 7).

The use of the nomogram is illustrated by the following example. The transit time over the femoral and posterior tibial segment was 130 msec. for a patient with a superficial femoral block, and the damping factor over the segment was 2·5. A straight line drawn from the 130-msec. point on the *T*-axis to the 2·5 point on the Δ-axis intersects the flow-rate axis at 12·0 ml. per min. per 100 ml. tissue. The hyperaemic flow-rate actually measured with the strain-gauge was 11·5 ml. per min. per 100 ml. tissue. The standard deviation of the regression lines in *Figs.* 3 and 4 is ± 4·0 ml. per min. per 100 ml. tissue. Therefore, about 70 per cent of any flow values derived from the nomogram may be expected to lie within these limits.

COMMENT

From the foregoing we would suggest that values of Δ and *T* derived from the ultrasonic measurements can be used not only to grade the collateral arteries and to infer their elastic state, as reported elsewhere (Woodcock, 1970; FitzGerald and others, 1971a; Gosling and others, 1971), but also to indicate indirectly the actual limb perfusion. This combination of vessel-specific and whole-limb information obtained atraumatically and non-invasively from a supine resting patient makes the ultrasonic technique an attractive one for initial screening and repeated examination of patients with peripheral arterial disease.

APPENDIX

The instantaneous blood-velocity, $\bar{v}$, averaged across the cross-section of any vessel, is a function of time, and may be written $\bar{v}(t)$. One of the most simple and elegant ways of mathematically describing such a complex wave-form was first pointed out by Fourier in 1892. Thus $\bar{v}(t)$ may be regarded as a steady forward flow-velocity on which is superimposed a purely sinusoidal oscillatory flow consisting of a number of harmonic components, the first having the same period as the cardiac cycle, the second, half of this period, the third harmonic, one-third of the period, and so on. It should be noted that the net flow over one cardiac cycle owing to these oscillatory harmonics is zero. They are, however, directly related to the elasticity of the system, hence their importance.

Therefore we may write

$$\bar{v}(t) = V_0 + \sum_{r=1}^{r=n} V_r \cos(rwt - \theta_r), \tag{1}$$

where V_0 is the mean forward flow over one cardiac cycle, $V_r \cos(rwt - \theta_r)$ is the *r*th harmonic of flow-velocity and varies with time, *t*, over the cardiac cycle of period $2\pi/w$ seconds, V_r is the amplitude and θ_r the phase angle of this harmonic, and n is the number of harmonics required to give a true representation of $\bar{v}(t)$. In most experimental determinations of $\bar{v}$ the noise level of the apparatus is reached by $n \sim 10$.

In the work presented here the maximum Doppler-shift signal $\Delta \wedge f$ at any instant is taken as being proportional to $\bar{v}$, and we examine the maximum frequency envelope over one cardiac cycle, $\Delta \wedge f(t)$. Thus, we may write $\bar{v}(t) = \Delta \wedge f(t) . C$, where C is some constant of the apparatus/patient arrangement. Fourier analysis of the $\Delta \wedge f(t)$ wave-form then allows us to write

$$\begin{aligned} \bar{v}(t) &= \Delta \wedge f(t) . C \\ &= C . \Delta \wedge f_0 + \sum_{r=1}^{r=n} \mathrm{C} . \Delta \wedge f_r \cos(rwt - \theta_r). \end{aligned} \tag{2}$$

Thus, if we define P.I. as the sum of the maximum oscillatory energy of the Fourier harmonics of the flow-velocity wave-form divided by the energy of mean forward flow we have

$$\text{P.I.} \equiv \sum_{r=1}^{r=n} V_r^2 \Big/ V_0^2,$$

and on equating (1) and (2),

$$\text{P.I.} = \sum_{r=1}^{r=n} \Delta \wedge f^2 r \Big/ \Delta \wedge f_0^2,$$

the calibration constant C having cancelled out, making P.I. a function of the maximum frequency envelope which is independent of the calibration constant.

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THE FATE OF AORTIC VALVE HOMOGRAFTS

AN EXPERIMENTAL STUDY

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SUMMARY

Segments of homograft aortic valve cusp and aortic sinus wall have been inserted as patches in the abdominal aortic wall of sheep. The donor valves were prepared in one of three ways: (1) fresh valves, (2) freeze-dried valves sterilized with antibiotics and ethylene oxide, and (3) valves which had been cooled at a controlled rate to −70° C. in a medium containing the cryoprotective agent, dimethyl sulphoxide. Histological examination of the implanted tissue obtained at intervals up to 2 years failed to show survival of any donor cells, whichever method of preparation had been used. The elastic tissue in the freeze-dried series had become calcified by 2 years, and although valves prepared in this way appeared to elicit no immunological response, both the fresh and frozen tissue were infiltrated by lymphocytes and plasma cells by 2 weeks. This round-cell infiltration reached a peak at 4 weeks and then subsided again. The response to fresh valves was more marked and more prolonged than that to frozen valves.

WHETHER it is better to replace a diseased aortic valve with a prosthesis or a homograft remains undecided (Duvoisin and McGoon, 1969). Homografts have the advantage of a central flow path and a negligible incidence of thrombo-embolism, but problems of procurement, sterilization, and storage have restricted their popularity. Many methods of sterilizing and storing homografts destroy the cells of the valve, leaving a dead biological prosthesis (Hudson, 1966; Smith, 1967). Moreover, the elastic and collagen structures of the valve are often weakened by these same methods (Harris, Kowalik, Marks, and Malm, 1968). Dimethyl sulphoxide (DMSO) is a cryoprotective agent which has been used successfully to preserve cells and tissues at low

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temperatures (Smith, 1961, 1965; Farrant, 1965a, b). This paper compares the long-term fate of aortic valve homografts in sheep; the valves which were used were either fresh, freeze-dried, or frozen in a medium containing DMSO.

MATERIALS AND METHODS

Segments of aortic valve of sheep consisting of a separate cusp and the adjacent ascending aortic wall were prepared in one of three ways:—

1. Fresh valves were obtained aseptically from sacrificed animals and were placed in normal saline at room temperature for approximately 45 minutes before being transplanted.

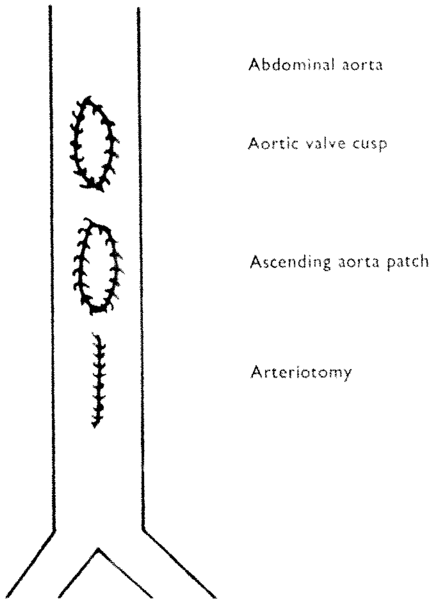

FIG. 1.—Diagram showing the types of patches which were inserted in the abdominal aorta.

2. Valves obtained from freshly sacrificed animals were either processed immediately or stored at −12° C. After trimming, the valve segments were soaked in normal saline containing penicillin, streptomycin, and nystatin for 24 hours at 4° C. before being rinsed with saline and placed in freeze-drying tubes. The tubes were filled with a mixture of ethylene oxide, 5 per cent, and carbon dioxide, 95 per cent, and the segments were left in the gas at 4° C. for a further 24 hours. After this, the tissue was flash-frozen and connected to a freeze-drying machine for 24 hours. The sealed tubes were stored at room temperature until required, when the material was reconstituted by adding sterile water at room temperature (Longmore, Lockey, Ross, and Pickering, 1966).

3. Fresh hearts were obtained aseptically immediately after death and valve segments were incubated for 30 minutes at 20° C. in a Pyrex tube containing a tissue-culture medium (Parker 199) with penicillin and streptomycin, 25 per cent calf serum, and 10 per cent DMSO. The tubes were heat-sealed and cooled at a rate of 1° C. per minute to −15° C., then at 5° C. per minute to −40° C., and then as rapidly as possible to −70° C., at which temperature the tissue was stored until required. The valve was reconstituted by warming it rapidly in a water-bath at 40° C. until all the ice had melted. The ampoule was opened aseptically and the concentration of DMSO was reduced in stages.

Young Clun Forest Cross sheep were used as the recipient animal. Under general anaesthesia an extraperitoneal approach to the abdominal aorta was made. Using a shunt within the aortic lumen to maintain distal arterial blood-flow, segments of the donor cusp and the adjacent aortic wall were inserted as patches to close holes cut in the aortic wall (*Fig.* 1). Each animal received one patch of aortic cusp and one patch of aortic wall from the same donor prepared in one of the three ways already described. No anticoagulants, steroids, or cytotoxic drugs were used.

Animals were sacrificed at 2, 4, and 8 weeks, 6 months, and 1 and 2 years after operation. On recovery of the patches, special note was made of the degree of periarterial reaction, the presence of aneurysms of the patches, the state of the intima, and whether any thrombus was present. The patches were examined histologically for general structural appearance and degree of cellular infiltration, the presence of calcification, and pyroninophilic cells. Bacterial infection was excluded with Gram's stain.

RESULTS

Eighty-eight sheep were operated on over a period of 16 months. Nine animals died either at operation or within 12 hours of operation, and 6 animals were found to be paraplegic. The combined operative mortality and morbidity in the first 20 operations was 55 per cent, and in the next 68 operations 5·8 per cent.

Gross Appearance.—*Table I* shows the incidence of gross aneurysm and abnormal dilatation of the cusp and aorta patches in the three groups at different time intervals. The freeze-dried patches show an increasing tendency to fail the longer they have been in place, while some of the fresh and frozen patches failed early. Flecks of fibrin and some areas of platelet thrombi were seen on the intimal surfaces of a few patches in the early weeks after transplantation. Thrombosis of the aorta occurred in only 3 animals, 2 of which had received freeze-dried patches, all of which had become aneurysmal. In those animals free of aneurysm formation, peri-adventitial reaction in the form of a thick layer of fibrous tissue was present in some specimens from all groups in the early weeks. The reaction was most marked in the fresh series.

Histological Appearance.—It was difficult to identify the cusp patches microscopically in many specimens even at 2 weeks, and attention was concentrated on changes in the aorta patches. Very few donor cells were seen in the freeze-dried patches at 4 weeks and those that remained were often pyknotic. Loss of cellularity was also noted in the fresh and frozen patches, but although the process continued at a slower rate than in the freeze-dried series all the patches were completely acellular by 6 months. Careful examination of the aorta patches for evidence of fibroblast proliferation failed to show convincing evidence that active tissue repair was being carried out in any of the three series of patches. Areas of collagen deposition, however, were seen in all specimens as part of the reparative process, becoming organized at the host–graft junction and on both the adventitial and intimal surfaces of the patches. New elastic fibrils were also seen in these areas, but no definite elastic lamina was ever formed. The surface of the graft in contact with the blood-stream rapidly became covered with a layer of fibroblast-like cells, and, later, collagen fibres were laid down in this pseudo-intima. Elastic tissue degeneration steadily progressed in all three groups of patches, and no particular method of preparation appeared to be advantageous. Calcification occurred almost exclusively in the freeze-dried series, all the specimens showing calcium deposits in the elastica of the aorta patches at 2 years (*Fig.* 2). In both the fresh and the frozen series the patches were surrounded by pyroninophilic lymphocytes and plasma cells by 2 weeks. This round-cell accumulation reached a peak of activity by 4 weeks and then subsided again (*Fig.* 3). The response to fresh valves was both more marked and more prolonged than that to frozen valves, but very little activity was present in either the fresh or frozen group after 6 months. Valves in the freeze-dried series did not stimulate round-cell reaction.

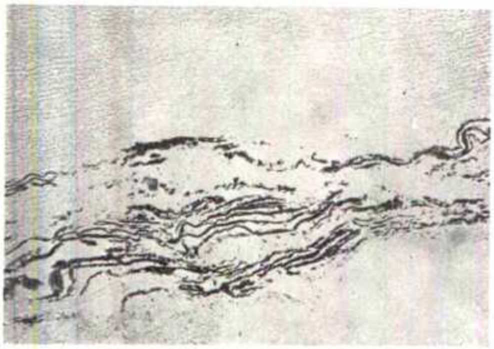

FIG. 2.—Calcification in a freeze-dried aorta patch at 2 years. Von Kossa. (×64.)

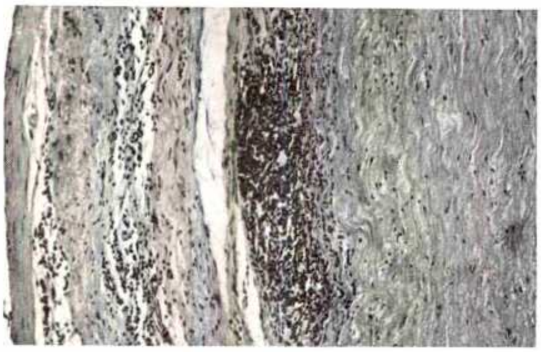

FIG. 3.—Cluster of lymphocytes and plasma cells in a frozen aorta patch at 8 weeks. H. and E. (×46.)

Table I.—INCIDENCE OF PATCH DILATATION AND ANEURYSM IN FRESH, FREEZE-DRIED, AND FROZEN AORTIC VALVE PATCHES

TYPE OF GRAFT	DURATION OF EXPOSURE											
	2 Weeks		*4 Weeks*		*8 Weeks*		*6 Months*		*1 Year*		*2 Years*	
	Patch Dilatation	Aneurysm	Patch Dilatation	Aneurysm	Patch Dilatation	Aneurysm	Patch Dilatation	Aneurysm	Patch Dilatation	Aneurysm	Patch Dilatation	Aneurysm
Cusp patches												
Fresh	0	0 (3)*	0	0 (4)	3	0 (4)	0	1 (4)	0	1 (4)	1	1 (3)
Freeze-dried	0	0 (3)	1	0 (1)	0	0 (4)	0	0 (4)	1	1 (4)	1	1 (4)
Frozen	0	0 (4)	1	0 (3)	1	0 (3)	1	0 (4)	0	1 (4)	0	2 (4)
Aorta patches												
Fresh	0	0 (3)	0	0 (4)	2	0 (4)	0	0 (4)	0	0 (4)	0	0 (3)
Freeze-dried	0	0 (4)	1	0 (4)	0	0 (4)	0	0 (4)	1	1 (4)	0	1 (4)
Frozen	0	0 (4)	1	0 (3)	1	0 (3)	1	0 (4)	0	1 (4)	1	1 (4)

* The number of patches in each group is given in parentheses in the Aneurysm columns.

DISCUSSION

By placing segments of aortic valve cusp and ascending aortic wall as patches in the abdominal aorta of sheep we have used a simple model in order to obtain material for histological examination over a 2-year period. For all three methods of preparation, fresh, freeze-dried, and frozen, there is no definite histological evidence that any donor cells survive homotransplantation. Previous work has established that sterilizing with ethylene oxide and then freeze-drying arterial segments destroys the cells (Creech, DeBakey, Cooley, and Self, 1954). It has also been reported that single-leaflet aortic valve replacements in dogs retained their cellularity over a period of 2½ years (Cleveland, Madge, and Lower, 1967), and that at 12 months, female (donor) cells were present on culture from the free edge of the grafted tissue (Barnes, Mohri, and Merendino, 1968). The reason that we have been unable to confirm this is probably due to the positioning of our material as patches in the aortic wall, and also due to the difficulty in identifying the site of the cusp patch after a period of time. We have also been unable to show histologically the persistence of viable cells in fresh-tissue patches which were grafted into the recipient animal within 45 minutes of sacrifice. The aorta patches were acellular by 6 months, and although an infiltration of a few elongated cells between the elastic fibres was apparent at 1 and 2 years there was little evidence of any new elastic or collagen fibres being laid down actually in the patches, and the elongated cells were almost certainly host cells which had migrated from the edge of the patch.

The calcification of freeze-dried arterial homografts led to this method of preparation being abandoned in the late 1950's (Creech, Debakey, Cooley, and Halpert, 1956; Szilagyi, McDonald, Smith, and Whitcomb, 1957; DeWeese, Woods, and Dale, 1959), and the calcification of human aortic valve homografts prepared in a similar way was forecast by Lord Brock (1968) and has since been confirmed (Missen and Roberts, 1970). In our series, calcification occurred almost exclusively in the freeze-dried series, and all the specimens showed deposits of calcium in the aorta patches at 2 years. None of the cusp patches became calcified. Elastic tissue degeneration was steadily progressive with time in all three groups of aorta patch, and no particular method of preparation was advantageous.

Patches in the freeze-dried series elicited very little in the way of immunological activity, whereas there was a brisk immunological response, which was well developed at 2 weeks, reaching a peak at 4 weeks, and then subsiding again, in both the fresh and frozen series. The response to fresh valves was more marked and more prolonged than that to frozen valves, but very little activity was present in either the fresh or frozen group after 6 months. Complete rejection, however, does not appear to have taken place, as many patches survived the period at which immunological activity would have been at its height.

Although no direct evidence of the viability of the frozen patches is presented, the immunological response to homografts of aortic valves preserved in this way is so similar to that stimulated by fresh homografts that it is possible that the frozen grafts may have been viable at the time of transplantation. However, as it is unlikely that freshly transplanted cells survive, there seems little to be gained from transplanting living valves until tissue-matching techniques are used in the selection of donor valves or unless the immunological response is suppressed with immunosuppressive drugs. More emphasis needs to be placed on finding ways of sterilizing and preserving these biological prostheses which do not seriously reduce the durability and functional behaviour of homograft valves.

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SHORT NOTES OF RARE OR OBSCURE CASES

CROSSED RENAL ECTOPIA WITHOUT FUSION ASSOCIATED WITH CARCINOMA OF THE RENAL PELVIS

A CASE REPORT

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SUMMARY

A case of crossed renal ectopia complicated by hydronephrosis, calculus, pyelonephritis, and tumour is described. The aetiology of the complications is discussed and the incidence of tumours in non-fused, crossed renal ectopia is described.

CROSSED renal ectopia is characterized by the kidney being on the opposite side to normal and its ureter crossing the midline to enter the bladder on the correct side. In 57 reported cases the ectopic and normal kidney had not fused and in 3 of these cases the ectopic kidney contained a malignant tumour. The case presented here is the fourth case of malignant tumour in a non-fused, crossed ectopic kidney.

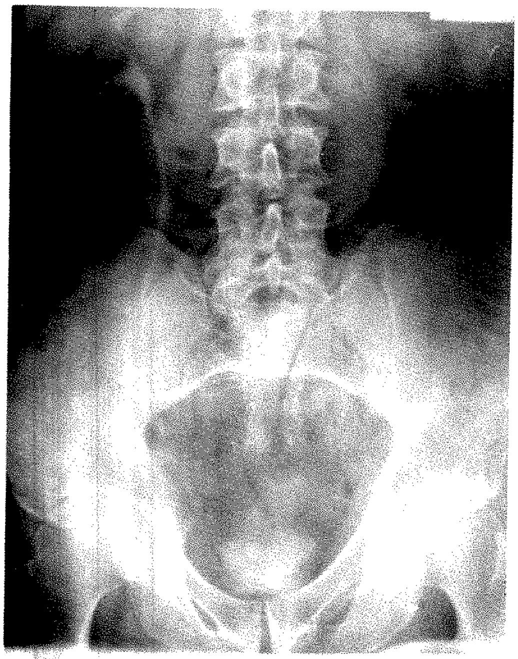

FIG. 1.—Excretion urogram to show a normal right kidney but no concentration in the left kidney.

CASE REPORT

Mr. A. E. Y., a 61-year-old builder and undertaker, was admitted in July, 1969, for investigation of 2 months' persistent haematuria in which blood was mixed with the urine. There was associated discomfort in the left iliac fossa, but no colic, loin pain, dysuria, or pyrexia. His general health was good but 6 months previously he had passed a small calculus per urethra. On physical examination the patient was obese and no organs or masses were felt; the blood-pressure was 170/110 mm. Hg.

INVESTIGATIONS.—Microscopic examination of the urine showed 1 white and 250 red blood-cells per high-power field but the urine was bacteriologically sterile. Blood-urea was 29 mg. per 100 ml. and serum electrolytes were normal. Serum uric acid was 6·6 mg. per 100 ml., corrected serum calcium 9·5 mg. per 100 ml., inorganic phosphate 3·1 mg. per 100 ml., and skeletal radiology

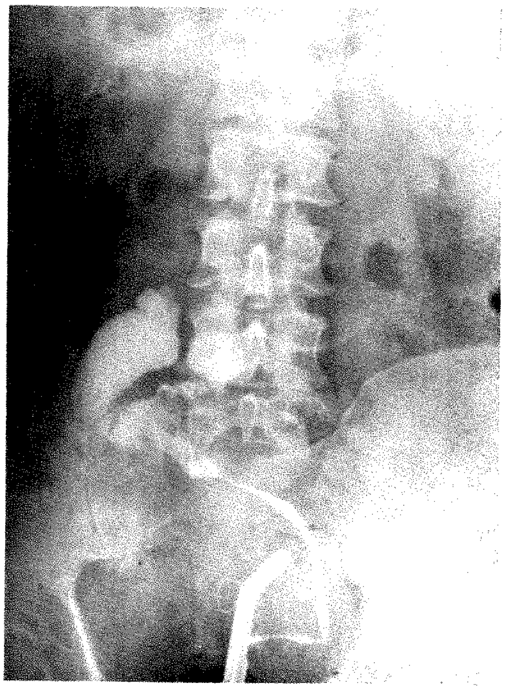

FIG. 2.—Left bulb ureterogram showing crossed ectopia of the left kidney. The ectopic kidney is pyelonephritic and hydronephrotic with a filling defect in the pelvi-ureteric junction.

showed no evidence of hyperparathyroidism. Haemoglobin was 99 per cent, the white-cell count 11,500 (with a normal differential), and the E.S.R. was 3 mm. per hour. Chest radiography was normal and excretion urography (*Fig.* 1) showed a normal right kidney but no concentration in the left kidney. Cystoscopy under general anaesthesia revealed a normal bladder and ureteric orifices. A left bulb ureterogram (*Fig.* 2) unexpectedly demonstrated crossed renal ectopia with the ectopic kidney lying in front of the right sacro-iliac joint. The kidney was small and pyelonephritic and there was a filling defect in the pelvi-ureteric junction, suggestive of a tumour or a blood-clot. A right transfemoral aortogram was carried out but failed to demonstrate the blood-supply to the abnormal kidney.

The ectopic kidney was explored through an oblique muscle-cutting incision in the right iliac fossa. An extraperitoneal approach was used and the kidney was found lying over the pelvic brim but not fused to the normal right kidney. It was small, but hydronephrotic, with a solid mass palpable at the pelvi-ureteric junction. The vascular pedicle descended from above but the origin was not clearly defined. The blood-vessels were ligated, the kidney removed, and the ureter was traced across the midline behind the mesorectum and was excised. Because of the patient's obesity a Pfannenstiel incision was necessary to remove the remaining 6 cm. of extravesical ureter, the intramural part of the ureter, and a cuff of bladder. His postoperative convalescence was unremarkable except for some infection of the nephrectomy wound. His subsequent follow-up will include urine cytology and cystoscopy.

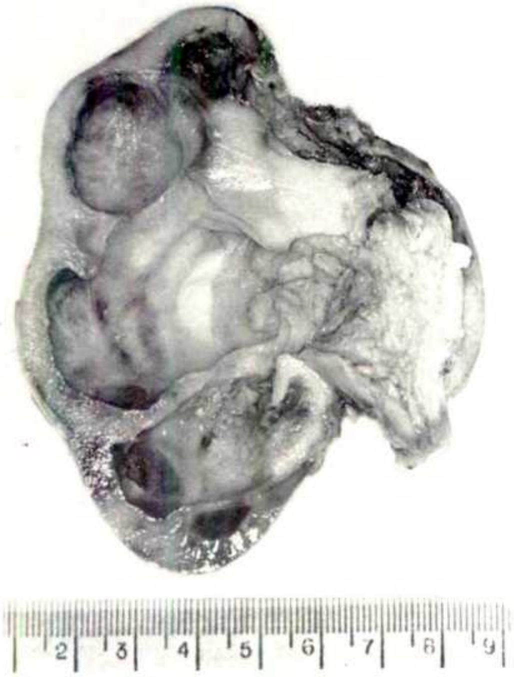

FIG. 3.—Operation specimen showing a tumour of the renal pelvis.

Table I.—INCIDENCE OF CROSSED RENAL ECTOPIA WITHOUT FUSION

Author	*No. of Cases*
McDonald and McClellan (1957)	40
Pathak (1965)	7
Caine (1956)	1
Weiss, Maloney, and Beland (1965)	1
Hurley and Kelley (1969)	1
Dworin (1969)	1
Yui and Ojeda (1964)	1
Wadskier (1967)	1
Awstric and Jankau (1965)	1
Kovalkovits and Ertsey (1966)	1
Castro and Ashken (1972)	1
Total	56

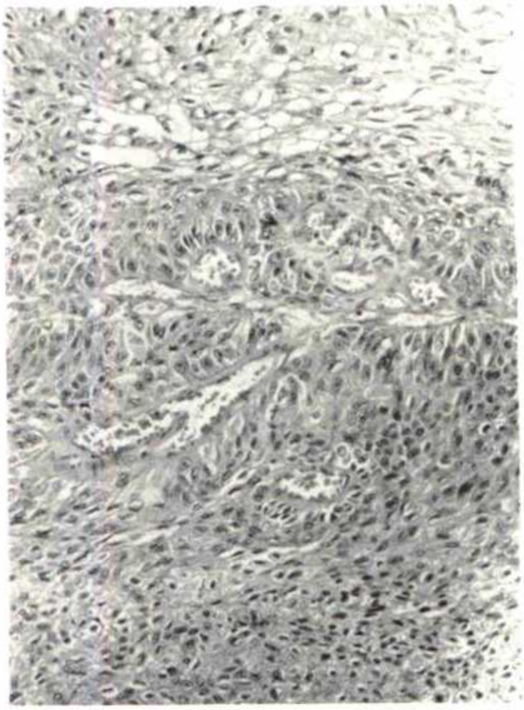

FIG. 4.—Histological section showing tumour of the renal pelvis. H. and E. (× 240).

PATHOLOGY.—The kidney was small, 9·5 × 5 × 3·5 cm. (*Fig.* 3), with reduction of renal substance and corresponding caliceal dilatation. The dilated renal pelvis contained soft grey tumour which also covered part of the caliceal mucosa and there were also tiny papillary nodules on the mucosa of the upper ureter. Histological examination (*Fig.* 4) showed a part solid and part papillary, transitional-cell carcinoma with foci of squamous differentiation. Mitoses were not very numerous but there was superficial invasion. There was no macroscopical or histological evidence of tumour in the lower ureter and microscopic examination of the kidney showed the changes of pyelonephritis.

DISCUSSION

Crossed renal ectopia was reported once in 7000 autopsies by Kretschmer (1925) and once in 5300 pyelographic examinations by Takahashi and Iwashita (Abeshouse, 1947). In most instances the normal and ectopic kidneys fuse to form one of the anatomical abnormalities described by Amesur and Singh (1963). Abeshouse (1947) reviewed the literature and found 337 such cases and later McDonald and McClellan (1957) found another 41.

Crossed renal ectopia without fusion accounts for only 10 per cent of cases (Malament and Majnarich, 1960). McDonald and McClellan (1957) found 40 cases and Pathak (1965) added a further 7. Since these reports 9 further cases have been described including the present one (*Table I*). Crossed renal ectopia of a solitary kidney has been reported in only 11 cases (Dworin, 1969).

Crossed ectopic kidneys are subject to more disease than normal kidneys (McDonald and McClellan, 1957), and the complications include infection, calculus formation, volvulus (Ranshoff, 1920), hydronephrosis (Diaz, 1953), giant hydronephrosis (Hurley and Kelley, 1969), and tumour (Lee, 1949). The present case possibly demonstrates four complications, namely, pyelonephritis, calculus formation, hydronephrosis, and tumour (it is, of course, not possible to be certain that the calculus came from the ectopic kidney).

Table II.—INCIDENCE OF TUMOUR IN CROSSED RENAL ECTOPIA WITHOUT FUSION

SEX	ECTOPIC SIDE	HISTOLOGY	AUTHOR	NO. OF CASES
M.	Left	Adenocarcinoma	Patch (1937)	1
M.	Right	Adenocarcinoma	Langworthy and Drexler (1942)	1
F.	Right	Squamous carcinoma of the pelvis	Lee (1949)	1
M.	Left	Squamous and transitional carcinoma of the pelvis	Castro and Ashken (1972)	1

Only 3 previous cases of malignant tumour in a non-fused, crossed ectopic kidney have been described (*Table II*); 2 of these were adenocarcinomas and 1 a squamous carcinoma of the renal pelvis. In the present case the tumour was in the renal pelvis and the histology was a mixture of squamous and transitional epithelia. The association of the latter with renal calculi is well established (Oberkircher, Straubitz, and Blick, 1951).

Hydronephrosis is the commonest complication of ectopic kidneys (Diaz, 1953), owing possibly to adherent blood-vessels or extrinsic pressure on abnormally placed ureters. This predisposes to infection and calculus formation, and the latter may cause squamous metaplasia and tumour of the renal pelvis. It is submitted that such a sequence occurred in the present case.

Crossed renal ectopia may be associated with spina bifida occulta (King and Holland, 1964) and solitary crossed ectopic kidney was associated with other congenital abnormalities in 9 of the 11 cases described by Dworin (1969). No congenital abnormality was found in the present case.

ADDENDUM

On follow-up Mr. A. E. Y. has had no urinary symptoms but in July, 1970, cytological examination of his urine showed neoplastic cells. Cystoscopy confirmed multiple foci of papillary tumour on the left bladder wall extending down to the bladder neck, and they were treated by transurethral resection and cystodiathermy, histology showing low-grade transitional-cell carcinoma.

A further check cystoscopy in October, 1970, showed further papillary tumour on the left bladder wall which responded well to cystodiathermy, but histology now showed evidence of superficial invasion in places so a course of cobalt-60 teletherapy was given (tumour dose 2200 rad). Further check cystoscopies have not revealed any further tumour, the last cystoscopy being in September, 1971.

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AORTIC ANEURYSM FOLLOWING EXTERNAL CARDIAC MASSAGE

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SUMMARY

Various hazards of external cardiac massage, such as rib fracture and bone-marrow emboli, are well known. This paper describes an unusual hazard, aortic aneurysm. The mechanism of production of this lesion differs in several respects from that of most closed-chest aortic lesions.

EXTERNAL cardiac massage must be vigorous to be successful, and this implies a high risk of complications, a risk which is usually acceptable under the circumstances. The complications have been reported by Barringer, Salzman, Jones, and Friedlich (1961), Jude, Kouwenhoven, and Knickerbocker (1961), Himmelhoch, Dekker, Gazzaniga, and Like (1964), Silberberg and Rachmanninoff (1964), Smith and Anthonisen (1965), Linko, Koskinen, Siitonen, and Ruosteenoja (1967), Roser (1967), Poulsen (1968), Fletcher (1969), and Jeresaty, Godar, and Liss (1969). Rib fractures and bone-marrow emboli have commonly been found. Other complications which have been less frequently reported have included traumatic lesions variously involving the pericardium, the pleural cavities, the peritoneum, and the abdominal viscera. Four cases of transient oliguria, 1 case of laceration of the diaphragm, and 3 cases of permanent severe brain damage have also been recorded as complications. Aortic aneurysm formation as a hazard of external cardiac massage has not been reported before.

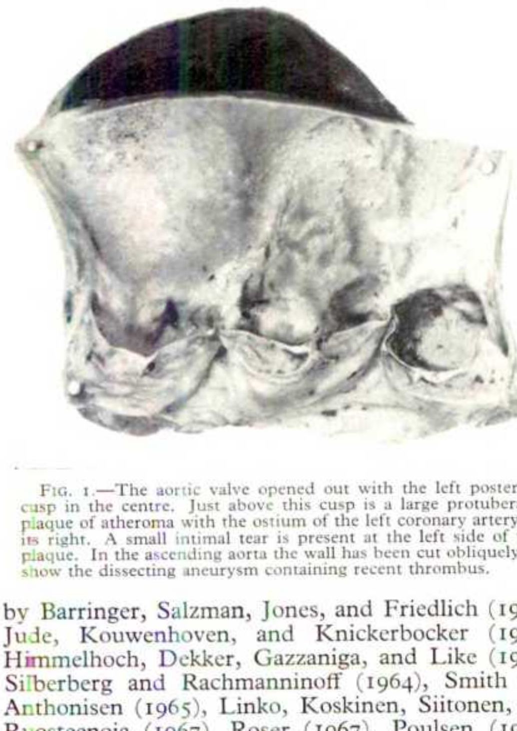

FIG. 1.—The aortic valve opened out with the left posterior cusp in the centre. Just above this cusp is a large protuberant plaque of atheroma with the ostium of the left coronary artery to its right. A small intimal tear is present at the left side of the plaque. In the ascending aorta the wall has been cut obliquely to show the dissecting aneurysm containing recent thrombus.

CASE REPORT

A hypertensive woman, aged 55 years, was admitted with a subarachnoid haemorrhage. After right brachial and left carotid angiography a bilateral frontal craniotomy was performed and clips were applied to two congenital aneurysms, each about 5 mm. in diameter, on the right anterior and on the left posterior communicating arteries.

The patient did not fully regain consciousness after the operation, and later became unconscious. Severe brain oedema developed. External cardiac massage was required, and cardiopulmonary resuscitation was initiated. She was subsequently maintained on a ventilator for 24 hours, after which time an iso-electric electro-encephalographic pattern was found. There was no spontaneous breathing when the ventilator was switched off.

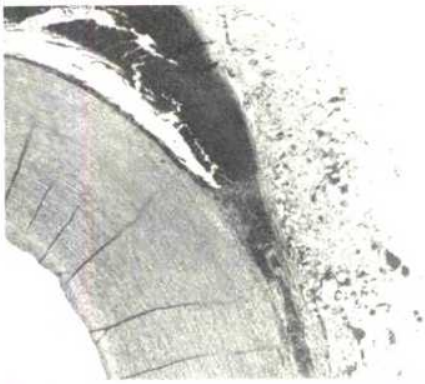

FIG. 2.—A section through the wall of the ascending aorta at the margin of the dissecting aneurysm. The aorta shows degeneration of the medial lamina, particularly in the outer third where the aneurysm has separated it into two layers. H and E. (× 17.)

NECROPSY SUMMARY.—

1. The presence of two clipped aneurysms was confirmed. There was gross herniation of the frontal lobes at the craniotomy site. The cerebral hemispheres, brainstem, and cerebellum were soft and swollen, and serial coronal sectioning showed recent, widespread, patchy, ischaemic damage in all areas and in all arterial territories.

2. Superficial bruising of the anterior chest wall was present, without fracture of the ribs or costochondral separation. There was also some bruising in the adventitia of the pulmonary trunk just above the pulmonary valve ring.

3. A recent dissecting aneurysm was present in the medial lamina of the wall of the ascending aorta (*Fig.* 1). It extended from just above the anterior aortic valve sinus upwards and posteriorly to involve the whole of the posterior wall of the aortic arch, and extended between 1 and 3 cm. along each of the three major branches of the aortic arch. It was also noted that the medial lamina was weak, and that further separation of the layers of the medial lamina could readily be produced by blunt dissection.

A small 4 × 1-mm. triangular intimal tear which communicated with the aneurysm was present on the left side of the anterior aortic valve sinus just above the level of the valve cusp and at the edge of a 1-cm. calcified and protuberant plaque of atheroma.

4. Widespread and severe patchy atheromatous degeneration was present in all the major arteries.

5. There was moderate hypertrophy of the myocardium of the left ventricle.

There were no macroscopic or microscopic features to other conditions that may be associated with aneurysm formation, such as Marfan's syndrome, coarctation of the aorta, syphilitic aortitis, or pregnancy.

HISTOLOGICAL FINDINGS.—The sections of the aorta showed atheromatous thickening of the intima, together with degeneration of the medial lamina (*Fig.* 2). The aneurysm was between the inner and outer layers of the medial lamina and contained recent unlaminated thrombus, with only slight reactive changes at the margins.

None of the sections showed any evidence of bone-marrow emboli.

DISCUSSION

The site of the intimal tear at the edge of a large, unbendable, atheromatous plaque and the presence of bruising in the anterior chest wall and around the root of the pulmonary trunk suggest that the precipitating cause of this lesion was compression of the inflexible great vessel against the vertebral column. The presence of necrosis in the medial lamina of the aorta presumably facilitated subsequent dissection from the intimal breach. The mechanism of production in this case differs in several respects from that of most closed-chest aortic lesions, which are mainly found in young atheroma-free adults who have been injured in road-traffic accidents. In such cases the lesions appear to be due to fixation and stretching of the thoracic aorta (Parmley, Mattingly, Marion, and Jahnke, 1958; Sevitt, 1968).

The possibility that the lesion in the present case had been produced by arteriography was investigated. Discussion with the radiologist revealed that the catheters which had been inserted for arteriography had extended only as far centrally as the right brachial artery and the bifurcation of the left common carotid artery. At no time had the catheters reached as far as the right subclavian artery or the main part of the left common carotid artery, and this possibility was therefore discounted.

The histological appearance of recent thrombus with only early reactive changes at the edges suggested that the haemorrhage must have occurred at about the time that external cardiac massage was applied. It would be an improbable coincidence of events if the lesion was to be regarded as having arisen spontaneously.

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LEIOMYOMA OF THE OESOPHAGUS WITH CALCIFICATION

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SUMMARY

The successful removal of a leiomyoma of the oesophagus in a man aged 64 years is described. The exceptional feature was the presence of calcification within the tumour which is almost unknown. The differential diagnosis from extrinsic causes which produce a similar appearance is discussed in view of this misleading feature. A brief general description of the clinical, radiological, and surgical aspects of leiomyomata of the oesophagus is given.

LEIOMYOMA of the oesophagus is a rare tumour and up to 1968 only about 200 cases had been recorded. Flavell (1953) records that Sussins in 1559 was the first to describe a case. Deverall (1968) reports that 876 carcinomata of the oesophagus and only 12 leiomyomata occurred in his department in a 23-year period, an incidence of 1·5 per cent. The tumours may rarely be multiple and Storey and Adams (1956) report their occurrence in about 7 per cent of cases while Allison (1967) mentions multiplicity in association with Schatzki's ring. The tumour may appear in any part of the oesophagus, but the lower third is the commonest site. Johnston, Clagett, and McDonald (1953) report 53 per cent in the lower third, 35 per cent in the middle third, and 12 per cent in the upper third. This latter figure is of interest because of the muscular layers of the upper third. *Gray's Anatomy* recalls 'in the upper quarter, both layers consist of striped muscle, in the second quarter bundles of smooth muscle appear and these gradually replace the striped muscle more caudally'.

The unusual and misleading feature of this case was the presence of stippled calcification; this is almost unknown.

CASE REPORT

A male patient aged 64 was admitted to the Princess Margaret Hospital, Swindon, on 5 Nov., 1968, with a history of intermittent hoarseness and indigestion for 2 years, and central retrosternal pain for 3 months with a sensation of food sticking at the back of the throat. On examination he had minimal clubbing of the fingers but no other abnormal physical signs. The blood-pressure was 140/90, haemoglobin, 106 per cent, and W.B.C., 9300.

On 30 and 31 Oct., barium swallows were carried out followed by tomography.

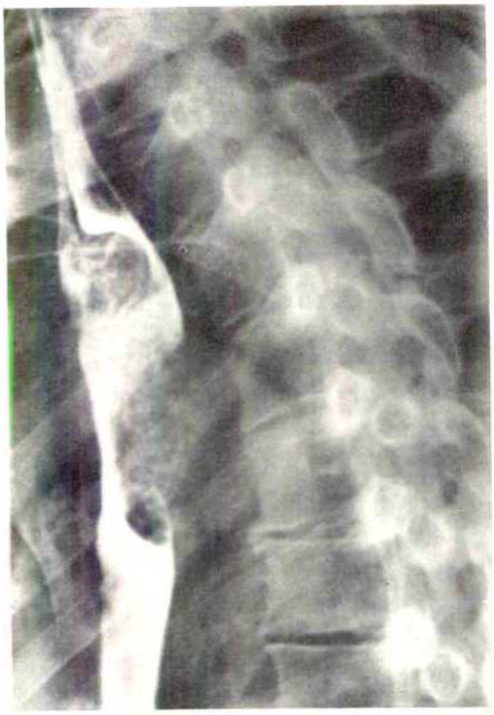
FIG. 1.—Barium swallow showing a filling defect but no obstruction caused by a mass which showed marked stippled calcification.

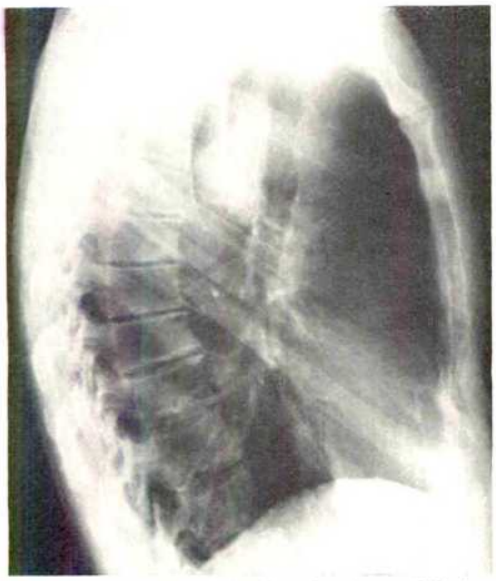
FIG. 3.—Lateral view of the chest showing a calcified mass lying immediately posterior to the trachea above the bifurcation. The dorsal spine appears normal apart from slight lipping. The lung fields appear clear.

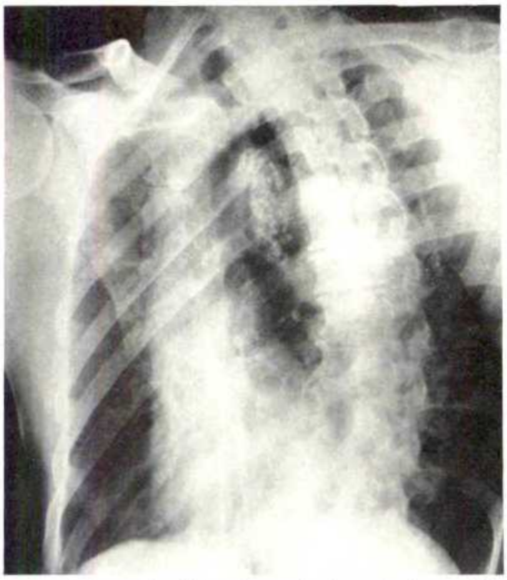
FIG. 2.—Left anterior oblique view of the chest showing a calcified mass lying in the upper mediastinum.

These investigations showed that there was a filling defect approximately 7 cm. in length (*Fig.* 1) on the antero-lateral aspect of the oesophagus close to the aortic knuckle. In this area the oesophagus was dilated and the filling defect exhibited marked stippled calcification (*Figs.* 2, 3). The defect did not move on swallowing and it did not show pulsation. It was thought that the mass was somewhat nodular superiorly. The upper and lower extremities of the filling defect were clearly defined, and a general impression was gained that the filling defect was probably either within the lumen or in the wall of the oesophagus, rather than outside. The tomographs showed that the calcification apparently fused with the oesophageal shadow, suggesting that the tumour might actually be within the oesophageal wall. The first reaction to this filling defect was that it was a neoplasm, but the presence of calcification was unknown and other causes outside the oesophagus were considered. It was thought not to be vascular as there was no pulsation and the type of calcification did not suggest a dermoid. A neurofibroma was considered in view of a lump on the left forearm but, on 13 Nov., it was excised and shown to be a lipoma. Other possibilities considered were a hamartoma or a calcified abscess, but there was no abnormality seen in the adjacent spine or lung fields.

On 6 Nov., oesophagoscopy was carried out and 25 cm. from the top of the oesophagus there was a lesion consisting of two lumps both bulging into the left wall of the oesophagus with a slightly yellow appearance and thought to be covered with normal oesophageal mucosa. They were non-pulsating and they were not hard. The oesophagus below was quite normal. A biopsy of the mucosa was taken which was shown to be normal. Bronchoscopy was carried out on 13 Nov., by Dr. J. Waddell, which showed a normal trachea with slight bulging of the posterior wall with possibly slightly anticlockwise rotation of the carina. The bronchi looked normal; no biopsy was taken.

On 27 Dec. the patient was admitted to the London Hospital under Mr. Geoffrey Flavell, and was operated on on 1 Jan., 1969. He had been of the opinion that, although the filling defect looked exactly as one sees in a leiomyoma, calcification of oesophageal leiomyomata appears to be unrecorded, although it does occur in uterine fibroids. He considered the most likely diagnosis was a mass of calcified glands or possibly a bronchogenic cyst or true ectopic thyroid. He did not think it was vascular.

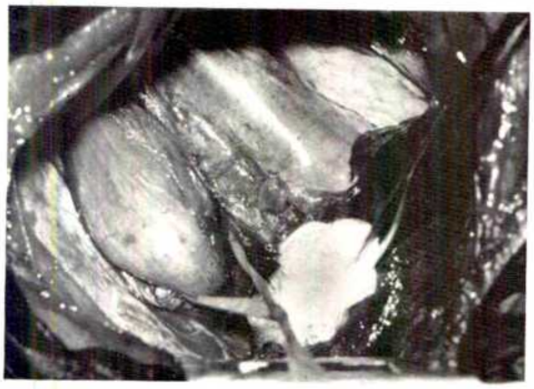

FIG. 4.—Fusiform swelling demonstrated at operation distending the upper oesophagus.

At operation the patient was explored through the right chest and a fusiform swelling of the upper oesophagus, which was crepitant to the touch and clearly calcified, was found (*Figs.* 4, 5). It was thought that this might have been a haemangioma, but when the muscle coat was incised, a white fusiform tumour partly encircling the mucosal tube shelled out with great ease and had all the macroscopic characters of a leiomyoma.

On section of the material, calcified areas up to 3–4 mm. in diameter were demonstrated, situated in an oedematous ground substance which contained scanty cells, singly or in bundles, some of which had nuclear characteristics of smooth muscle, together with other cells which appeared to be fibroblasts (*Fig.* 6).

The patient was discharged on 11 Jan., having completely lost his dysphagia, and is well at the present date.

DISCUSSION

The sex distribution of these rare tumours has been reported as a 2 : 1 ratio of males to females by Gilfillan (1966), but in the pooled reported cases of Barrett (1964), Glanville (1965), Deverall (1968), Engelmann and Scialla (1968), and ourselves, there were 15 males to 16 females.

The diagnosis may be puzzling and treatment may be difficult (Glanville, 1965). The presenting symptom is variable, the majority presenting with dysphagia, retrosternal pain, or reflux, although Barrett (1964) states that 50 per cent are symptomless. More unusual is the presence of bleeding. Respiratory symptoms occur occasionally presumably due to the 'spill over' phenomenon. Weight-loss may be marked, as occurred in 2 of Glanville's cases. Its presence does not necessarily signify malignancy as it may be due to starvation. Cases have been recorded of leiomyomata being on long pedicles appearing in the mouth and then disappearing again. They may also present in the fundus of the stomach. At the lower end of the oesophagus they may be associated with hiatus herniation, oesophagitis, and subsequent ulceration and haemorrhage, and the presence of such associated conditions make the diagnosis in the lower third more difficult than in the middle third (Deverall, 1968). A leiomyoma may be discovered incidentally at thoracotomy carried out for another lesion.

Radiologically, leiomyomata usually present as mediastinal shadows or as well-defined filling defects of the oesophagus. The findings may be bizarre as some tumours become very large and the mediastinal shadow is due to a combination of the tumour itself and the dilated oesophagus above. The mediastinal shadow, however, may be only very small and barely perceptible (Deverall, 1968).

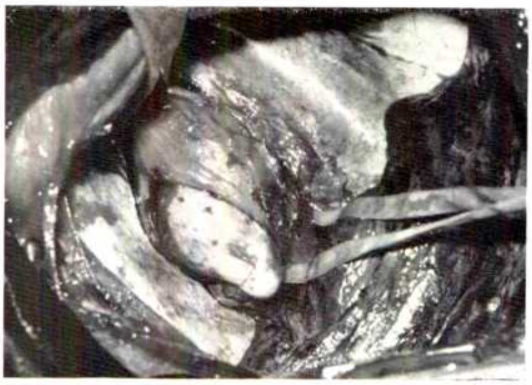

FIG. 5.—Calcified leiomyoma, crepitant to the touch, protruding through the incised oesophagus.

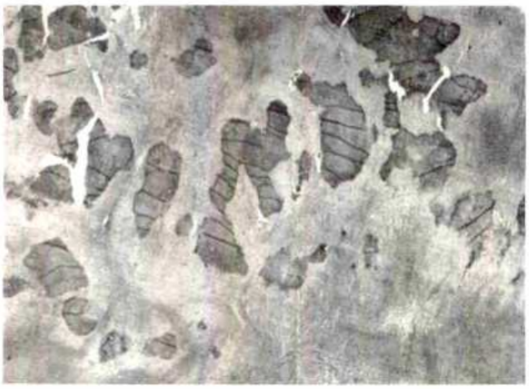

FIG. 6.—Section of the leiomyoma showing calcified areas up to 3–4 mm. in diameter lying in an oedematous ground substance together with cells having nuclear characteristics of smooth muscle with fibroblasts. (× 4.)

Leiomyomata may be either pedunculated or intramural. A pedunculated tumour may move up and down. Hence it may be difficult to diagnose and radiographic examination in the head-down position may be helpful (Barrett, 1964; Glanville, 1965; Deverall, 1968). The intramural tumours may become large and encroach on the lumen of the oesophagus, stretching the oesophagus over the tumour and producing dilatation. Dysphagia is not produced by this, but certain intramural tumours encircle the oesophagus and as soon as this occurs dysphagia supervenes. These cases are often mistaken for a carcinoma (Barrett, 1964). At the lower end of the oesophagus the condition may be mistaken for achalasia, owing to the dilatation (Shanks and Kerley, 1959). Conversely, the presence of a leiomyoma may be related to the failure of hiatal function (Deverall, 1968).

The case recorded here presented with almost all the radiological features of an intraluminal leiomyoma, the exceptional feature being the presence of calcification. On screening one had the impression that there was a lobulated mass within the oesophagus, the extent of the calcified mass corresponding with the filling defect. The dilatation of the oesophagus and the clearly defined diverging and converging folds of mucous membrane above and below the tumour were typical. It did not, however, move on swallowing which one usually finds in a leiomyoma of the upper oesophagus. There was no pulsation which made a vascular cause and an aberrant vessel unlikely.

It may be extremely difficult to distinguish between an intrinsic and an extrinsic tumour especially if the latter is fixed to the oesophagus by adhesions (Harper and Tiscenco, 1945). Shanks and Kerley (1959) illustrate an example of an abscess due to tuberculous glands, the pressure of which produced a filling defect on the oesophagus, exactly similar to that of a leiomyoma.

The two essential investigations are barium swallow and oesophagoscopy. Oesophagoscopy must complement the barium swallow to confirm or correct the diagnosis as differentiation from carcinoma may be very difficult and it is essential that the correct diagnosis is established to enable the correct surgical approach to be made (Gilfillan, 1966). A leiomyoma may also occur in association with other conditions, including a carcinoma (Barrett, 1964). Storey and Adams (1956) report that 7 cases out of 63 leiomyomata were diagnosed as carcinoma, and presumably they were treated accordingly. Carcinoma may present as an apparent leiomyoma as in 2 cases of Engelmann and Scialla (1968). Oesophagoscopy and biopsy corrected the impression of a leiomyoma demonstrated at barium swallow. The converse may also occur and Gilfillan (1966) reports a case which was thought to be a carcinoma radiologically but which subsequently proved to be a leiomyoma. Ulceration in a carcinoma may be minute. Enlarged mediastinal glands caused by malignant infiltration from a carcinoma may produce smooth filling defects on the oesophagus which simulate primary carcinoma and, conversely, large glandular masses may arise owing to associated non-malignant hyperplasia, simulating malignant glands macroscopically. Microscopic calcification may occur (Gilfillan, 1966; Pawlowski, 1966; Deverall, 1968). This is not surprising histologically as leiomyomata are very much like uterine fibroids which calcify fairly commonly. Unlike fibroids, however, the degree of calcification does not assume macroscopic proportions. Barrett (1964), however, describes a case in a woman of 60 years with a calcified leiomyoma at the lower end of the oesophagus which produced dysphagia and vomiting after meals owing to obstruction. This was clearly demonstrated radiologically on plain films.

Bronchoscopy is usually carried out to exclude bronchial lesions producing pressure.

At oesophagoscopy, in this particular case, the instrument passed easily down the lumen, the mucosa was seen to be intact, and a yellowish swelling was seen bulging into the left wall.

We can foresee difficulty in making a diagnosis in obstructive cases, where the submucosal spread of a carcinoma often holds up the instrument and makes visualization at biopsy difficult or impossible. The question of biopsy of a leiomyoma is of doubtful value, when a carcinoma can be excluded, because it may destroy the plane of enucleation of a tumour and make perforation at operation more likely.

Treatment of these tumours should usually be by their removal, presuming the patient to be fit. Three principal methods are available. Enucleation with repair of the muscle wall is the ideal method for most cases because it involves little local trauma and the mortality is low. For pedunculated lesions the best method of removal is probably by oesophagotomy with excision of the tumour at the base of its stalk. Thirdly, if there is a likelihood of the tumour having undergone malignant change (which is a rare complication) or if there is doubt about the diagnosis, resection and reconstruction is the method of choice.

Acknowledgements.—We wish to thank Mr. Geoffrey Flavell for access to, and inclusion of, his operative notes and comments on this case, and for his help in the preparation of this paper.

We would also like to thank Dr. Robert Martlew for his comments on the section, Mrs. Sheila Huddy and Miss B. Griffiths for their secretarial help, and the Photographic Departments of the London Hospital, and the Princess Margaret Hospital, Swindon, for their help with the illustrations.

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A CASE OF TRAUMATIC RUPTURE OF THE THORACIC AORTA ASSOCIATED WITH HYPOTHERMIA

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SUMMARY

This communication reports a case of traumatic rupture of the thoracic aorta. The literature on this subject is reviewed, the problem of diagnosis is discussed, and the importance of acute hypertension as a diagnostic sign is stressed. In view of the fact that the hypertension in the case reported here occurred in the presence of good femoral pulses and persisted after operation, the cause of the hypertension may not be simply an acute coarctation syndrome but may be due to damage to the cardiac plexuses around the site of rupture. It also emphasizes the importance of not rewarming severely traumatized hypothermic patients until facilities are available to replace blood-loss.

TRAUMATIC rupture of the thoracic aorta usually occurs adjacent to the ligamentum arteriosum in young males, and is associated with accidents involving rapid deceleration. It is surprising that many survive this injury. Strassmann (1947) reported 18 per cent surviving 1–18 hours, and Parmley, Mattingly, Marion, and Jahnke (1958) reported 19 per cent surviving from 24 hours to 10 weeks. It is probable that the incidence of this condition will increase with the development of high-speed travel.

As aortic rupture is often associated with other severe injuries the diagnosis may not be made immediately. However, as it is particularly amenable to surgical repair (Gerbode, Braimbridge, Osborn, Hood, and French, 1957; Eiseman and Rainer, 1958; Spencer, Guerin, Blake, and Bahnson, 1961; Dobell, MacNaughton, and Crutchlow, 1964; Jahnke, Fisher, and Jones, 1964; McKnight, Meyer, and Neville, 1964; Schonholtz and Jahnke, 1964; Bromley, Hobbs, and Robinson, 1965; McClenathan and Brettschneider, 1965; Rey Balter, 1965; Alley, 1966; Beall, Arbregast, Hallman, and Cooley, 1967; Clarke, Brandt, Cole, and Barratt-Boyes, 1967; Kiser, 1968; Keen, Brabrook, and McGinn, 1969; Malloy, 1970) there should be a high index of suspicion of aortic rupture in high-velocity accidents so that an early diagnosis can be made.

CASE REPORT

A 19-year-old university student was buried under a pile of rocks after falling about 9 m. while pot-holing in Derbyshire.

During his rescue from the caves the general practitioner in charge of the operation decided against using a rubber protection suit, being in favour of getting the patient out of the cave as quickly as possible.

On admission to the Sheffield Royal Infirmary Casualty Department 8 hours after the fall the patient was chilled, shivering, and had peripheral cyanosis. He was covered with minor lacerations and abrasions, but there was no external evidence of severe injury. On examination his pulse was 120 per minute, his blood-pressure was 90/40, and his rectal temperature was 32·2° C. He was tender on compression of the chest and had minimal physical signs in the left chest. He was tender in both hypochondria, and bowel-sounds were absent. Radiographs showed a crack fracture of the ilium on both sides and avulsion of the transverse process of the third lumbar vertebra.

The patient was transferred to the ward and was slowly warmed with blankets. Six hours after admission his temperature was 38·4° C., his blood-pressure had fallen to 80/50, and his pulse was 120 per minute. At this time he was becoming dyspnoeic and was developing physical signs of a left haemopneumothorax, which a chest radiograph confirmed. After transfusion with 400 ml. of plasma, his blood-pressure rose to 110/60 and he was transferred to the operating theatre.

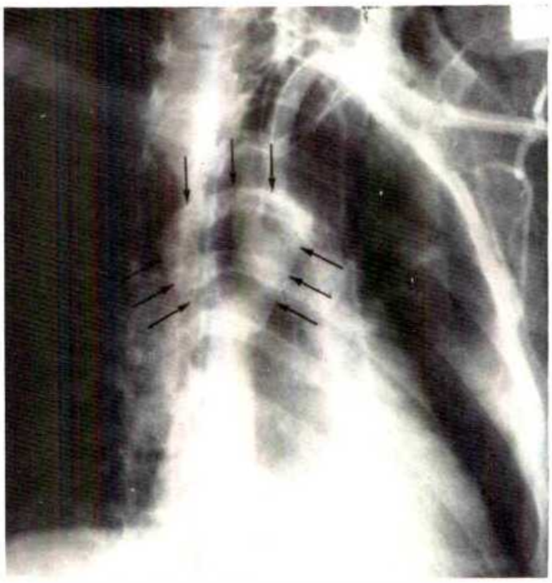

FIG. 1.—Aortogram showing an aneurysm just distal to the left subclavian artery.

A left-sided anterolateral chest drain was inserted and a left paramedian abdominal incision was made. A ruptured spleen was removed and a ruptured liver was repaired.

Postoperatively the patient was at first greatly improved. However, 3 days after the operation he had developed a collapsing pulse with a blood-pressure of 200–190/60. He had also developed a systolic murmur over the left scapula region, and a chest radiograph showed widening of the mediastinum and cardiomegaly. There were good femoral pulses on both sides.

Four days after admission the heart continued to increase in size, the systolic murmur was louder and could be heard in the lumbar region, and the left hypochondrium and the blood-pressure continued to be raised. The blood-pressure varied from recording to recording, involving mainly the systolic reading with a correspondingly high pulse-pressure. An aortogram was then performed (*Fig.* 1) and this showed an aneurysm of the aorta, distal to the left subclavian artery. At thoracotomy there was a complete tear of the aorta at the usual site just below the left subclavian artery. The aneurysm was resected and a Teflon graft was inserted.

Postoperatively the patient made a good recovery but his blood-pressure remained raised and varied between 200/60 and 140/80. At the time of his discharge, 5 weeks after admission, his blood-pressure was fairly stable at 140/80.

Table I.—CASES OF TRAUMATIC RUPTURE OF THE THORACIC AORTA ASSOCIATED WITH ACUTE HYPERTENSION

AUTHORS	BLOOD-PRESSURE BEFORE OPERATION	BLOOD-PRESSURE AFTER OPERATION	COARCTATION SYNDROME IF KNOWN
Rice and Wittstruck (1951), *Case* 1*	205/136	—	—
Wyman (1953)	170/90	—	—
Jay and French (1954)	160/90	—	—
Passaro and Pace (1959)	150/70	—	—
Spencer and others (1961)	140/100	—	—
Dobell and others (1964), *Case* 1	160/90	—	Peripheral pulses normal
Fleischaker, Mazur, and Baisch (1964), *Case* 1	180/80	—	Weak femoral pulses
Jahnke and others (1964), *Case* 3	180/90 left arm 110/80 right arm	— —	— —
Case 4	200/90	—	—
Case 5	160/70–180/72	—	—
Case 6	160/90–210/110	—	—
Schonholtz and Jahnke (1964)	200/90	—	—
Bromley and others (1965), *Case* 1	—	Hyperdynamic hypertension on third day post-operatively	—
Laforet (1965)	200/120	—	—
Clarke and others (1967), *Case* 4	Mild hyper-tension	Mild hyper-tension	—
Case 5	No record	Hypertension	—
Pate and Richardson (1968), *Case* 2	170/80	—	Good femoral pulses
Case 3	180/40 right arm 140/30 left arm	— —	Absent lower limb pulses
Malloy (1970)			
Case 1	150/90	—	—
Case 2	230/130	—	—
Case 3	230/100	—	—
Present case	200/60	180/60	Femoral pulses at first normal, becoming weaker

* This case was complicated as the patient was pregnant and had a previous history of mild hypertension.

DISCUSSION

The patient arrived at the hospital 8 hours after sustaining a ruptured spleen, liver, lung, and aorta. His initial shocked state was due to trauma, blood-loss, and hypothermia. The peripheral vasoconstriction secondary to hypothermia probably helped to maintain his blood-pressure.

Slow rewarming may result in cutaneous vasodilatation and a fall in arterial blood-pressure, because of the shunting of a considerable proportion of the cardiac output into the periphery (Cooper and Ross, 1960). This would have been particularly dangerous in this case and the decision not to stop the journey to dress the patient in a rubber exposure suit may have saved his life.

McClenathan and Brettschneider (1965), in a discussion of traumatic aortic rupture, list the following points which should make one wary of this condition. The first four were present in the case described here.

1. A history of horizontal deceleration and chest pain even without external injury to the chest.
2. Widening of the mediastinum on chest radiographs.
3. The development of a soft systolic murmur heard over the lower thoracic or lumbar vertebrae.
4. Unexplained haemopneumothorax.
5. Development of an acute coarctation syndrome.

All these points suggest the advisability of carrying out angiograms. McClenathan and Brettschneider (1965) also stress that the key to the treatment of this condition is a high index of suspicion, early diagnosis, and surgical repair in all cases.

Eiseman and Rainer (1958), Malm and Deterling (1960), and Jahnke and others (1964) have described cases associated with hypertension, and Laforet (1965) has suggested that acute hypertension with a coarctation syndrome is probably caused by aortic obstruction at the site of rupture. However, as the case described here had hypertension both before and after operation and associated with normal femoral pulses it would suggest that raised labile systolic hypertension, not necessarily associated with an acute coarctation syndrome, should be added to the points of McClenathan and Brettschneider (1965) in helping to make a diagnosis. *Table I* lists other reports of cases of acute hypertension associated with traumatic rupture of the thoracic aorta.

The aetiology of the hypertension may be, as suggested by Rice and Wittstruck (1951), due to local segmental spasm of the aorta and/or reflex irritation of the cardiac plexuses which are related to the site of rupture. The latter would explain the persistence of hypertension for some time after the repair.

Acknowledgements.—I would like to thank Mr. Clifford Jones and Mr. A. G. Norman for permission to publish details of this case, Professor M. A. Epstein for his helpful criticism, and Miss R. E. Menheneott for secretarial services.

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THE NON-ABSORBABLE CYSTIC DUCT LIGATURE

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SUMMARY

A case is reported of a common bile-duct calculus which had formed around a non-absorbable cystic duct ligature used during cholecystectomy 6 years previously. Although there are advantages in the use of the non-absorbable cystic duct ligature, the risk of migration to the common duct and consequent stone formation is probably greater than is recognized.

POST-CHOLECYSTECTOMY choledocholithiasis is usually due to stones which were present at the original operation. However, stones may form around non-absorbable sutures used to close a choledochotomy and for this reason absorbable sutures are generally used for this purpose. The occurrence of common-duct stones around non-absorbable cystic duct ligatures which have migrated into the common duct is less widely appreciated, and random personal inquiries amongst registrars revealed that non-absorbable cystic duct ligatures are still used by many surgeons throughout Britain, in some centres more so than in others. In Scandinavia, however, Milbourn (1949) reported 2 cases of common-duct stones which had formed around silk ligatures used during cholecystectomy, and further cases have been reported in Scandinavia by Silvennoinen and Asp (1956) and Ahleberg (1959). Recently, Sigler and Sahler (1969) reported a case in America of a common bile-duct calculus with a silk cystic duct ligature as a nidus.

A case is reported of a common bile-duct calculus in association with a thread cystic duct ligature used during cholecystectomy 6 years previously, and attention is drawn to this complication of non-absorbable cystic duct ligatures.

CASE REPORT

A 49-year-old multiparous woman had a cholecystectomy in September, 1964, the cystic duct and artery being ligated with thread. There was no history of jaundice and the common bile-duct looked and felt normal although an operative cholangiogram was not performed. Postoperatively she developed clinical and radiological evidence of a right subphrenic abscess which settled on conservative treatment and she was discharged home 1 month after the operation.

The patient was readmitted to Manchester Royal Infirmary in May, 1970, with an 18-month history of intermittent severe pain in the right hypochondrium, radiating to the right scapular region. On closer questioning she said that she had suffered an occasional mild ache in the right hypochondrium ever since the previous operation. She had passed dark urine during attacks of the pain. The serum alkaline phosphatase was raised at 21 K.A. units per 100 ml. and a drip-infusion cholangiogram showed a dilated common bile-duct.

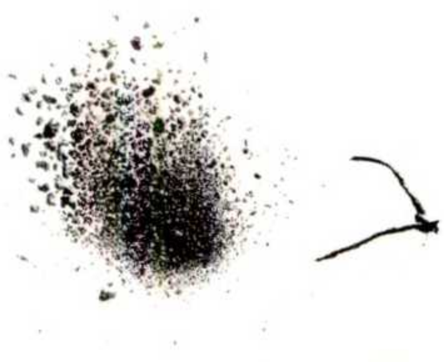

FIG. 1.—The fragmented stone removed from the lower end of the common bile-duct together with a thread ligature.

At laparotomy on 13 May a dilated common bile-duct of 1·5 cm. was confirmed by an operative cholangiogram with a filling defect in the lower duct. The common bile-duct was opened and a fragmented stone was removed from its lower end together with a thread ligature (*Fig.* 1). A transduodenal sphincteroplasty was performed and the duct was flushed with normal saline. The patient made a smooth postoperative recovery and the T-tube was removed on the eleventh day after a cholangiogram had shown no residual stones. She was well and symptom-free 5 months after the operation.

DISCUSSION

Sigmoidoscopic examination often reveals the extrusion of non-absorbable serosal ligatures into the lumen of the rectum after an anterior resection (Goligher, 1967), and presumably cystic duct ligatures may similarly migrate into the common bile-duct. This may be helped by necrosis of the cystic duct stump, and Sigler and Sahler (1969) postulate that local infection predisposes to this event. Certainly in the case reported here there was evidence of a subphrenic abscess.

Many surgeons prefer a non-absorbable ligature for the cystic duct because of its superior knot-holding qualities and the sometimes serious consequences of a leaking cystic duct stump. The occurrence of common-duct stones in association with non-absorbable cystic duct ligatures, however, is probably more common than is recognized, and Ahleberg (1959) gives an incidence of at least 0·6 per cent. The recent introduction of an absorbable material with improved handling and knot-holding properties (polyglycolic acid) may prove an effective compromise.

Acknowledgement.—I am indebted to Mr. W. F. Nicholson for permission to report this case admitted under his care.

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REVIEWS AND NOTICES OF BOOKS

Transplantation Today. Edited by Hans Balner, D. W. van Bekkum, The Netherlands, and Felix T. Rapaport, New York. 10 × 6¾ in. Pp. 978. Illustrated. 1971. New York: Grune & Stratton Inc. $25.

This large volume contains the Proceedings of the Third International Congress of the Transplantation Society, which was held at The Hague, The Netherlands, in September, 1970.

The volume is dedicated to Sir Peter Medawar, and there is a pleasing photograph of Sir Peter at the commencement of the book.

The volume is a truly international production and papers from all the important centres are included in this book.

Professor R. Y. Calne, of Cambridge, contributes an interesting paper on Antigen-induced Immunosuppression for Organ Grafting, in which he gives a selective review on this subject.

As one would expect in a work such as this, the various chapters are equally divided between animal experimentation and human material.

The preservation of organs and tissues is discussed at length. The mode of action of antilymphocyte sera (ALS) is considered in some detail.

This book is most comprehensive in its outlook and every facet of this important subject has been covered.

There is an extended author index at the end of the book.

This book will have a wide appeal and will remain the reference volume *par excellence* for some years to come.

Ischemic Forms of Venous Thrombosis. By Henry Haimovici, M.D., New York. 9 × 6 in. Pp. 230 + x. Illustrated. 1971. Springfield, Ill.: Charles C. Thomas. $23.

This is a useful monograph on a rather neglected subject, for venous gangrene or gangrene due to venous occlusion is not well documented in world medical literature.

From the surgical point of view, postoperative ischaemic thrombophlebitis includes phlegmasia caerulea dolens and venous gangrene. The former is likely to occur after operations on the gastro-intestinal tract and the latter after operations within the pelvis.

Professor Haimovici has put the medical profession in his debt by publishing a comprehensive and detailed review of the well-documented published cases. This book will be of great assistance to anyone who wishes to do some further research work on this subject.

There seems to be very little consensus of opinion as to the best method of treatment for these forms of venous thrombosis. Sympathetic blocks and anticoagulants are advocated, and so is thrombectomy, local excision, and skin-grafting. Whatever treatment is advocated, a considerable proportion of patients will require amputation, and this is not without risk.

This is an excellent reference volume on this not too well-known condition.

Fortschritte der Kiefer- und Gesichts-Chirurgie. Edited by K. Schuchardt, Hamburg. 10½ × 7⅝ in. Pp. 290. Illustrated. 1970. Stuttgart: Georg Thieme Verlag. DM.156.

This volume on faciomaxillary surgery is one of a series of annual productions. This particular volume deals with the diagnosis and treatment of mesenchymal tumours and hyperplastic lesions of the mouth, jaw, and face. The volume contains no less than forty-four separate papers presented by different authors, many of which are case reports or reports of a small series. However, malignant lesions such as sarcoma are dealt with in detail. Each chapter has an extensive list of references and there is a full summary not only in English but also in French and Spanish. Although there is no statement to the effect, the final section dealing with discussion suggests that this volume is in fact the report of a meeting. Unfortunately, all the discussions had been collected at the end of the book and it might have been more helpful to have the relevant discussion at the end of each chapter. The volume is beautifully produced with a large number of high-quality photographs, and although expensive it should be available to all those specializing in faciomaxillary surgery.

Surgery for Nurses. Twelfth edition. By JAMES MORONEY, M.B., Ch.B., F.R.C.S., L.R.C.P., Consultant Surgeon, Broadgreen Hospital, Liverpool. 8½ × 5½ in. Pp. 632 + x. Illustrated. 1971. Edinburgh: E. & S. Livingstone. £2·75.

THE popularity of this book speaks for itself—twelve editions in 20 years is a great achievement for any author. This new twelfth edition has been extensively revised and rewritten and many new illustrations have been added.

The book provides an excellent, well-illustrated up-to-date text for student nurses. This book will help nurses pass their Final State Examination, and will prove as popular as former editions.

Pathogenese und Klinik des akuten Nierenversagens. Edited by ULRICH GESSLER, KARL SCHRÖDER, and HORST WEIDINGER, Nürnberg. 9 × 6 in. Pp. 261 + x, with 138 illustrations. 1971. Stuttgart: Georg Thieme Verlag. DM.42.

THIS is a report of a symposium held in December, 1969, and deals with the aetiology and clinical picture of renal failure. Twenty-eight separate papers dealing with pharmacology, animal experiments, and various forms of treatment are discussed and each paper has an appended discussion reported in full. A large number of the papers are published in English, and those published in German have a long English summary. The book is extremely well produced and illustrated and should find its place on the shelves of everyone interested in nephrology.

Methods in Mammalian Embryology. Edited by JOSEPH C. DANIEL, jun., University of Colorado. 10 × 6½ in. Pp. 532 + xv, with 186 illustrations. 1971. Reading: W. H. Freeman & Co. Ltd. £10·70.

THIS important book will make a strong appeal to a great variety of scientific research workers, for it contains a wealth of material.

Since the Second World War the field of experimental mammalian embryology has expanded to an enormous extent. This book is very practical in its outlook and contains some excellent chapters on practical subjects such as the collection and preservation of spermatozoa, obtaining eggs and embryos from sheep and pigs, and egg storage and transfer.

Tissue culture of various parts of the genital system receives considerable attention.

Today research workers can observe the inside of the living uterus, and study the exposed guinea-pig foetus.

This book, which gives extensive coverage to this important subject, will interest not only embryologists, zoologists, and cancer research workers, but also a wide variety of scientists who are interested in associated subjects.

Atlas röntgenologischer Befunde am operierten Magen. By E. BAUDISCH, Friedrich-Schiller-Universität, Jena. 11⅜ × 8½ in. Pp. 344. Illustrated. 1970. Jena: Veb. Gustav Fischer Verlag. DM.134.

THIS book offers a large quantity of radiographs of patients who were operated upon for oesophageal and gastric diseases, mostly resections. The principal goal of the author is to give an impression to the radiologist of the surgical techniques that were applied by offering him a series of postoperative X-rays. Nevertheless surgeons can profit as well, obtaining information about the aftermath of their operations.

Though one would be happier if, besides the pictures after Billroth-II gastrectomies, the situation after Billroth-I gastrectomies and vagotomies had been demonstrated, nevertheless, the numerous reproductions of radiographs are impressive.

Some conclusions might be drawn: after oesophageal resections many fistulae appear; in cases of total gastrectomy interposition of a piece of small intestine (more than 15 cm. long) appears satisfactory; when an antecolonic Billroth-II resection is performed, an anastomosis of the Braun type might be useful.

Proceedings of the Fourth Annual Leucocyte Culture Conference. Edited by O. ROSS MCINTYRE, Hanover, New Hampshire. 9¼ × 6½ in. Pp. 580 + xxiii. Illustrated. 1971. New York: Appleton-Century-Crofts. $19.50.

THIS large volume contains the forty-two original papers presented at the Fourth Annual Leucocyte Culture Conference, which was held at Dartmouth Medical School, Hanover, New Hampshire, in June, 1969.

It may be said after reading these numerous papers that they provide an excellent detailed survey of the current knowledge and recent advances in the field of lymph culture and cellular immunity.

The field of lymphocyte culture is a large and expanding one, and much more research work still remains to be done. The cell membrane has come in for much extended work, and the role of pinocytotic vacuoles is discussed at some length. One of the features of this book is the discussion at the end of each paper. The illustrations, especially the electron micrographs of various cultures of cells fixed in situ, are of a high order.

Doctor Barbara Brain is to be congratulated on her verses on the lymphocyte, two of which we record:—

> The Lymphocyte is small and round,
> And innocent of face,
> Which is extremely handy
> For a cell that circulates.
>
> Its size and shape allow our friend
> The Lymphocyte to squeeze
> Through tissue spaces, nodes, and spleen,
> And small capillaries.

Colposcopy. A Scientific and Practical Approach to the Cervix in Health and Disease. By MALCOLM COPPLESON, M.D. (Syd.), F.R.C.O.G., Sydney; ELLIS PIXLEY, M.B., B.S. (Qld), M.R.C.O.G., Perth; and BEVAN REID, M.D. (Syd.), B.V.Sc., D.T.M. and H., Sydney. 9¾ × 6¾ in. Pp. 346 + xi. Illustrated. 1971. Springfield, Ill.: Charles C. Thomas. $21.50.

THIS is an important monograph on an important subject. Anything which will help in the early diagnosis of cancer of the cervix is very worth while.

In this book the colposcopic appearances of the cervix uteri in health and in disease are interestingly and practically described in detail. In addition, the unique value of colposcopy in defining the precise sites of preclinical carcinoma and other epithelial conditions is graphically illustrated. Although there are two forms of instrument, the Zeiss one is probably the better. It is a modified operating microscope mounted on a heavy mobile base and is positioned upon a system of arms allowing universal movement and easy manipulation. The optical head provides high-intensity illumination along the optical pathway and a variable magnification, ranging from × 6 to × 40, which may be changed without refocusing. To the head may be attached a photographic unit with a separate optical pathway which can be focused with the plane of the viewing optics. An electronic flash is fitted for photography.

The atlas portion of the monograph includes many colpophotographs illustrating the variations in appearance in native, physiological, and atypical epithelia, carcinoma, and miscellaneous conditions. All the colpophotographs are of a very high order and are most instructive.

This is a book which all gynaecologists and research workers should read.

The Plain X-ray in the Diagnosis of the Acute Abdomen. By M. H. GOUGH, M.S. (Lond.), F.R.C.S., and MICHAEL W. L. GEAR, D.M., M.Ch. (Oxon.), F.R.C.S., Gloucester. 9 × 6 in. Pp. 188 + xi. Illustrated. 1971. Oxford: Blackwell Scientific Publications. £3·50.

THIS is a surgical handbook with notes on Clinical Presentation and Differential Diagnosis. It is a useful book not only for the student but also for house-surgeons and casualty officers, for it presents practical ways in helping to make a diagnosis in abdominal conditions. The book is divided into six chapters, each of which is illustrated with good X-ray pictures. Besides the diseases of the alimentary system, diseases of the genito-urinary system and trauma are all covered in a good practical way.

Diseases occurring in infancy and childhood are dealt with in a very sound manner.

The matured clinical acumen of the authors is clearly manifested in this book.

Autologous Transfusions. By GEORGE MILLES, M.S., M.D., HIRAM T. LANGSTON, M.S., M.D., and WILLIAM DALESSANDRO, B.S., M.D., F.A.C.P., Chicago. 9¾ × 6¾ in. Pp. 127 + viii, with 11 illustrations. 1971. Springfield, Ill.: Charles C. Thomas. $11.75.

THIS book certainly convinces the reader of the value of autologous transfusions during or after operations, especially in the aged. Venesection of the patient prior to all types of elective surgery make up the bulk of this book. The authors record the details of more than 500 thoracic surgical cases as well as many other patients subjected to presurgical venesection of one or more units of blood for later transfusion. They conclude that all patients selected for elective surgery whose haematological reserve is adequate can serve as the source of more than 50 per cent of the blood that they may need, thereby reducing the drain on the blood banks.

This book stimulates the modern surgeon to a new approach in the pre- and postoperative treatment of his patients.

Biochemical Consequences of Chronic Renal Failure. By M. R. WILLS, M.D., M.R.C. Path., London. 9 × 6 in. Pp. 218, with 9 illustrations. 1971. Aylesbury: Harvey Miller & Metcalf Ltd. £3.

THIS is a most useful book and it appears at an opportune time when surgeons in particular are interested in their patients who are likely to develop uraemia.

It is true that today chronic renal failure is treated by long-term intermittent dialysis, yet the clinician wants to know how his patient is progressing, and this book will be his constant guide, and as a reference volume it could not be bettered.

This monograph gives a lucid and excellent survey of the state of our knowledge of the function of the kidney in controlling the various biochemical systems in the body, and of the consequences to those systems of renal failure.

There can be no doubt that this book will appeal not only to postgraduate students but also to physicians, surgeons, and pathologists.

A most complete list of references is given at the end of this book, comprising 39 pages.

The Hand. By LEE MILFORD, M.D., Memphis, Tennessee. 10½ × 7 in. Pp. 282 + viii, with 308 illustrations. 1971. London: Henry Kimpton. £8·75.

THIS large monograph on the hand is an expanded edition of the author's chapter on the hand in the fifth edition of Campbell's *Operative Orthopaedics*

The importance of the hand from a surgical point of view is manifested in the fact that so many 'hand clinics' have emerged in hospitals up and down the land.

This volume considers the hand from every point of view, including congenital deformities, injuries, nerve palsies, and tumours—in fact every facet of the surgery of the hand has been adequately covered.

The illustrations, over 300 of them, have been well chosen and are a feature of the book. The line drawings are particularly good and so are the X-ray pictures. The various and numerous operative techniques are illustrated in a very clear and practical way.

The list of references at the end of the book is extensive and covers some 14 pages.

This book should be in every medical library, for it is an excellent reference volume. Casualty officers and residents will find the book of real value to them.

Immunobiology. Edited by ROBERT A. GOOD, M.D., and DAVID W. FISHER, Minnesota. 11 × 8½ in. Pp. 305 + xii. Illustrated. 1971. Reading: W. H. Freeman & Co. Ltd. £5·20.

THIS large volume is concerned with common knowledge of basic concepts in immunology and their clinical applications.

There are some thirty contributors to this volume, two of whom come from England, namely Sir Peter Medawar and James L. Gowans, both of whom have made considerable advances in our knowledge of immunology.

The book is divided into five large sections: Section 1 is devoted to the development of the immune systems: cellular mechanisms of immune response. Section 2 deals with humoral antibodies. Section 3 is concerned with mediators and effectors of immunity. Section 4 is devoted to the pathogenetic mechanisms involving immunologic factors, while Section 5 deals with clinical applications of immunology in prophylaxis and in therapy. It is in this last section that Sir Peter Medawar writes on antilymphocytic serum, its properties and potential.

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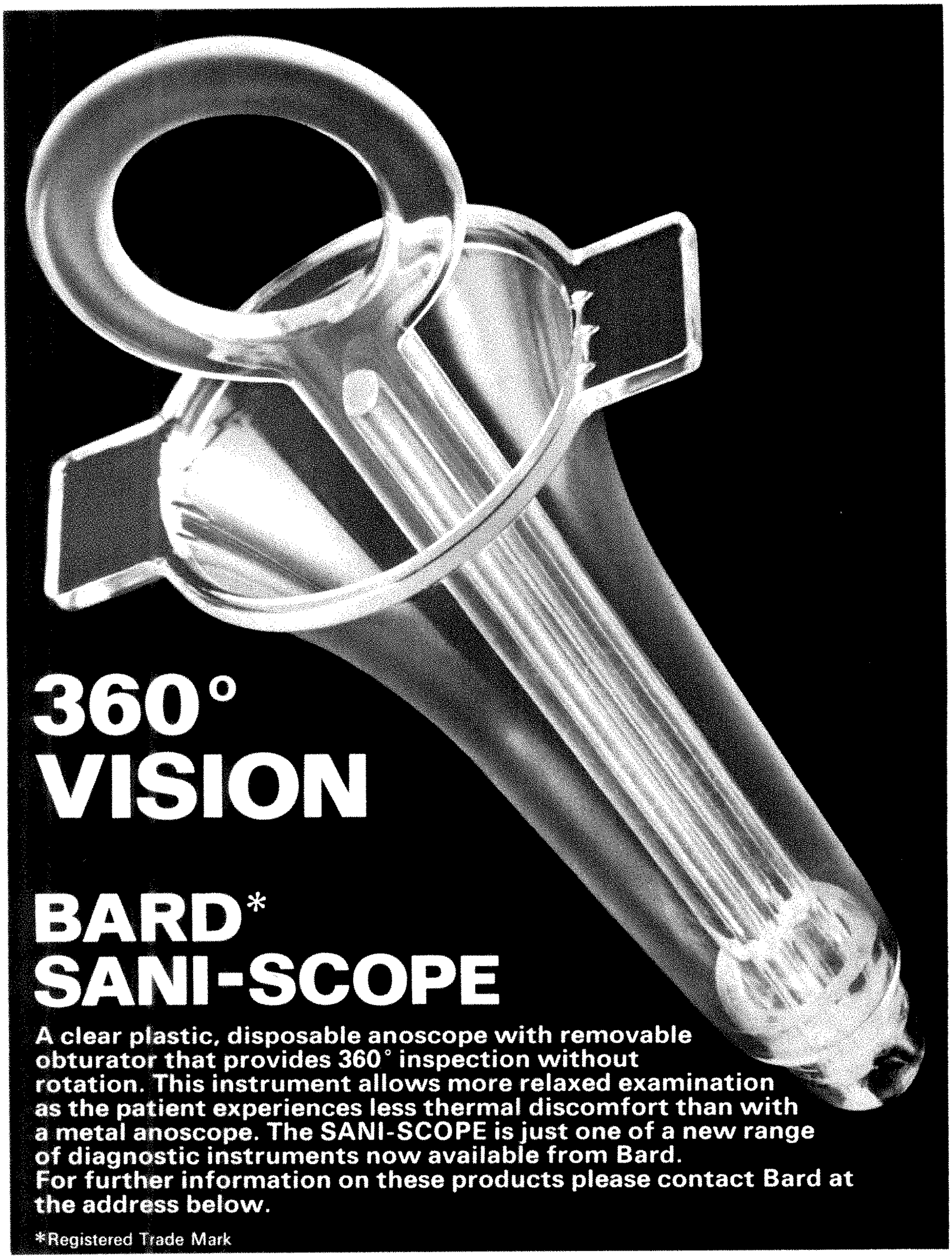

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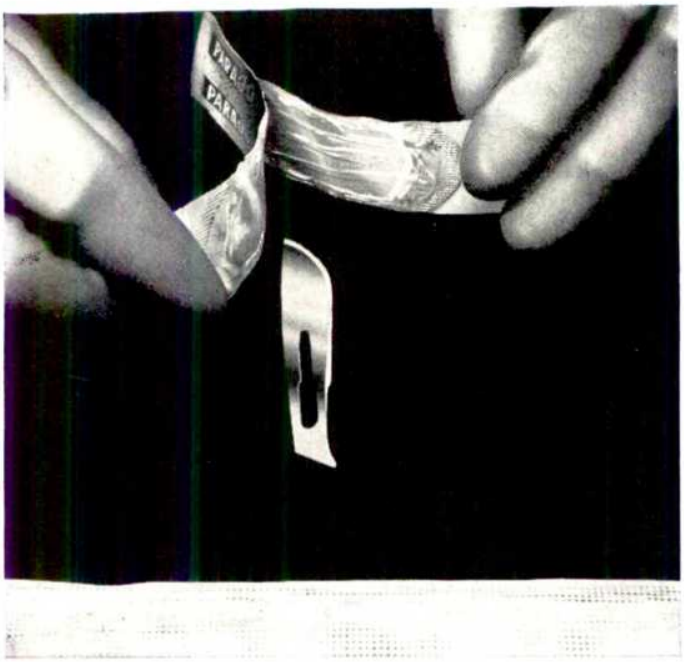

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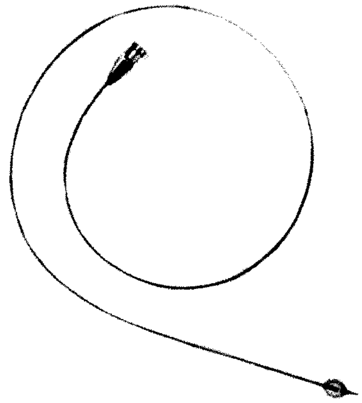

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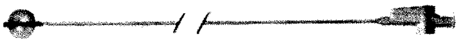

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92-060-6F (Whistle Tip)	1.75	3.0	13
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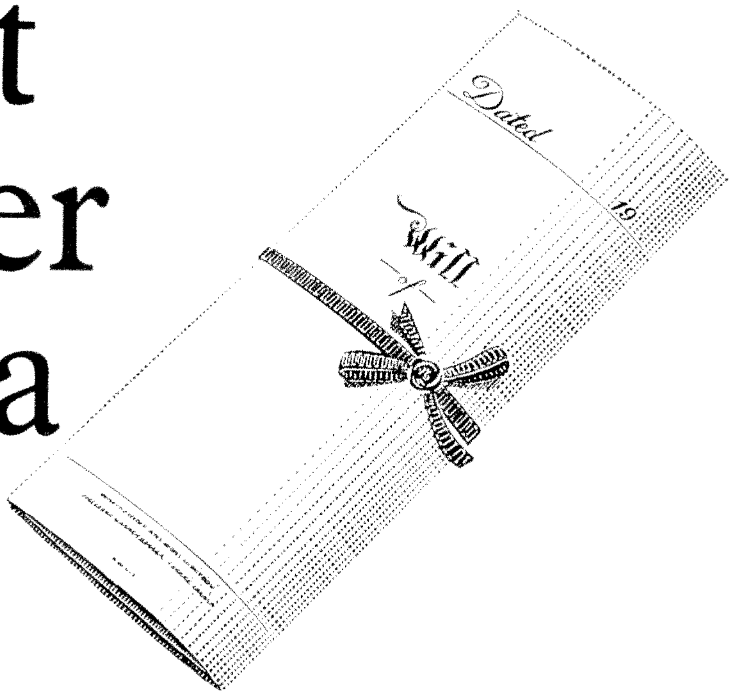

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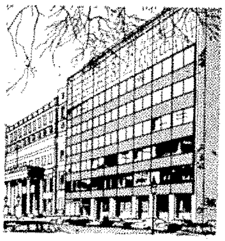

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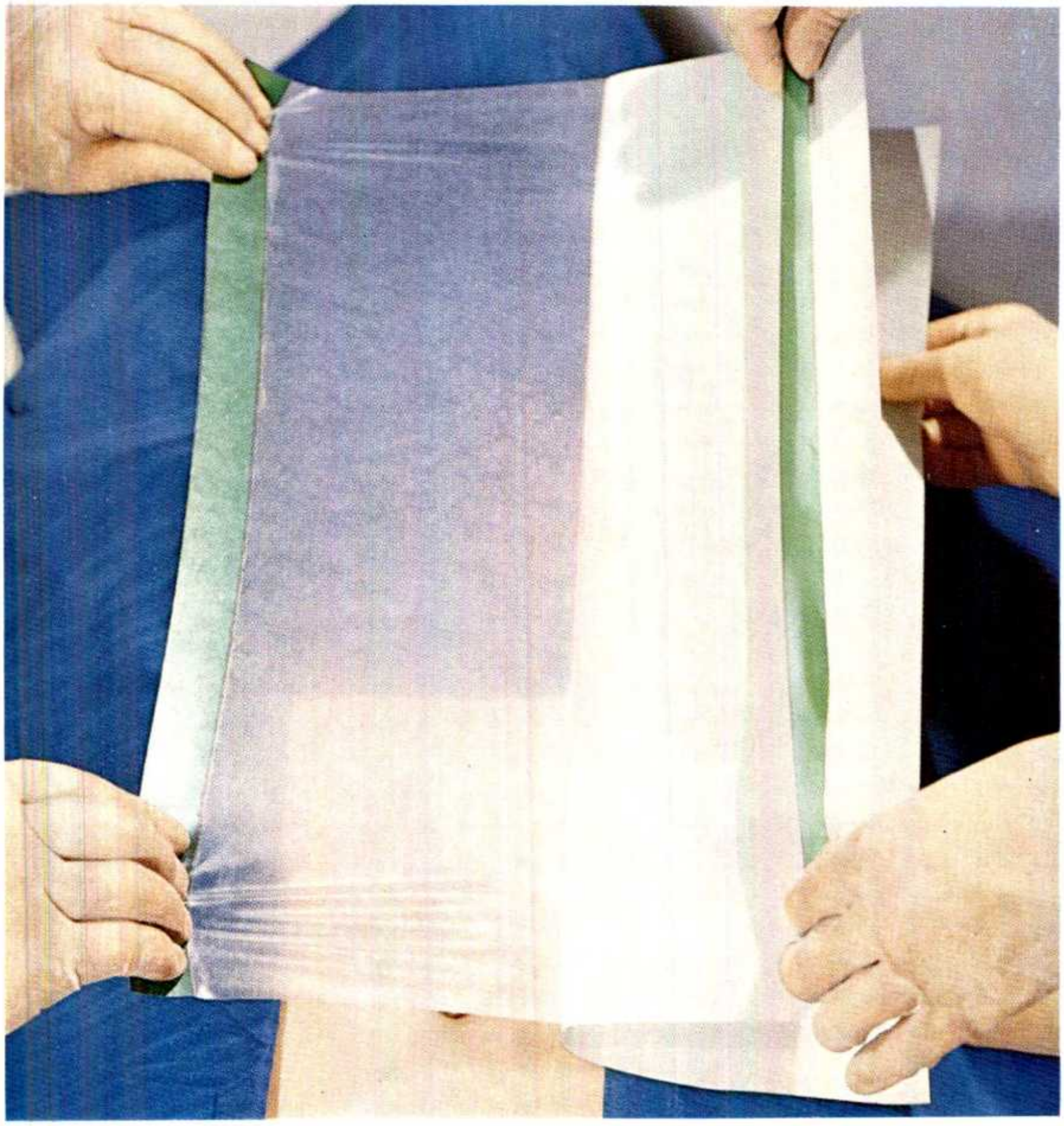

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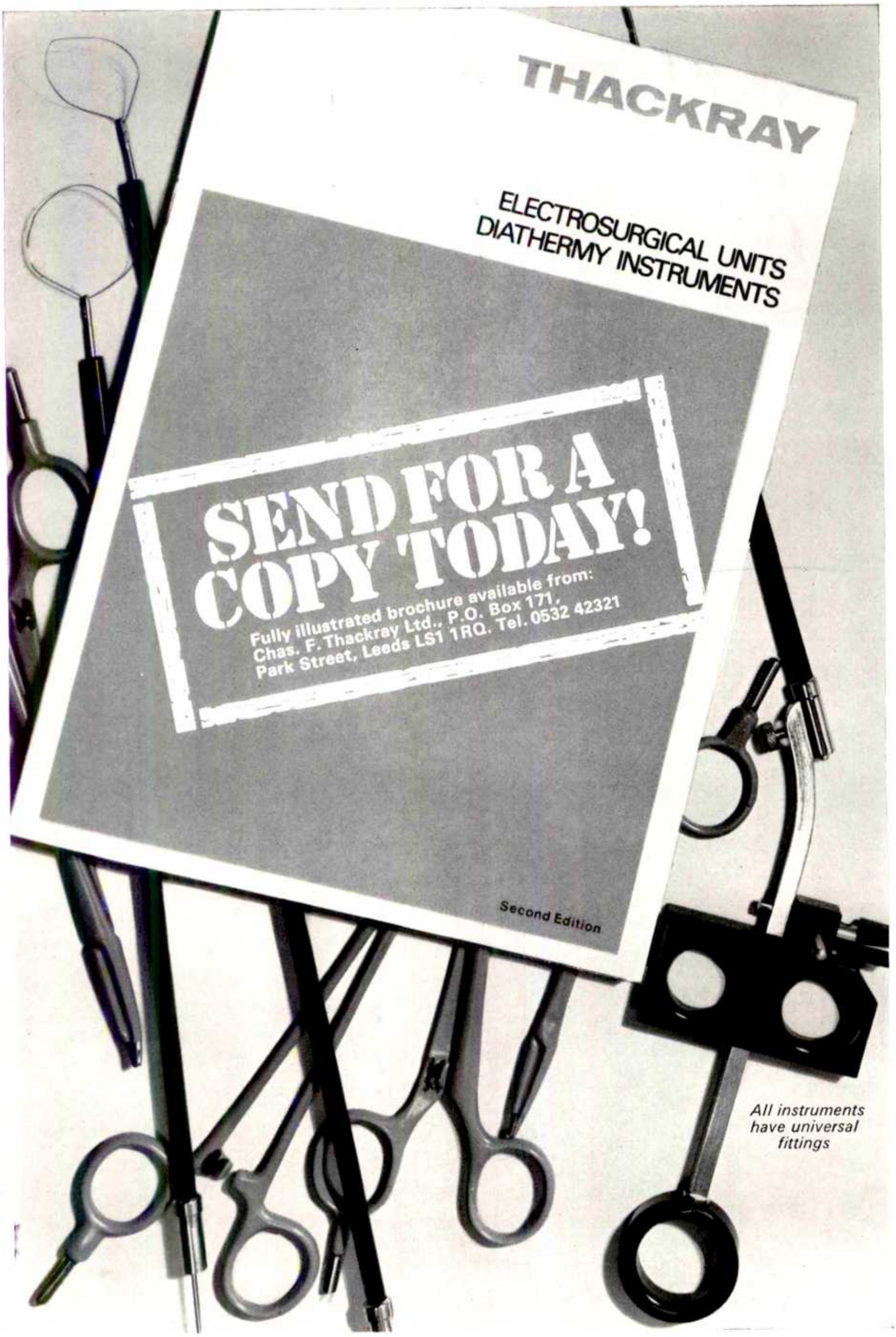

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CONTENTS

PAGE

ORIGINAL PAPERS

ULCERATION OF THE MOUTH, PHARYNX, AND LARYNX IN CROHN'S DISEASE OF THE INTESTINE *C. B. Croft and A. R. Wilkinson* 249

ILEAL RECURRENCE AFTER ILEOSTOMY AND EXCISION OF THE LARGE BOWEL FOR CROHN'S DISEASE *J. C. Goligher* 253

THROUGH-KNEE AMPUTATION - - - - - - *J. F. Newcombe and R. W. Marcuson* 260

BILIARY-PRESSURE STUDIES DURING CHOLECYSTECTOMY - - *A. Cushieri, J. Howell Hughes, and M. Cohen* 267

TWELVE-HOUR LIVER PRESERVATION IN THE PIG USING HYPOTHERMIA AND HYPERBARIC OXYGEN *Harold Spilg, C. J. Uys, Rosemary Hickman, Stuart J. Saunders, and John Terblanche* 273

CHOLEDOCHODUODENOSTOMY - - - - - - *A. G. Johnson and A. J. Harding Rains* 277

THE TREATMENT OF ACHALASIA BY CARDIOMYOTOMY - - - *H. V. Wingfield and A. Karwowski* 281

THE RESULTS OF FUNDOPLICATION FOR THE RELIEF OF OESOPHAGEAL REFLUX DUE TO HIATUS HERNIA *I. K. Shah and O. Daniel* 285

PERFORATED DUODENAL ULCER IN CHILDHOOD - - - - *J. M. S. Johnstone and R. F. Rintoul* 288

TUBERCULOSIS OF THE GALL-BLADDER - - - - - *Leif Bergdahl and Lennart Boquist* 289

DRAINAGE FOLLOWING CHOLECYSTECTOMY - - *C. B. Williams, D. S. Halpin, and A. J. S. Knox* 293

ANTERIOR DISLOCATION OF THE HIP AND DIASTASIS OF THE CONTRALATERAL SACRO-ILIAC JOINT—THE REAR-SEAT PASSENGER'S INJURY? - - - - - - - - *D. E. Markham* 296

SURGICAL RESEARCH SOCIETY - - - - - - - - - - - 299

SHORT NOTES OF RARE OR OBSCURE CASES

GASTRIC NECROSIS: A RARE COMPLICATION OF CHLORAL HYDRATE INTOXICATION *I. D. A. Vellar, J. P. Richardson, J. C. Doyle, and M. Keating* 317

A CASE OF XANTHOGRANULOMATOUS PYELONEPHRITIS - - - *Clive Bartram and David Jagelman* 319

A CASE OF CARCINOMA OF THE COLON IN ASSOCIATION WITH NEUROFIBROMATOSIS *D. H. R. Jenkins and W. Gill* 322

A CASE OF INTRALUMINAL DIVERTICULUM OF THE DUODENUM - *Hugh P. Guerrier and Maurice J. Turner* 324

AN UNUSUAL DISLOCATION OF THE HIP - - - - *R. F. Brown and F. A. Simmonds* 326

REVIEWS AND NOTICES OF BOOKS

Current Concepts in the Management of Leukemia and Lymphoma—ed. *J. E. Ultmann, M. L. Griem, W. H. Kusten, and R. W. Wissler.* Clinical Anatomy—*Harold Ellis.* Mechanical Devices for Cardiopulmonary Assistance—ed. *R. H. Bartlett, P. A. Drinker, and P. M. Galletti.* Oral Pathology—*Donald A. Kerr and Major M. Ash.* Diseases of the Urinary Tract—*British Medical Journal.* Diseases of the Ear, Nose and Throat—ed. *John Ballantyne and John Groves.* Outline of Orthopaedics—*J. Crawford Adams.* A First Notebook of Head Injury—*Kenneth G. Jamieson.* Intensive Care of the Surgical Patient—ed. *Marshall D. Goldin.* Today's Drugs—*British Medical Journal.* Scoliosis and Growth—ed. *P. A. Zorab.* Special Topics in Sterotaxis, Epilepsy, Disorders of Behaviour, and Autonomic Balance—ed. *W. Umbach.* Methods of Ossiculoplasty—*James R. Tabor.* Regeneration of Liver and Kidney—*Nancy L. R. Bucher and Ronald A. Malt.* The Craft of Surgery—ed. *Philip Cooper.* The Illness of Trauma—*Garbett Pipkin and Victor Buhler.* Atlas for Surgical Repair of Cleft Lip, Cleft Palate, and Noncleft Velopharyngeal Incompetence—*Richard B. Yules.* Chest Injuries: Physiologic Principles and Emergency Management—*Emil A. Naclerio.* Occult Traumatic Lesions of the Cervical Vertebrae—*Martin S. Abel.* Gynaecology: Essentials of Clinical Practice—*Thomas H. Green.* Cleft Lip and Palate: Surgical, Dental and Speech Aspects—ed. *William C. Grabb, Sheldon W. Rosenstein, and Kenneth R. Bzoch.* Klinische Sudeckprophylaxe und Therapie—*Jost L. Bircher.* Atlas of Transbronchial Biopsy: Early Diagnosis of Peripheral Pulmonary Carcinomas—*Eitaka Tsuboi.* Frontiers of Nuclear Medicine—ed. *Wolfgang Horst.* Encyclopedia of Urology—ed. *C. E. Alken, V. W. Dix, W. E. Goodwin, and E. Wildbolz.* Traumatismes Ostéo-articulaires de la Main—ed. *R. Vilain.* 328

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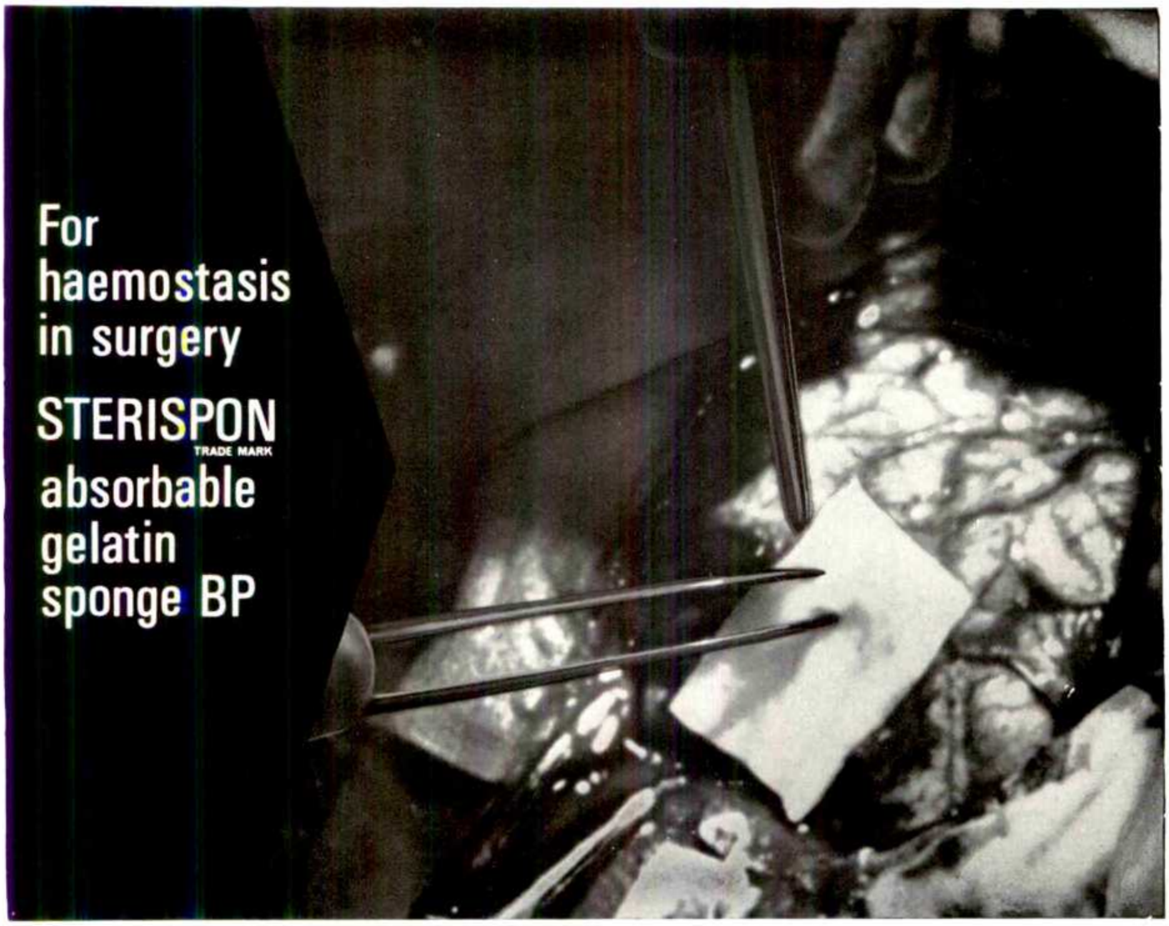

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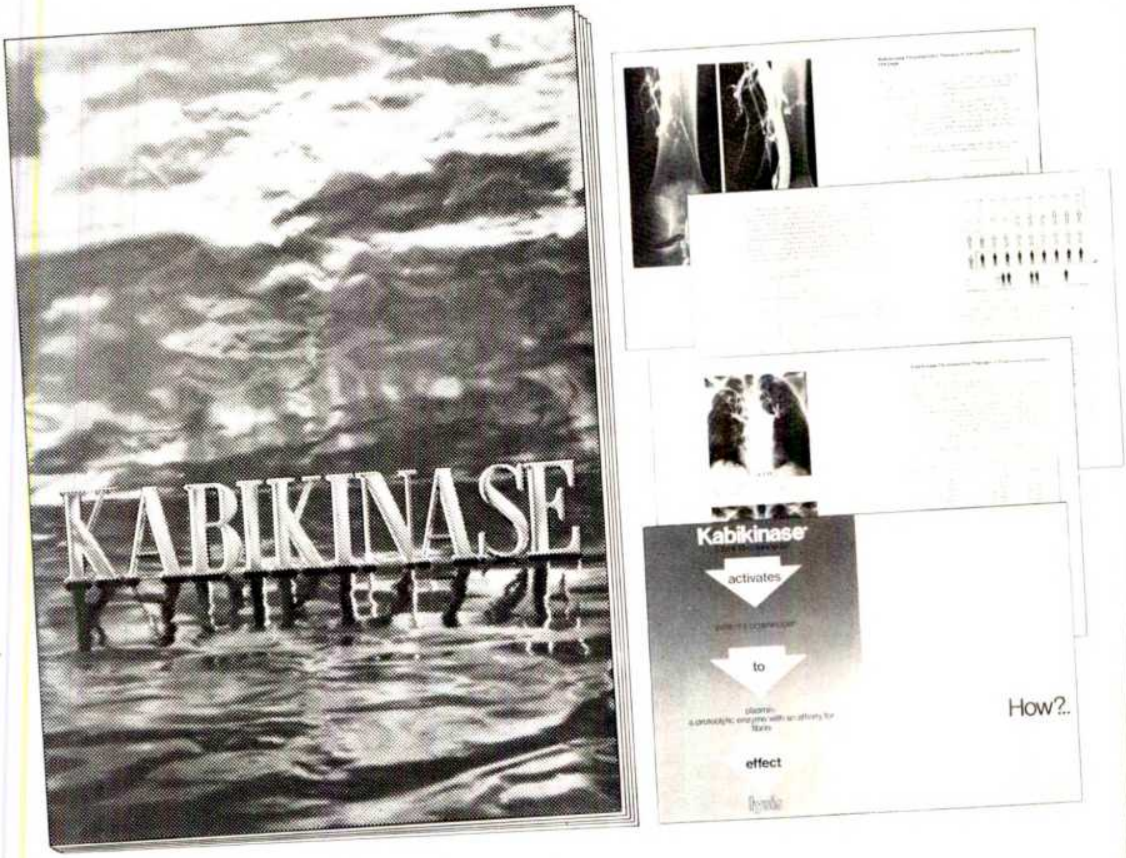

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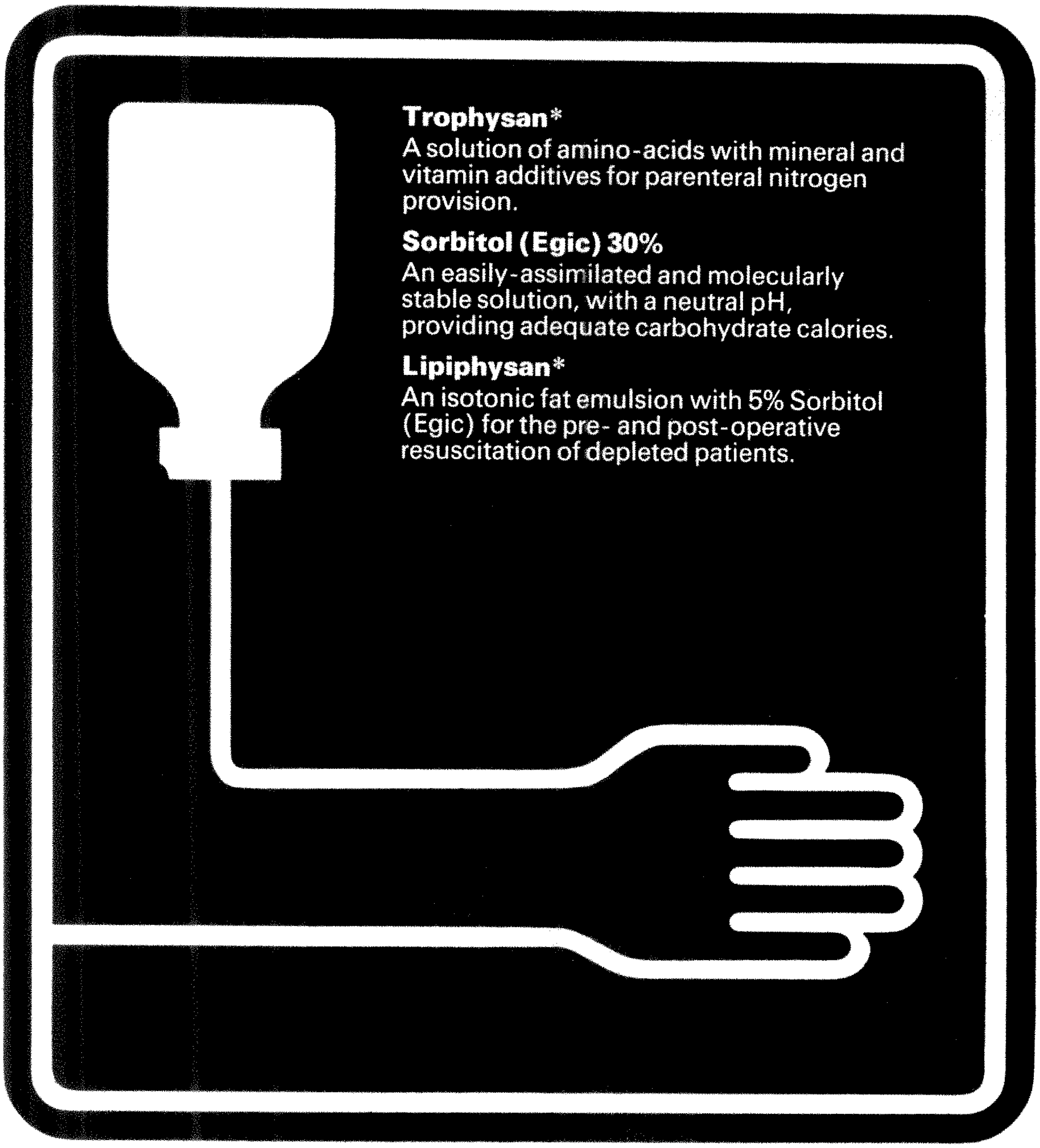

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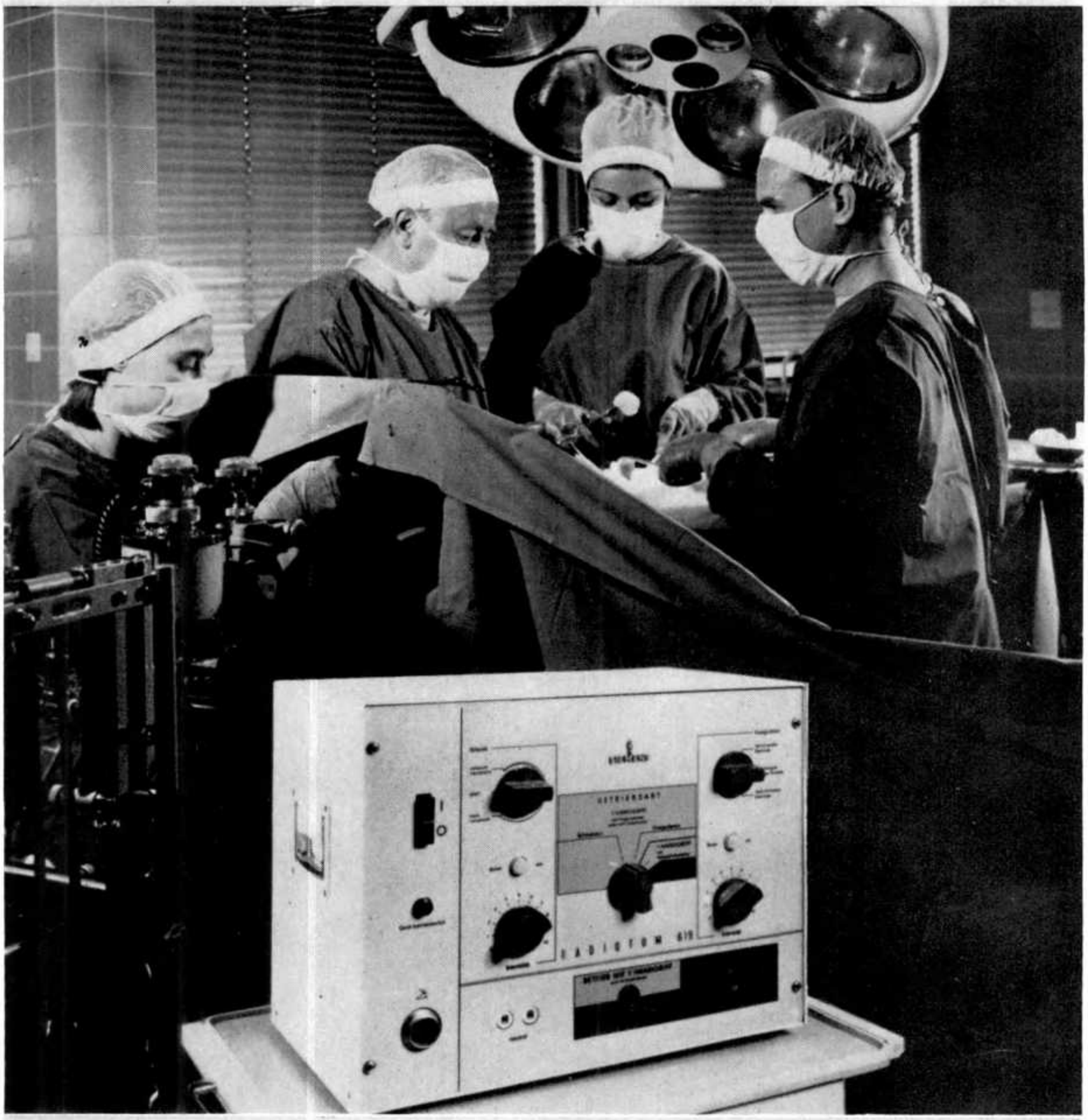

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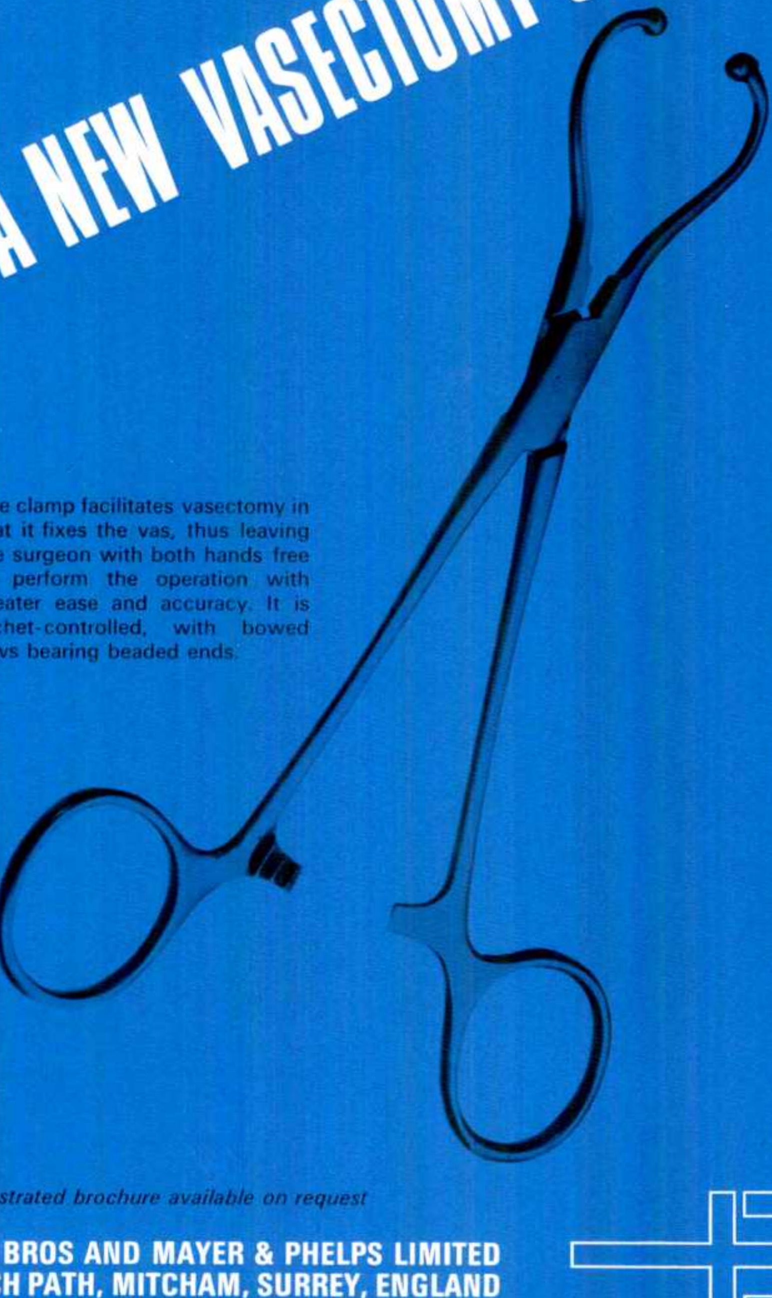

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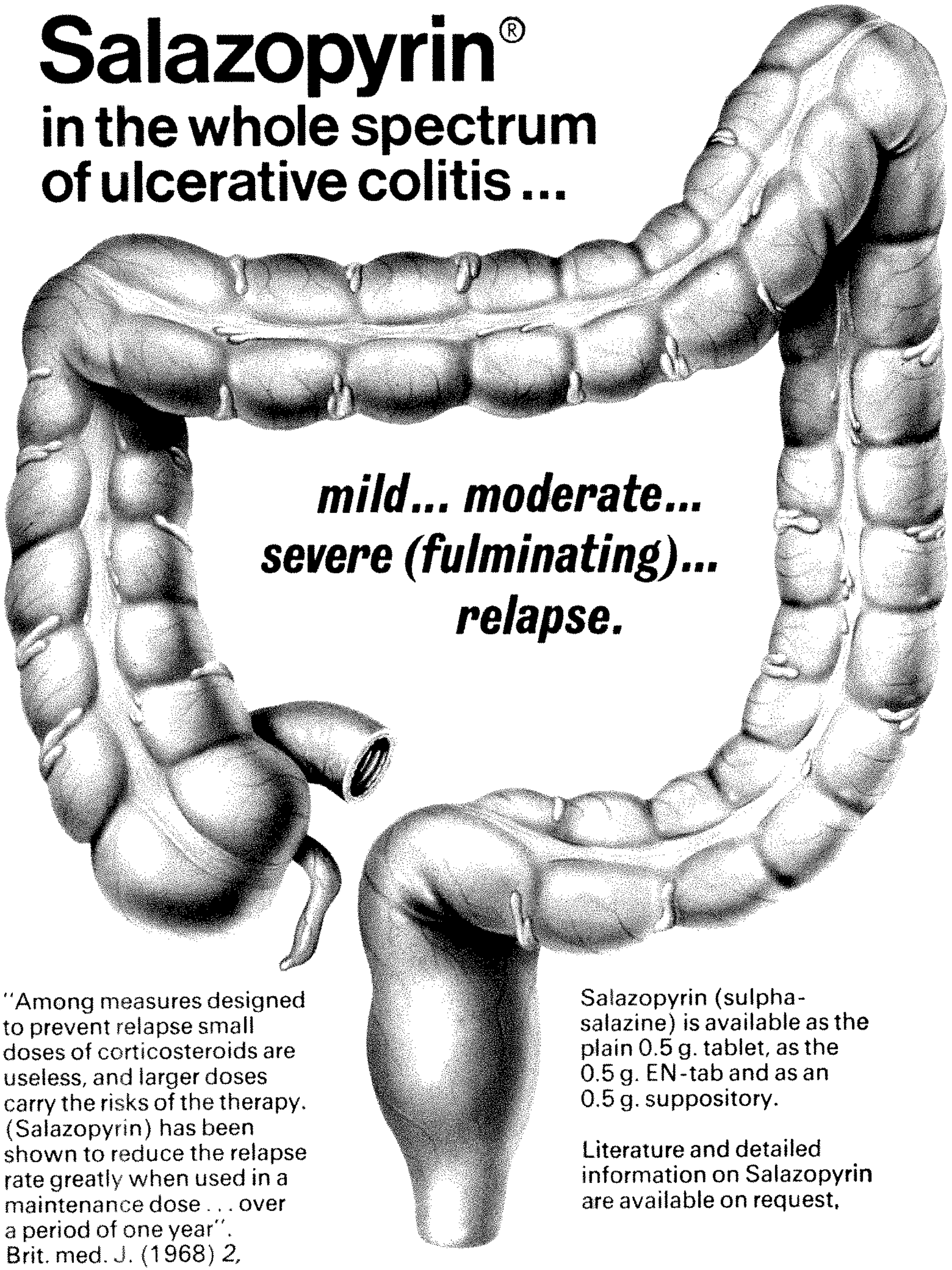

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ORIGINAL PAPERS

ULCERATION OF THE MOUTH, PHARYNX, AND LARYNX IN CROHN'S DISEASE OF THE INTESTINE

By C. B. CROFT and A. R. WILKINSON
THE GENERAL INFIRMARY, LEEDS

SUMMARY

Three hundred and thirty-two cases of Crohn's enteritis were reviewed retrospectively and 20 or 6·1 per cent were found to have suffered from oral ulceration at some stage during their illness. One of these patients with histological evidence of Crohn's disease in the mouth, pharynx, and larynx is described in detail.

WITHIN the past decade Crohn's disease has been diagnosed with increasing frequency, and it has been recognized, moreover, that the distribution of the condition is much more protean than Crohn, Ginzburg, and Oppenheimer (1932) had imagined when they described their first cases affecting the terminal ileum. The same disease is now known to occur anywhere in the small bowel, in the colon and rectum (Lockhart-Mummery and Morson, 1960), in the stomach or duodenum (Comfort, Weber, Bagenstoss, and Keely, 1950; Pryse-Davies, 1964; Wise, Kyriakos, McCown, and Ballinger, 1971), and in the oesophagus (Gelford and Krone, 1968). Recently, 2 cases have been reported of alleged Crohn's disease invading the mouth (Dudeney and Todd, 1969; Issa, 1971), which has stimulated us to review the records of the series of 332 cases of Crohn's disease treated at Leeds Infirmary between 1939 and 1968 inclusive to see how many had suffered from oral ulceration. Twenty patients with this complication were discovered.

CLINICAL MATERIAL AND FINDINGS

Of the 20 patients with Crohn's disease and concomitant oral ulceration, 14 were interviewed and re-examined. Four patients who now live a considerable distance from the hospital were contacted by postal questionnaire. The remaining 2 patients had died and were not considered further in this study. Details of the 18 cases reviewed are listed in *Table I.*

Sex Incidence.—It will be seen that there were 9 males and 9 females, a ratio of 1 : 1, which is the same sex ratio as for the parent series of 332 cases of Crohn's disease.

Relation to Bowel Symptoms.—In 3 patients oral ulceration occurred as a presenting feature of the illness, and in 1 patient the onset of oral ulceration actually preceded bowel symptoms by 1 month. In 10 patients oral ulceration appeared from 2 weeks to 3 years after the onset of bowel symptoms (within 6 months in half of them). Four patients developed oral ulceration in the postoperative period, 2 of these occurring within 1 month of operation. It could be argued that oral lesions encountered postoperatively may be due to other specific causes such as candidiasis or vitamin deficiencies, but it is much less likely that the commoner oral ulceration occurring preoperatively could be so caused.

Severity of Ulceration.—Oral ulceration was described as severe in 10 patients, meaning that the lesions were bad enough to cause dysphagia. The majority of these cases exhibited recognizable oedema of the lips and bleeding from the mouth. The remaining 8 patients gave histories of recurring attacks of oral ulceration but these were deemed to be mild.

Site of Intestinal Lesions.—In 8 patients—7 with severe mouth ulcers—Crohn's lesion in the intestine was confined to the large bowel. As there were 70 cases in the original series with colonic or rectal lesions, the incidence of oral ulceration in association with Crohn's disease of the large bowel was 11·4 per cent. Five patients with oral ulceration had involvement of the terminal ileum alone, out of 136 patients with this distribution of intestinal disease, an incidence of 3·6 per cent. The remaining 5 cases with oral ulceration had Crohn's lesions involving both the colon and the terminal ileum and were derived from the group of 115 cases with mixed lesions of the bowel, an incidence of 4·3 per cent.

Physical Findings at Review.—On examination of the 14 patients who attended for review at hospital only 4 showed signs of previous oral ulceration. Three of them had diffuse scarring of the soft palate (*Fig.* 1). One patient still has florid changes in his mouth and laryngopharynx (*see* Case Report).

Treatment.—Four patients were ill enough to require treatment for their oral condition with

Table I.—DETAILS OF PATIENTS PRESENTING WITH MOUTH ULCERS IN THE COURSE OF CROHN'S DISEASE

PATIENT	AGE AND SEX	SITE OF CROHN'S LESION IN BOWEL	OPERATION FOR INTESTINAL LESION	ORAL ULCERATION	INTERVAL BETWEEN ONSET OF BOWEL SYMPTOMS AND ORAL LESIONS	INTERVAL BETWEEN APPEARANCE OF ORAL LESION AND BOWEL OPERATION	FINDINGS OF ORAL EXAMINATION AT REVIEW	DURATION OF ORAL ULCERATION	TREATMENT OF ORAL ULCERATION
P. C.	27 M.	Colon	Proctocolectomy with ileostomy	Severe	Simultaneous	15 years	Gross oedema of epiglottis and larynx	15 years	Prednisone 10 mg. t.d.s.
D. A.	29 M.	Colon	Colectomy, ileorectal anastomosis, rectal excision, ileostomy	Severe	6 months	1 year	Scarring of soft palate	6 months	Prednisone 10 mg. t.d.s.
A. B.	31 M.	Colon	Colectomy, ileorectal anastomosis	Severe	1 week	6 weeks	Nil	3 weeks	Cortisone acetate 100 mg. q.d.s.
R. K.	24 F.	Colon	Proctocolectomy, ileostomy	Severe	2 months	3 months	Nil	3 months	Local anaesthetic, lozenges, steroids
L. B.	21 F.	Colon	Partial colectomy	Severe	1 year	Immediate post-operatively	Nil	2 months	Parenteral vitamins
E. J.	17 F.	? Terminal ileum	No operations	Severe	Simultaneous	—	Nil	1 year	Salazopyrine 1 g. q.d.s.
D. M.	52 F.	Colon	Proctocolectomy, ileostomy	Severe	20 years	Post-operatively, 1 year	Nil	3 months	No specific treatment
J. W.	34 F.	Colon	Proctocolectomy, ileostomy	Severe	Simultaneous	2 years	Scarring of soft palate	2 years	No specific treatment
R. S.	27 M.	Colon, ileum	Colectomy, ileorectal anastomosis, rectal excision, ileostomy	Mild	2 months before bowel symptoms	1 year	Diffuse scarring of soft palate	1 year	No specific treatment
M. A.	50 F.	Terminal ileum	Right hemicolectomy	Mild	3 years	2 years	Nil	2 months	No specific treatment
G. G.	41 M.	Ileum	Right hemicolectomy, ile-ectomy	Mild	15 years	Post-operatively	Nil	Intermittent	No specific treatment
P. M.	20 F.	Colon, ileum	Proctocolectomy, ileostomy, ile-ectomy	Mild	9 months	Pre-operatively	Not seen	3 weeks	No specific treatment
P. M.	24 M.	Colon, ileum	Proctocolectomy, ileostomy	Severe	2 years	9 months	Nil	1 month	No specific treatment
M. S.	51 F.	Ileum	Ile-ectomy	Severe	6 months	7 years	Not seen	7 years	No specific treatment
P. G.	24 M.	Colon	Proctocolectomy, ileostomy	Mild	2 weeks	6 weeks	Nil	1 month	No specific treatment
D. S.	31 M.	Ileum, colon	Right hemicolectomy, with ile-ectomy, sigmoid colectomy	Mild	Unknown	Pre-operatively	Not seen	Unknown	No specific treatment
M. W.	37 F.	Ileum, colon	Right hemicolectomy, subtotal colectomy, resection ileum I, resection ileum II	Mild	Unknown	Pre-operatively	Not seen	Unknown	No specific treatment
P. H.	40 M.	Ileum	Right hemicolectomy	Mild	2 months	1 month post-operatively	Nil	2 months	No specific treatment

systemic steroids, and all responded well to this therapy. One patient who developed oral ulceration postoperatively was treated with parenteral vitamin supplements with good effect, which suggests that the cause of the oral ulceration in this case may have been a deficiency state rather than Crohn's disease. The remaining 13 patients received no specific treatment for their oral lesions. However, 9 patients stated that after undergoing surgery for their intestinal lesion the oral ulceration disappeared and did not recur.

Histological Examination of Mouth Lesions.—Unfortunately, biopsy of the oral ulcers was performed in only 1 of the 18 cases where the oral lesions were active, the resulting histological examination producing clear evidence of a granulomatous lesion that could be diagnosed as Crohn's disease. This case is recorded in detail below.

CASE REPORT

P. C., a 27-year-old male, was referred to the Professorial Surgical Unit at Leeds General Infirmary in April, 1970. He gave a 15-year history of recurrent diarrhoea with the intermittent passage of blood and mucus and recurrent oral ulceration. This condition had been serious enough to warrant hospital admission on three occasions. Over the years his general condition had steadily deteriorated, with weight-loss, recurrent chest infections, and increasingly frequent bouts of diarrhoea.

On examination the patient was emaciated and clinically anaemic. Abdominal examination was unremarkable. No abnormality was evident in the anal region. Sigmoidoscopy to 14 cm. revealed relatively normal mucosa, with normal vessel pattern and no contact bleeding. There was a good deal of mucus visible in the bowel lumen. A barium-enema study showed loss of haustral pattern throughout the large bowel, with appearances of colitis polyposa. Examination of the mouth revealed widespread 'aphthous' ulceration of the buccal mucosa and palate.

In view of the patient's long-standing history and steady deterioration it was decided to proceed to total proctocolectomy with ileostomy.

At laparotomy on 4 May the terminal 30 cm. of the ileum and the large bowel from the caecum to the upper descending colon were found to be contracted and thickened, but the sigmoid colon and rectum appeared normal. A proctocolectomy was performed and an ileostomy was established. Postoperative progress was uneventful, apart from a chest infection which responded to physiotherapy and antibiotics (ampicillin), and the patient was discharged home on 20 May with his wounds healing satisfactorily.

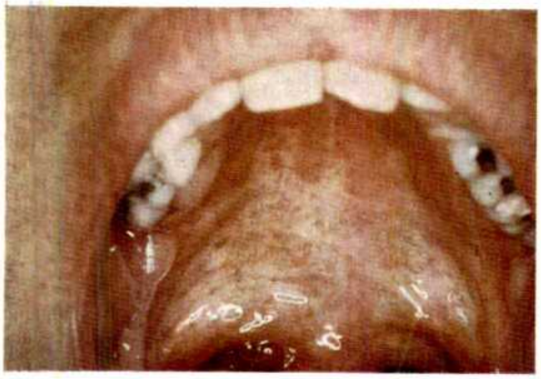

FIG. 1.—D. A. Scarring of the soft palate.

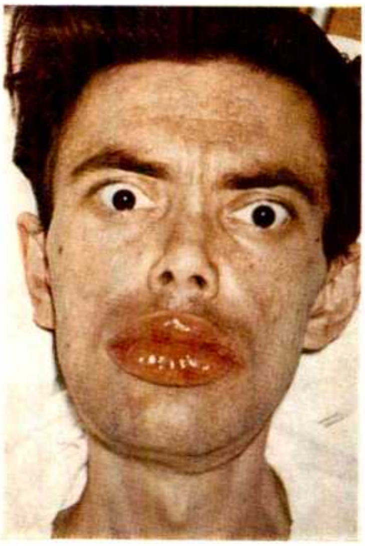

FIG. 2.—P. C. Facial features.

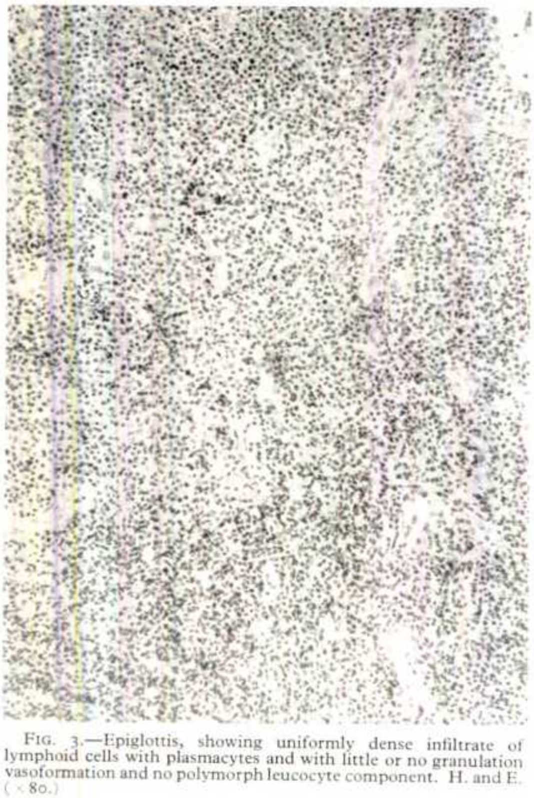

FIG. 3.—Epiglottis, showing uniformly dense infiltrate of lymphoid cells with plasmacytes and with little or no granulation vasoformation and no polymorph leucocyte component. H. and E. (×80.)

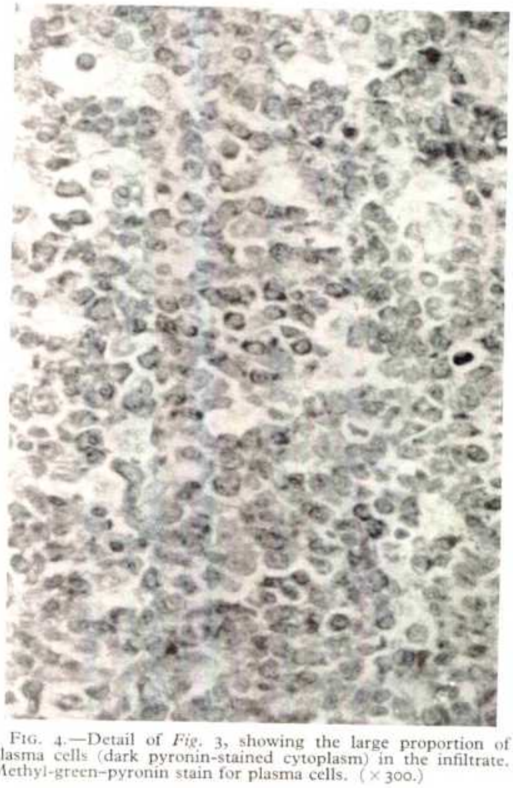

FIG. 4.—Detail of *Fig.* 3, showing the large proportion of plasma cells (dark pyronin-stained cytoplasm) in the infiltrate. Methyl-green–pyronin stain for plasma cells. (×300.)

Pathological examination of the operative specimen showed characteristic changes of Crohn's disease of the large intestine.

SUBSEQUENT PROGRESS.—On 13 June the patient was seen in the out-patients' clinic complaining of severe ulceration of the mouth with dysphagia. On examination he had grossly oedematous swollen lips and tongue (*Fig.* 2), and also inflammation and ulceration of the oral and pharyngeal mucosa. A tentative diagnosis of oral candidiasis was made and treatment with nystatin lozenges was instituted. During this period the patient was also using a local steroid application prescribed by his general practitioner. On 17 June he was readmitted because of the failure of his oral ulceration to respond to treatment. Medication with nystatin lozenges was continued and was augmented by the application of gentian violet to the lips. On this régime his oral condition improved and he was discharged home again on 24 June.

On review 3 weeks later he reported increasing ulceration of the lips and throat with expectoration of blood and mucus. He was experiencing considerable pain and dysphagia and had lost 1 stone in weight since discharge from hospital. His symptoms were so severe that he was immediately readmitted. Under general anaesthesia direct pharyngolaryngoscopy (Mr. Oliver Lord) showed generalized ulceration and oedema of the mucosa of the oral cavity, pharynx, and larynx. The epiglottis was surrounded by a mass of granulation tissue, the arytenoids and false cords were oedematous, but the vocal cords appeared normal. Several biopsies were taken from affected areas, but they were reported to show merely lymphoblastic and plasma-cell infiltration of the tissues, which did not admit of a firm histological diagnosis.

In view of the patient's deteriorating clinical state he was started on prednisone, 10 mg. three times a day, on a tentative clinical diagnosis of Crohn's disease of the mouth, with subsequent reduction of the oedema and of the other changes in the appearance of the oral and pharyngolaryngeal mucosa. This improvement was maintained for several months, but at repeat laryngoscopy on 17 Feb., 1971, the alveolar and palatal mucosae were observed to be thickened and granular and similar changes were noted on the epiglottis and false vocal cords. Further biopsies were taken from each of these areas.

HISTOLOGICAL REPORT ON THE SECOND BIOPSIES.—Professor C. E. Lumsden reported that all biopsies on light microscopy (*Fig.* 3) showed an intensely packed infiltrate, predominantly of plasma cells and large lymphocytes, lying beneath an intact mucosa which did not show evidence of 'aphthous' ulceration. Although the infiltration of cells was intense there was no evidence of follicle formation. Histochemical studies showed the plasma cells to be pyroninophilic (*Fig.* 4). Immunofluorescence studies failed to reveal the presence of immunoglobulin A in any of the cells, but immunoglobulin G and M reactions were given by a proportion of the plasma cells in the infiltrate. The conclusion reached was that these histological findings indicated a variant of Crohn's disease affecting the mouth and laryngopharynx.

Currently, the patient still demonstrates the changes described above and also has developed bilateral sensorineural deafness following a viral illness in March, 1971. The deafness may be attributed to the damage caused by infection in a patient on systemic steroids, and it is of such degree as to require a hearing aid for perception of normal conversation.

DISCUSSION

Of the 2 cases of alleged Crohn's disease of the mouth previously reported by Dudeney and Todd (1969) and Issa (1971), the former exhibited suggestive but not diagnostic features of Crohn's disease in the oral lesion, and in the latter there was no definite evidence of an associated intestinal lesion. Of the 18 cases with oral ulceration discovered in our review of 332 patients with established Crohn's disease of the intestinal tract, only 1 had had a biopsy of the oral lesion taken; the histological report on this biopsy showed changes compatible with Crohn's disease of the mouth and laryngopharynx. As far as we are aware, involvement of the laryngopharynx in a patient with Crohn's disease of the intestine has not previously been reported.

In view of the lack of histological material from the mouth ulcers in our 17 other patients, the precise nature of their oral lesions and the relationship of these lesions to their intestinal conditions are matters for conjecture. It is of interest, and perhaps significant, however, that the lesions in the mouth were presenting features in 3 of these cases, as they were in the patient with a positive biopsy, whilst in 5 of the remaining 14 cases these lesions developed within 6 months of the onset of bowel symptoms. In 14 patients the oral ulceration appeared before operation was performed. The occurrence of the ulcers in the mouth early in the course of the disease in 9 of our cases certainly renders it much less likely that the ulceration was due to candidiasis or vitamin deficiency in these patients.

Against the theory that some of these oral lesions were manifestations of Crohn's disease involving the oropharynx is the fact that most of them healed on conservative management. This is a more satisfactory response than is usually obtained by conservative management of Crohn's lesions at other sites. However, it may be significant that in 17 of our 18 cases the associated intestinal lesion was ultimately excised and many patients noted an improvement in their oral condition following operation.

Acknowledgements.—We are deeply indebted to Professor J. C. Goligher for allowing us to report his cases and for helpful criticism during the preparation of the paper, to Mr. O. C. Lord for his help with the otolaryngological aspects of this paper, to Mr. F. T. de Dombal for advice on statistics concerning the present series of patients with Crohn's disease, to Professor C. E. Lumsden for advice concerning the histological report and for supplying the photomicrograph in *Fig.* 3, and finally to Miss E. Bartholomew for typing the paper.

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ILEAL RECURRENCE AFTER ILEOSTOMY AND EXCISION OF THE LARGE BOWEL FOR CROHN'S DISEASE

By J. C. GOLIGHER
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SUMMARY

Seven cases are recorded of 'recurrent' Crohn's disease in the terminal ileum following ileostomy and colectomy or proctocolectomy for Crohn's disease of the large intestine or alleged ulcerative colitis. The clinical, radiological, and pathological features are described and the management is discussed.

WHEN it was first recognized (Wells, 1952; Brooke, 1959; Lockhart-Mummery and Morson, 1960) that Crohn's enteritis could on occasions be mainly or entirely localized to the large intestine, the impression was quickly formed that this large-bowel version of the condition might carry a much more favourable prognosis after surgical treatment than did the more usual small-bowel lesion (Cornes and Stecher, 1961; Jones, Lennard-Jones, and Lockhart-Mummery, 1966). In this matter, however, a cynic might have felt that the wish could have been to some extent father to the thought, for recurrent Crohn's disease after large-bowel surgery involving creation of an ileostomy might be expected to present serious difficulties in management. A recent follow-up of our own sizeable series of patients at the Leeds General Infirmary treated surgically for Crohn's lesions in various parts of the intestinal tract (de Dombal, Burton, and Goligher, 1971a, b; Goligher, de Dombal, and Burton, 1971, 1972) has confirmed that the recurrence rate of disease mainly or exclusively restricted to the colon and rectum has indeed been significantly less than that of disease mainly or entirely confined to the small bowel. It has shown, further, that of the various forms of colectomy practised for Crohn's disease of the large intestine, the one that seemed to afford the greatest protection against recurrence was an ileostomy and proctocolectomy (combined with excision of more or less of the lower ileum, if diseased). However, the fact remains that

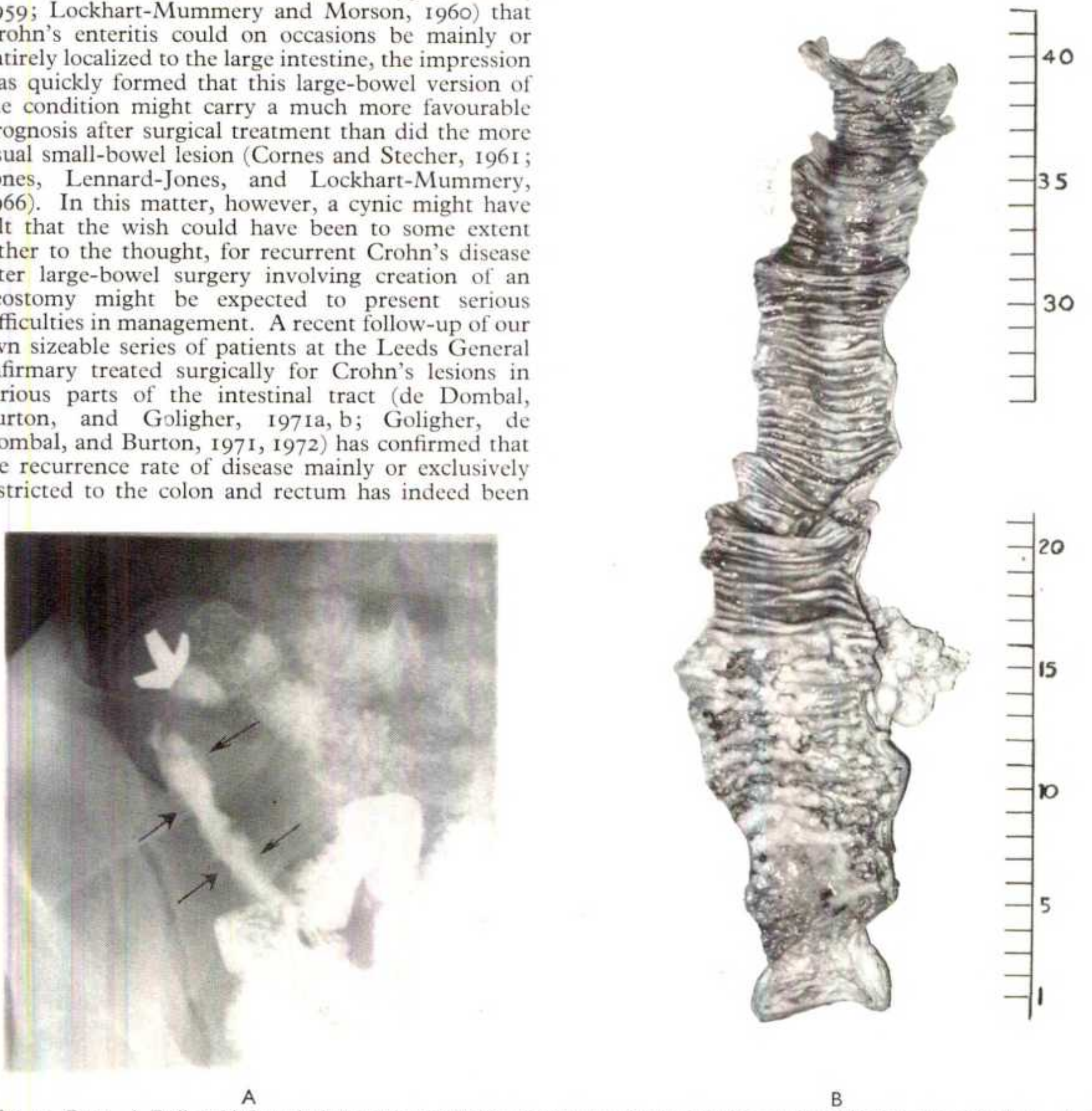


FIG. 1.—*Case* 1. A, Radiograph from the barium-meal and follow-through examination revealing a lesion of Crohn's disease in the terminal 10 cm. of ileum leading up to the ileostomy. B, Specimen of the lower ileum containing the recurrence.

patients may develop recurrence after excision of Crohn's disease of the large bowel, *even when the initial lesion was contained entirely within the colon and rectum and did not encroach at all on the small bowel, and even when it was removed by a complete proctocolectomy with ileostomy.*

During the past 2 years 7 patients have been seen with Crohn's disease in the distal small bowel following previous excisional surgery and ileostomy for inflammatory disease of the large bowel. Four of them were included, as regards both their primary lesions and the recurrence, in the series of cases of Crohn's disease that formed the basis of our recent reports on the long-term outcome of this condition (de Dombal and others, 1971a, b; Goligher and others, 1971, 1972). One patient was included in that series for the primary lesion, but the recurrence arose since the data were analysed. The remaining 2 patients are entirely outside our comprehensive survey, for they both presented after it had been completed, 1 of them, incidentally, having had her primary operation elsewhere. It seemed worth while to publish these cases because they illustrate well some of the problems involved in the diagnosis and treatment of this form of recurrence.

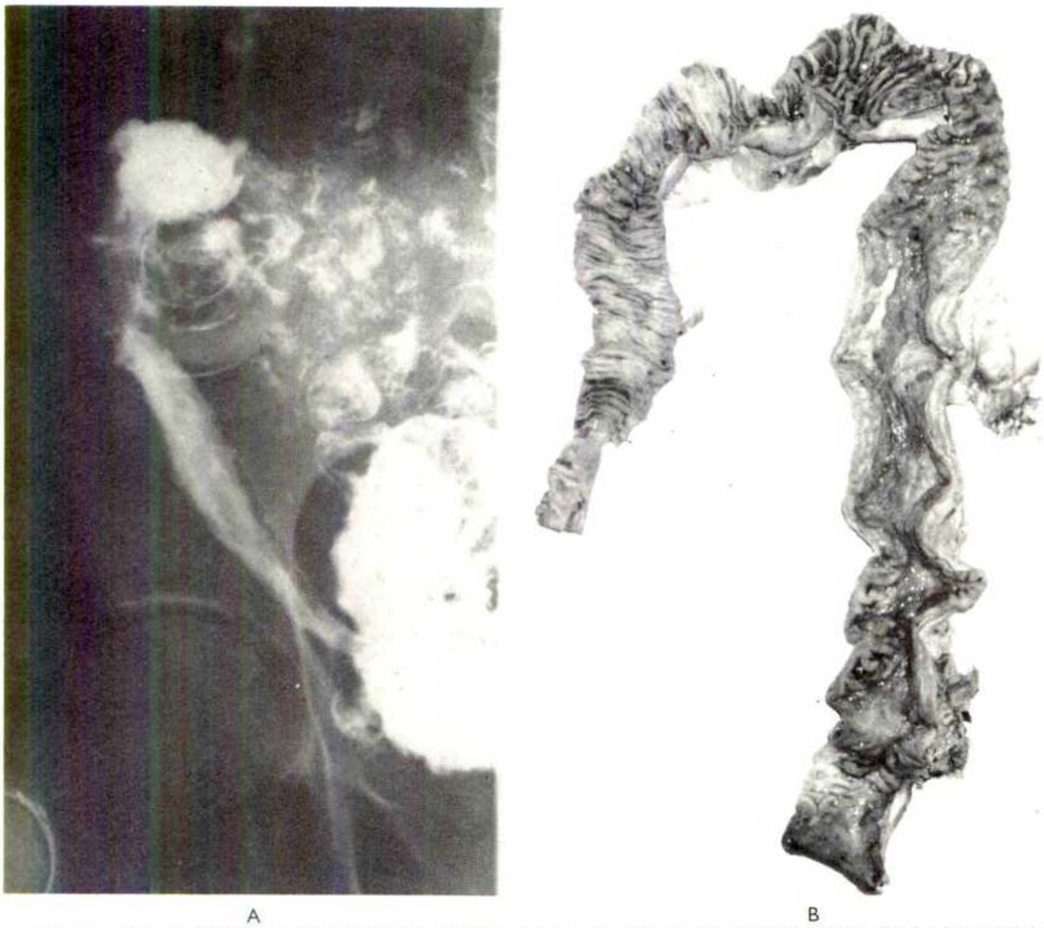


FIG. 2.—*Case* 2. A, Radiograph from the barium-meal and follow-through examination showing a recurrent lesion in the terminal ileum immediately proximal to the ileostomy. B, Specimen of the lower ileum with the recurrence.

CASE REPORTS

Case 1.—J. D. M., a male, born on 10 Aug., 1943.

In April, 1967, this patient underwent complete proctocolectomy with excision of 28 cm. of terminal ileum and establishment of an ileostomy for Crohn's disease of the rectum, colon, and distal ileum. Examination of the operative specimen showed gross disease in the upper rectum and colon as far proximally as the distal ascending colon. The proximal ascending colon and caecum were apparently normal, but there was a patch of enteritis in the last 6 cm. of ileum immediately adjacent to the ileocaecal junction. The more proximal ileum was normal.

The patient made a good recovery from this operation and remained well until September, 1969, when he reported that for 3 weeks he had been experiencing colicky abdominal pains and borborygmi with some abdominal distension and looseness of the ileal discharge. On one occasion he had noticed some blood with the faeces. Abdominal examination revealed no obvious abnormality. The ileostomy appeared satisfactory and digital examination excluded any significant narrowing at skin level, though the finger was not advanced into the abdomen because of discomfort. A barium-meal and follow-through examination showed a normal small bowel except for the last 10 cm. of ileum leading up to the ileostomy, which were narrowed and rigid (*Fig.* 1 A).

Treatment was by reoperation, at which the terminal 40 cm. of ileum were resected and a new ileostomy was established at the old site. Pathological examination of the resected bowel showed gross and microscopic changes of Crohn's disease in its distal 15 cm., the remainder being normal (*Fig.* 1 B). The general condition of the patient on review in September, 1971 (2 years later), was excellent and his ileostomy was functioning normally.

Case 2.—S. M., a male, born on 10 March, 1932.

In July, 1958, this patient was treated by ileostomy and complete proctocolectomy for what was thought clinically to be ulcerative colitis. Examination of the operative specimen, however, showed features more suggestive of Crohn's disease—multiple small areas of ulceration up to 1 cm. in diameter, a localized stenosis at the hepatic flexure, and, on histological section, occasional giant-cell follicles. The 8 cm. of lower ileum attached to the colon had a granular mucosa throughout and a few inflammatory polyps were noted, but no frank ulceration was present.

The patient enjoyed excellent health for 11 years following this operation. Then, in June, 1969, he began to have occasional colicky abdominal pains and looseness of the ileostomy discharge. Quite frequently he observed blood in the faeces. These symptoms gradually became more severe till he reported to hospital in January, 1970. Examination showed a normal-looking ileostomy. Digital examination and passage of the sigmoidoscope through the stoma revealed a thick, granular, partly ulcerated mucosa in the ileum for 8 cm. within the abdomen. A biopsy was taken and showed the histological picture of Crohn's disease. A barium-meal and follow-through study demonstrated characteristic changes of Crohn's enteritis in the terminal ileum (*Fig.* 2 A). Operation was advised and consisted of excision of the terminal 60 cm. of ileum including the ileostomy, a new ileostomy being fashioned at the old site. The postoperative course was marred by the development of an abdominal abscess, which had to be drained. Subsequent recovery was uneventful, and when seen in September, 1971, the patient was in excellent general health and was back at his old job; his ileostomy was acting normally. Pathological examination of the resected small bowel (*Fig.* 2 B) showed thickening of the wall with oedema and ulceration of the mucosa in the distal two-thirds; the proximal 25 cm. appeared grossly normal. Histological sections revealed typical changes of Crohn's disease, especially in the distal extremity of the loop, and also in two related lymph-nodes.

Case 3.—J. R., a male, born on 16 Sept., 1917.

In January, 1959, this patient had a typical segment of Crohn's enteritis in the terminal ileum removed by a right hemicolectomy and terminal ile-ectomy. He remained well till late 1961, when he developed a recurrence of his diarrhoea, and in the next 10 weeks he lost 15·8 kg. in weight. Barium-enema examinations revealed appearances of ulcerative colitis. Sigmoidoscopy to 12 cm. showed a normal mucosa throughout but mucopus was noted coming down from a higher level. In February, 1962, the patient underwent a further laparotomy and had the remaining colon removed and an ileorectal anastomosis established. On pathological examination of the specimen gross appearances compatible with a diagnosis of Crohn's disease of the colon were observed, with a 'skip' lesion in the caecum and two in the ileum.

Convalescence from this operation was slow owing to a wound infection, eventuating in a persistent fistula from the anastomotic site to the abdominal wall. Sometimes flatus escaped from the fistula. The patient's general condition remained indifferent, and after 6 months he had an abdominoperineal excision of the rectum with the establishment of a permanent ileostomy. Thereafter he made a rapid and complete recovery and quickly became reconciled to his ileostomy.

The patient led a normal active existence up to January, 1970, when he reported to hospital again, complaining of recurrent attacks of abdominal pain and loss of 6·3 kg. in weight in the preceding 3 or 4 months. Though no abnormality could be detected on clinical examination of the ileostomy and the abdomen, a recurrence of Crohn's disease was suspected and a barium-meal and follow-through examination was ordered. This confirmed the diagnosis by showing a narrowed segment of the lower ileum. In February, 1970, the patient proceeded to a further laparotomy and had the diseased portion of the bowel excised and a new ileostomy established. The operative specimen (*Fig.* 3) showed typical changes of Crohn's disease in its distal half. Since this operation, up to the latest review in September, 1971, the patient has been well and his ileostomy has functioned normally.

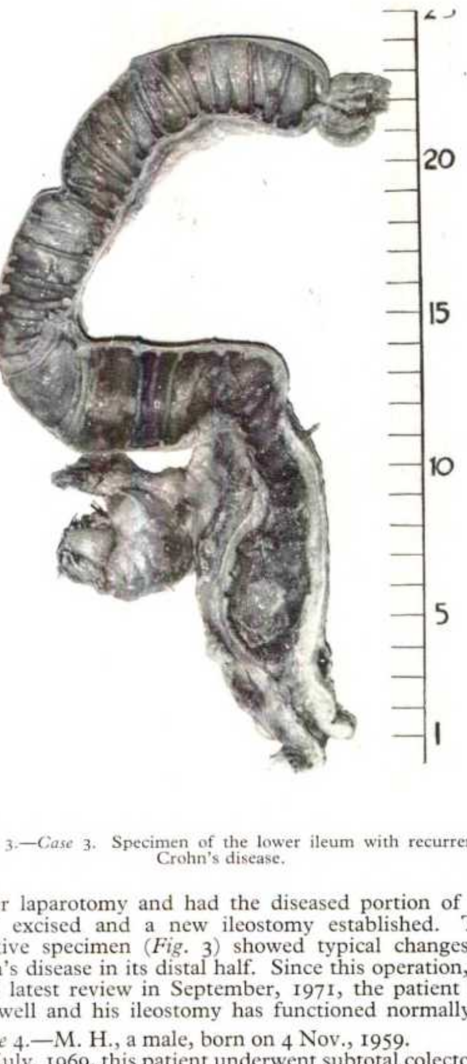


FIG. 3.—*Case* 3. Specimen of the lower ileum with recurrent Crohn's disease.

Case 4.—M. H., a male, born on 4 Nov., 1959.

In July, 1969, this patient underwent subtotal colectomy and ileostomy for a colitis, which it was suspected might be of Crohn's type because of the relatively slight involvement of the rectum compared with the rest of the large bowel. Pathological examination of the operative specimen (*Fig.* 4 A), however, showed gross and microscopical features that were considered to be diagnostic of ordinary ulcerative colitis. The short stump of ileum attached to the colon in the specimen was absolutely normal.

Following operation the patient made a reasonable recovery so far as the healing of his wound and the action of his ileostomy were concerned, but improvement in his general health seemed slow. Then in April, 1970, on attending for a periodic review, he was found to have a fistula through the inferior part of the ileostomy spout just beyond skin level. No other abnormality could be demonstrated in relation to the stoma on clinical examination, and it was thought that the fistula might be due to chafing by the flange of the ileostomy appliance. However, the patient also complained of occasional colicky abdominal pains and very loose faeces, and therefore a barium-meal and follow-through examination was ordered and showed clear evidence of Crohn's disease in the distal ileum (*Fig.* 4 B). In May, 1970, a further laparotomy was performed at which the terminal 40 cm. or so of small bowel, including the ileostomy, were excised and a new ileostomy was established at the same site. Pathological examination (*Fig.* 4 C) showed that the distal third of removed bowel was the seat of Crohn's disease. Since this second operation the patient has regained normal general health, and his ileostomy was working well at review in September, 1971.

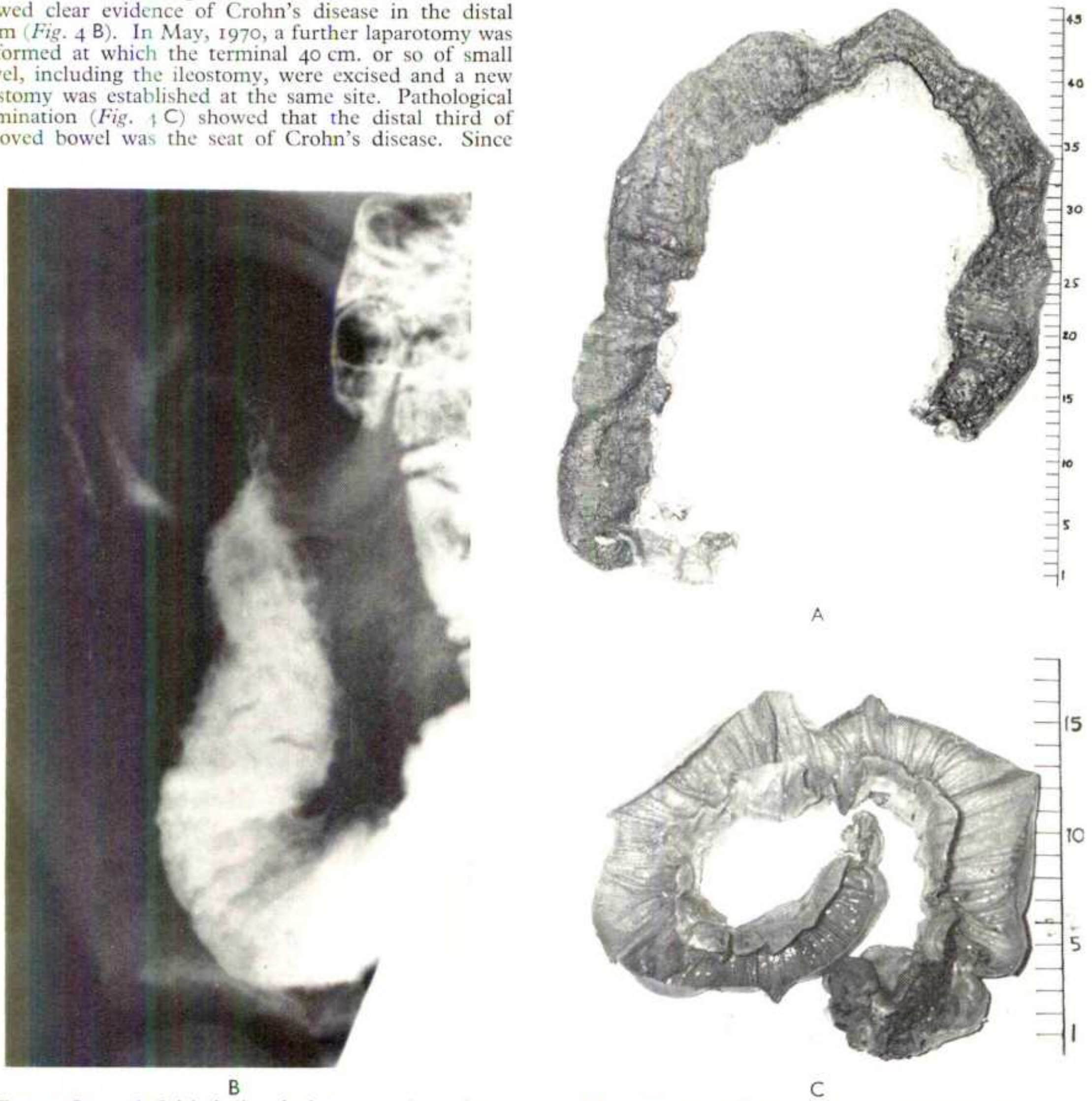


FIG. 4.—*Case* 4. A, Original subtotal colectomy specimen of apparent ulcerative colitis. B, Radiograph from the barium-meal and follow-through examination showing Crohn's lesion in the terminal ileum immediately proximal to the ileostomy. C, Specimen of the lower ileum containing Crohn's lesion.

Case 5.—H. A., a male, born on 10 April, 1940.

The illness of this patient commenced with rectal bleeding in 1961, and on sigmoidoscopy this was found to be due to a diffuse granular proctitis extending as far proximally as 12 cm. from the anal verge. Despite conservative management with salazopyrine and topical steroid enemas, under which there were occasional phases of improvement when the rectal mucosa reverted virtually to normal on sigmoidoscopic examination, the condition became complicated by the development of perianal and submucous abscesses, and the mucosal inflammatory changes gradually extended proximally beyond the reach of the sigmoidoscope. A barium-enema study in October, 1965, showed colitis confined to the rectum and sigmoid, but in January, 1966, the changes were found to have progressed as far proximally as the splenic flexure. At this stage the patient was treated by ileostomy and complete proctocolectomy, the appearances of the operative specimen being found to be those of Crohn's disease of the large bowel rather than of ulcerative colitis.

After this operation the patient remained well till February, 1970, when he began to have colicky abdominal pains and he noticed that the ileostomy discharge had become liquid. He was also anorexic. When he reported to hospital a month later he had lost about 6 kg. in weight. The ileostomy appeared normal on clinical examination, but on barium-meal and follow-through examination, changes of Crohn's disease were observed in the distal ileum. At a further laparotomy in March, 1970, the last 44 cm. of ileum were excised together with the ileostomy, and a new ileostomy was created at the former ileostomy site. Pathological examination of the resected specimen (*Fig.* 5) showed Crohn's disease in the terminal half. Following the operation the patient has remained in excellent health and has had no further trouble with his ileostomy up to the time of review in September, 1971.

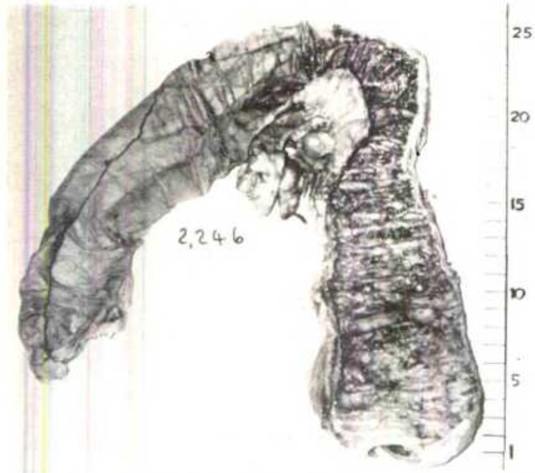
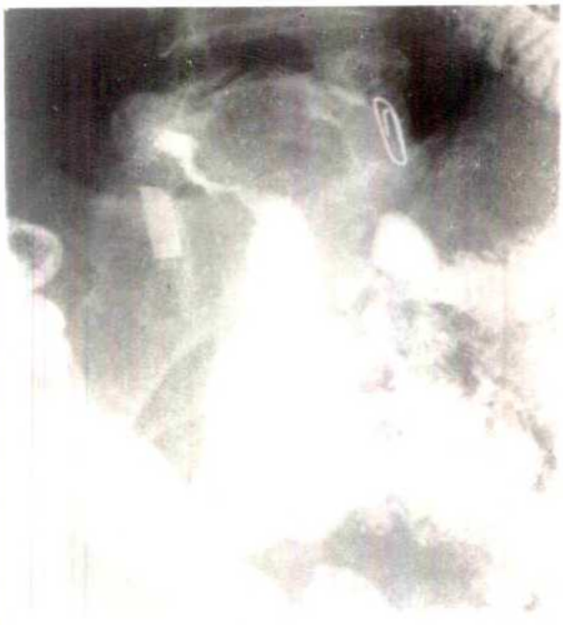


FIG. 5.—*Case* 5. Operative specimen of the lower ileum containing recurrent Crohn's disease.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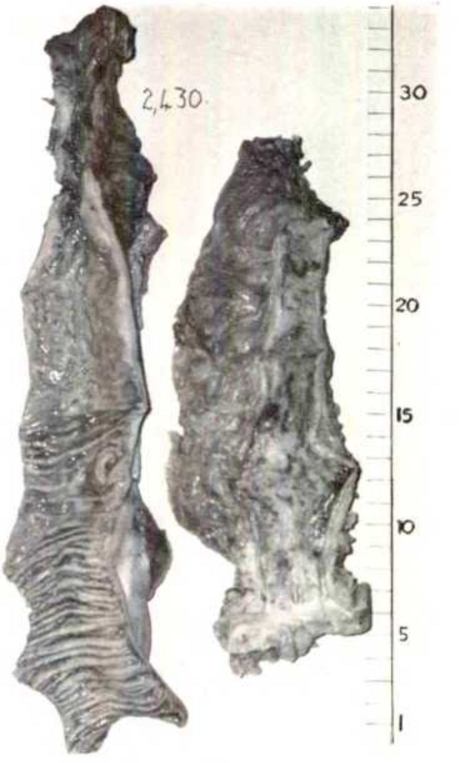

B

FIG. 6.—*Case* 6. A, Radiograph from the barium-meal and follow-through examination showing the diseased terminal ileum. B, Operative specimens of the terminal ileum and rectal stump, showing Crohn's enteritis in the distal half of the former and throughout the length of the latter.

Case 6.—D. B., a female, born on 14 Nov., 1926.

In 1958 this patient had an ileostomy and subtotal colectomy in another hospital for what was alleged to be ulcerative colitis. She was well thereafter till 1968, when she developed an abscess in the vicinity of the umbilicus. This was incised but continued discharging pus, flatus, and a slight amount of faecal-looking material intermittently. When seen in October, 1970, the patient had a very inadequate, contracted and deformed ileostomy, the skin around the stoma was reddened and digested from frequent leakage of faeces, and there was a fistulous opening at the umbilicus. A sinogram demonstrated that the fistula connected with the terminal ileum, which was diseased. On barium-meal and follow-through examination (*Fig.* 6 A) a narrowed segment of bowel was shown leading up to the ileostomy. Rectal examination with the sigmoidoscope revealed a thickened granular bleeding mucosa.

The patient was advised to have both the small-bowel recurrence and the rectal stump removed, and this was done in November, 1970, by an abdominoperineal operation, a new ileostomy being established on the opposite side of the abdomen. Pathological examination of the operative specimens (*Fig.* 6 B) showed that the rectal stump was inflamed and ulcerated throughout its length, and the ileal stump was similarly affected in its distal half. The histological appearances in both the specimens were those of Crohn's disease. Recovery from this operation was quite protracted because of severe sepsis in the perineal wound, which took 4 months to deal. The patient's ileostomy was entirely satisfactory when she was reviewed in September, 1971.

Case 7.—M. T., a female, born on 6 Sept., 1928.

In 1959 this patient had a complete proctocolectomy and excision of 2·5 m. of terminal ileum together with the establishment of an ileostomy for Crohn's disease of the large and small bowel. The postoperative course after the operation was complicated by very profuse ileostomy diarrhoea, with loss of up to 5–6 litres of fluid from the stoma in the 24 hours. With the aid of codeine phosphate in large doses this state of affairs was controlled to some extent, and it was possible to wean the patient off intravenous infusions of fluid and electrolytes. However, at the time of discharge from hospital 7 weeks after operation the ileostomy discharge still amounted to $2\frac{1}{2}$ litres, and the patient required oral supplements of sodium, potassium, calcium, and magnesium, as well as injections of cytamen.

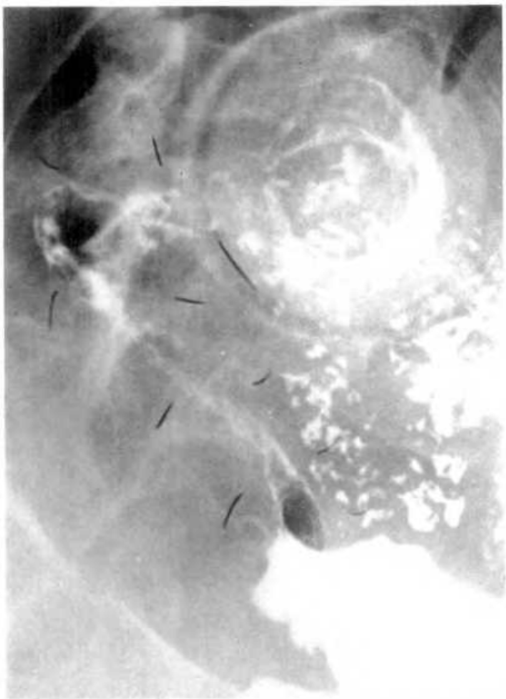

FIG. 7.—*Case* 7. Radiological appearances of the recurrence in the last 10 cm. of the small bowel proximal to the ileostomy.

During the succeeding years the patient led a somewhat precarious existence owing to impaired nutrition and lack of energy, and periodically she needed to come into hospital for short spells for correction of metabolic deficiencies. During one of these readmissions in 1964 a barium-meal and follow-through study was equivocally reported as showing possible recurrence in the small bowel. This was noted in our records, but no further surgical intervention was advised. In January, 1971, the patient was readmitted in a state of dehydration and depletion, which was corrected by suitable infusions. It appeared on interrogation that she had recently been having a good deal of colicky pain. Examination of the ileostomy with the finger detected some thickening and induration of the mucosa just within the abdomen, and, on passing a sigmoidoscope into the terminal ileum through the stoma, the mucosa was seen to be thickened and nodular. A mucosal biopsy revealed appearances of Crohn's disease. A barium-meal and follow-through study showed narrowing of the terminal 7·5 cm. or so of the ileum extending up to the stoma (*Fig.* 7). Elsewhere the small intestine seemed normal.

Although further operation was advised on this occasion to excise the recurrence, the patient and her physician felt that they would prefer to continue with medical management for the time being.

DISCUSSION

The early years of ileostomy surgery for ulcerative colitis were marred by the frequent occurrence of a special form of ileostomy obstruction or dysfunction (Warren and McKittrick, 1951; Counsell and Goligher, 1952) which was due in the early postoperative period to the oedematous state of that part of the ileum of which the serosa was exposed in the projecting ileal spout, and at a later stage to subsequent fibrous stenosis at skin level. With the introduction of the method of eversion of the end of the ileum and its primary suture to the cut edge of the skin (Brooke, 1952; Crile and Turnbull, 1954), this particular type of ileostomy dysfunction has largely been eliminated (Watts, de Dombal, and Goligher, 1966a, b; Goligher, 1967). However, patients with ileostomies are still rather prone to have episodes of partial or complete intestinal obstruction at a higher level owing to kinking or compression of the small bowel by an intraperitoneal adhesion or other mechanical cause. Another cause of obstruction to be considered in patients whose original large-bowel lesion was due to Crohn's disease is the development of a recurrence of this condition in the small bowel. With the steeply rising incidence of Crohn's disease of the large intestine in recent years and the greater number of patients with this condition being submitted to ileostomy, ileal recurrence is becoming an increasingly important cause of obstructive episodes in ileostomy patients. Because of the fact that until recent years not a few cases of Crohn's disease of the large bowel were wrongly diagnosed clinically and pathologically as ordinary ulcerative colitis—as in *Cases* 4 and 5 in the present group of patients—recurrent Crohn's disease of the small bowel should also be thought of as a cause of obstruction in patients whose ileostomies were said to have been performed for ulcerative colitis.

All but 1 of our 7 patients (*Case* 6) with Crohn's lesions in the ileum proximal to their ileostomies had had their original operation performed in the Department of Surgery at the General Infirmary, Leeds, and were known to have had an eversion technique used for construction of their stomas. It was thus unlikely that their recent bowel symptoms would be found to be due to stenosis at the ileostomy, and this tentative conclusion was confirmed by visual and digital examination of the ileostomy in each of the 6 cases, which showed that there was no significant narrowing at the stoma itself in any of them. In 2 patients (*Cases* 4 and 6) fistulas were found to be present in relation to the ileostomy. One fistula (*Case* 4) was in the actual ileostomy spout and could well have been due to repeated friction from a badly applied ileostomy bag. The other fistula (*Case* 6) was connected with the bowel at a somewhat higher level and opened at the umbilicus, which was highly suspicious of an ileal Crohn's lesion proximal to the stoma. This patient, who had had her original operation for 'colitis' performed elsewhere, also exhibited a very contracted and somewhat deformed ileostomy, which in itself suggested the possibility of recurrent Crohn's disease. In 2 patients (*Cases* 2 and 7) it was possible with deep digital palpation of the ileostomy under a short general anaesthetic to reach a zone of narrowing and induration in the ileum inside the abdomen, and in both of these cases the passage of a sigmoidoscope through the stoma for a short distance revealed 'cobblestoning' of the ileal mucosa and allowed biopsies to be taken showing histological appearances of Crohn's disease.

Two patients (*Cases* 1 and 2) complained not only of obstructive episodes with colicky pains and change of the faeces to a liquid consistency but also of *occasionally passing blood in the faeces*. This symptom seemed to establish beyond all doubt that there was some lesion in the bowel wall itself as the source of the bleeding, and made the diagnosis of recurrent Crohn's disease much more likely than that of obstruction due to adhesions.

What clinched the diagnosis in most cases, however, was the radiological appearance after a barium-meal and follow-through examination (*Figs.* 1 A, 2 A, 4 B, 6 A, 7). Not only did the barium study show clearly the narrowed irregular segment representing the site of the recurrence—usually in the last 7·5–10 cm. of ileum, just inside the abdominal cavity and leading up to the stoma—but it also demonstrated that most of the small bowel proximal to this segment was normal, which was a very important consideration in planning further therapy.

Elsewhere (de Dombal and others, 1971a, b; Goligher and others, 1971, 1972) we have emphasized the principle followed by us in the management of Crohn's disease, namely to operate and reoperate as required, the criterion of success being the relief of symptoms. In accordance with this policy all of the present 7 patients were offered further surgical treatment to excise the diseased portion of small bowel and to establish a fresh ileostomy. *Case* 7 declined, while the other 6 accepted. The operation performed was very similar in all instances. The abdomen was reopened through the old left paramedian incision. After a thorough exploration to determine the extent of the recurrence and to exclude any 'skip' lesions or other intra-abdominal abnormality, the diseased segment of ileum and the related mesentery were excised, together with the old ileostomy distally and 25 or 30 cm. of apparently normal small bowel proximally. The cut end of the remaining small gut was then brought out as a new ileostomy at the old site in 5 patients and at a new site in the left abdomen in *Case* 6, the stoma being fashioned by the usual eversion technique (Goligher, 1967).

The 6 surgically treated patients all made good recoveries from their operations and were out of hospital within 2 weeks, except for *Case* 6 who had a rectal stump removed by abdominoperineal excision at the same time and developed a very septic perineal wound which took 4 months to heal. All the patients were reviewed in September, 1971, and all appeared to be in excellent general health and to be enjoying normal ileostomy function. Admittedly the interval since operation, which ranges from 11 months to 2 years, is in no case very long, and further recurrence in the fullness of time in some of these patients is certainly a possibility, but they may well go for several years before this happens, or it may never occur, for it is difficult to prognosticate with any accuracy in Crohn's disease. *Case* 3 is particularly interesting in this respect, for this patient originally had a terminal ile-ectomy and limited right hemicolectomy for Crohn's disease of the terminal ileum in January, 1959. He developed a recurrence in the rest of the colon in 1961, and he had a subtotal colectomy with ileorectal anastomosis in February, 1962, followed a few months later by an abdominoperineal excision of the rectal stump and a permanent ileostomy. He then remained in perfect health, doing his ordinary work as a storeman for nearly 8 years till February, 1970, when he developed an ileal recurrence. After his latest ile-ectomy and new ileostomy for this condition he has been able to return to his former job again. In all, therefore, this patient has had 4 operations in over 12½ years, and at present, 18 months after his last operation, he rates himself as 100 per cent fit.

In view of the recent report by Knill-Jones, Morson, and Williams (1970) of a form of prestomal ileitis, distinct from recurrent Crohn's ileitis, arising proximal to the ileostomy for ulcerative colitis, it should be pointed out that in all our 7 cases, including the 2 whose original colectomy specimens were thought to show ulcerative colitis (*Cases* 4 and 6), the subsequent ileal lesion revealed clear histological evidence of Crohn's disease.

Acknowledgements.—I should like to record my sincere thanks to Drs. K. Simpkins and R. S. Harris for performing the majority of the radiological examinations on these patients, and to Drs. M. Cook, C. Abbot, F. G. Shiel, and H. Thompson for conducting the histopathological studies.

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THROUGH-KNEE AMPUTATION

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SUMMARY

Forty-three through-knee disarticulation amputations in 41 patients are reviewed. In 11 patients the procedure was entirely palliative, and 8 of these died within 1 month of operation. Of the 30 patients for whom a prosthesis was planned, only 2 died within this period. Ten patients were measured for a walking pylon preoperatively. The value of premeasurement is demonstrated by the speed of rehabilitation which was achieved by this group. The time scale of rehabilitation was much longer in those patients who were measured for their prostheses postoperatively. However, other adverse factors were present in this group, and their importance is discussed. Despite these factors, a very high rate of ultimate rehabilitation was obtained. Healing was obtained in 83 per cent of the entire series. The results indicate that the through-knee amputation is excellent for the elderly patient with atherosclerotic gangrene of the foot. The importance of an active programme of walking training in this advanced age-group is particularly stressed.

THE concept of amputation through the knee-joint is a very old one, but only relatively recently has there been a revival of this technique as applied to the problem of atherosclerotic gangrene (Early, 1968).

There appear to be two main reasons for the unpopularity of the through-knee procedure: first, the difficulty of designing an acceptable prosthesis, and, secondly, the poor reputation that this operation has acquired for primary healing (Taylor, 1967). It is this latter reason that has led many workers to advocate the Stokes-Gritti procedure in preference to simple disarticulation.

It is evident that any amputation in the ischaemic lower limb must be a compromise. The longer the stump, the greater is the control of any subsequent prosthesis, but unfortunately the smaller is the chance of primary healing. Thus, the standard below-knee amputation, although an excellent procedure when successful, has a failure rate of approximately 30 per cent (Dale and Capps, 1959; Tolstedt and Bell, 1961) when performed for atherosclerotic gangrene.

The above-knee amputation, on the other hand, has a good reputation for primary healing, but successful rehabilitation with a satisfactory prosthesis presents great problems in elderly patients. Furthermore, it carries an appreciable mortality, ranging from 18 to 30 per cent in published series (Gilchrist, 1961; Ham, MacKenzie, and Loewenthal, 1964; Otteman and Stahlgren, 1965).

It might be expected, therefore, that some form of through-knee procedure would prove a satisfactory compromise. Experience with the Stokes-Gritti operation indicates that this is indeed so. Martin, Stuart, and Maelor-Thomas (1967) found that this operation combines the advantage of a high rate of primary healing with the provision of good leverage for controlling the prosthesis. It is, however, not an easy amputation stump on which to fit a satisfactory prosthesis, although this has been denied by some workers (Middleton and Webster, 1962; Nayman, 1964; Lishman, 1965). The long conical shape of the stump provides a relatively small area for end-bearing, and the tendency of the prosthesis to rotate usually necessitates the added security of a pelvic band.

A through-knee disarticulation, besides being a technically simpler operation, does not have these disadvantages (Gillis, 1961). Its broad bulbous stump (*Fig.* 1) permits total end-bearing without discomfort, and its shape is such that with a close-fitting thigh corset the prosthesis cannot rotate (Vitali, Harris, and Redhead, 1967). This enables the final limb to be of light construction with no provision for ischial weight-bearing and without a pelvic band (*Fig.* 2).

An additional advantage of the through-knee procedure is that the length and shape of the stump are accurately known before the amputation is performed. Hence, in suitable cases, preoperative measurement can be made and the first walking pylon is therefore under construction while the stump is healing (Harding, 1967). This considerably shortens the duration of hospital care.

With these considerations in mind it seemed that the place of the through-knee operation in the management of atherosclerotic gangrene should be reassessed.

The present report analyses the results of 43 consecutive through-knee disarticulation amputations carried out on 41 patients in a district general hospital over a period of 4 years.

OPERATIVE TECHNIQUE

The technique used was essentially the same as that described by Batch, Spittler, and McFaddin (1954), but it was modified in several important respects.

With the patient supine and the knee flexed to a right-angle, *equal* flaps were marked out on the skin. The midpoint of the anterior flap was 3 cm. below the tibial tubercle, and the upsweep at the lateral and medial ends of the incision only reached a point at the same level as the tubercle (*Fig.* 3). We believe the construction of unequal flaps with the anterior flap longer than the posterior one to be a major cause of failure to heal in this operation.

With the incision we describe the extra length of the posterior flap ensures that the skin in the region of the stitch-line is completely slack. During the

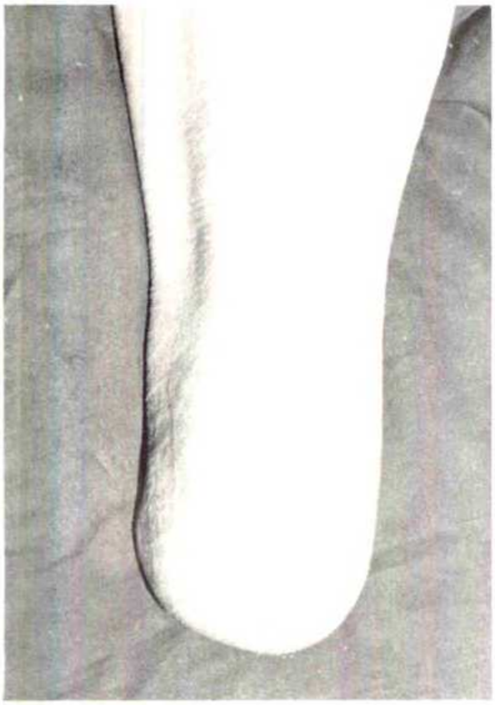

FIG. 1.—Anterior view of a through-knee disarticulation.

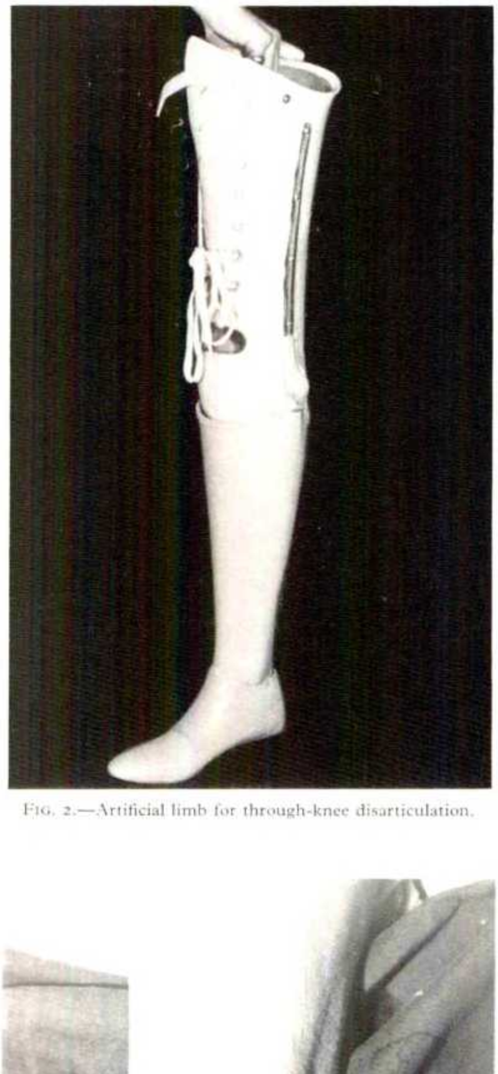

FIG. 2.—Artificial limb for through-knee disarticulation.

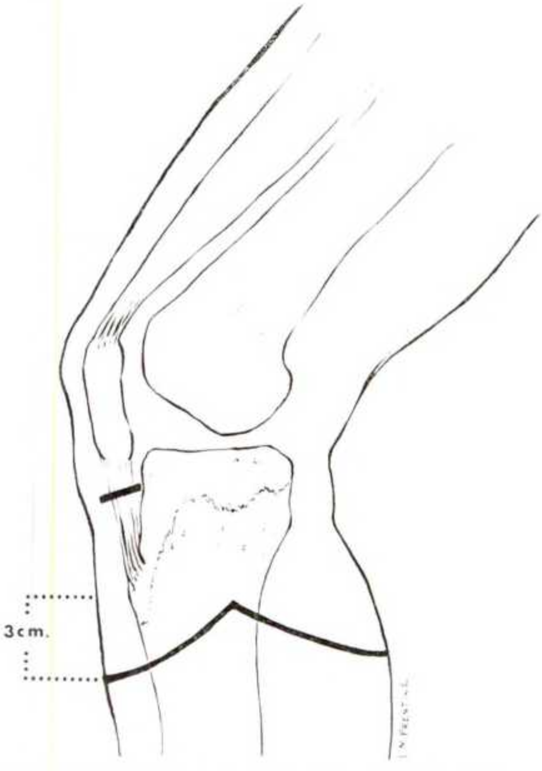

FIG. 3.—Showing the line of incision to give a suture-line without tension.

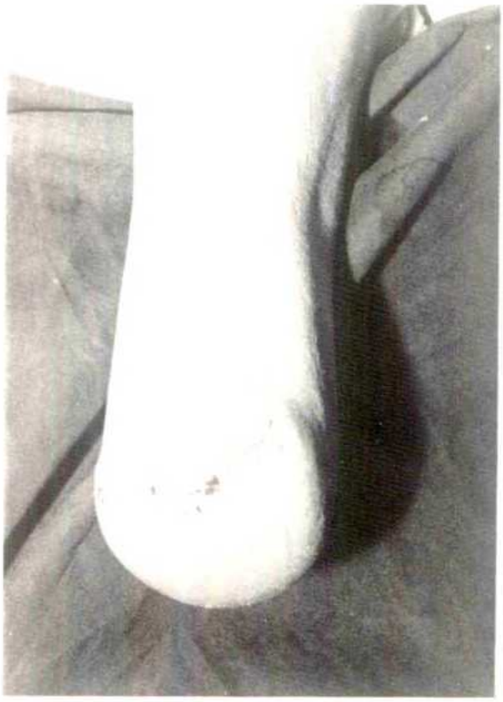

FIG. 4.—Posterior view of a through-knee disarticulation.

succeeding days this slackness is progressively taken up, and by the time the sutures are removed on the fourteenth day a perfect stump will be found (*Fig.* 4). A suture-line which is under the slightest tension when it is constructed will tend to be pulled apart during the postoperative period before the sutures are removed.

When the capsule of the knee-joint is reached it is reflected off the upper end of the tibia. The ligamentum patellae is divided and the joint is entered. The cruciate ligaments are divided and the tibia is displaced forwards to enable the posterior capsule to be divided as low down as possible. In some early cases the menisci were left behind, but we now routinely remove them.

With the division of the posterior capsule, the popliteal nerve and vessels are seen. The vessels are divided between clamps and are ligated individually. The popliteal nerve is cleanly transected and allowed to retract. The two bellies of the gastrocnemius are now divided as close to the femur as possible and the leg is now completely free.

With the assistant guiding the patella downwards the ligamentum patellae is sutured to the posterior capsule with interrupted No. 1 chromic catgut mattress sutures. Using the same suture technique, the cut edges of the capsule are then closed over the condyles of the femur. It has not been our practice to stitch the hamstring tendons to the cruciate ligaments, as described by Harding (1967), and no demonstrable weakness of hip extension has been apparent.

Table I.—DETAILS OF THE THREE GROUPS OF PATIENTS STUDIED

GROUP	NO. OF PATIENTS			AGE		NO. OF AMPUTATIONS
	Male	Female	Total	Mean	Range	
1	7	3	10	67	52–81	10
2	15	5	20	68	55–81	22
3	6	5	11	76	65–88	11

The skin is closed with interrupted sutures of 00 monofilament nylon, a Redivac suction drain being placed in the subcutaneous space for 24 hours.

Ampicillin and cloxacillin in a dosage of 250 mg. 6-hourly are given for 5 days postoperatively.

The stump is padded with cotton-wool and a firm 6-inch crêpe bandage is applied to prevent postoperative oedema. Normally the dressing is kept in place for 14 days, i.e., until the skin sutures are removed. After this a firm Rayelast bandage is applied and renewed daily.

ANALYSIS OF RESULTS

The patients have been divided into three groups:—

Group 1. Patients who were suitable for preoperative measurements and early postoperative fitting of a walking pylon.

Group 2. Patients for whom a prosthesis was planned but who were unsuitable for preoperative measurement and early postoperative fitting. There were four main reasons for allocation to this group:—

a. Poor general condition, making survival of the patient uncertain.

b. Severe rest pain leading to urgent amputation.

c. Failure of recent vascular reconstruction.

d. Doubt that the amputation stump would survive because of a high level of demarcation.

Group 3. Patients for whom the operation was entirely palliative.

The constitution of these groups is shown in *Table I.* It will be seen that the age structure of groups 1 and 2 is practically identical but that of group 3 is considerably higher.

Table II.—THE INCIDENCE OF POTENTIALLY ADVERSE FACTORS IN THE THREE GROUPS OF PATIENTS STUDIED

OTHER CONDITIONS	GROUP 1 (10 patients)	GROUP 2 (20 patients)	GROUP 3 (11 patients)
Diabetes	0	6	1
Cardiac failure	0	3	1
Recent coronary thrombosis	0	1	0
Hemiparesis	1	3	1
Senile mental changes	0	0	6
Recent failed arterial surgery	1	2	0
Previous contralateral amputation	0	3	0
Chronic bronchitis	1	0	1
Severe hypertension	1	3	0
Malignant disease	0	0	2

Table III.—NUMBER OF PATIENTS SURVIVING IN THE GROUPS STUDIED

GROUP	NO. OF PATIENTS	NO. OF PATIENTS SURVIVING			
		At 1 Week	At 1 Month	At 6 Months	At 12 Months
1	10	10	10	9	9
2	20	19	18	15	14
3	11	10	3	1	0

Table II shows the incidence of potentially adverse factors in the patients in the three groups. As would be expected, these were considerably more numerous in group 2 than in group 1. In group 3 the most common factor was senile mental deterioration of such a degree as to make rehabilitation with a prosthesis quite impossible.

It must be emphasized that advanced age alone was not considered a contra-indication to fitting a patient with a walking pylon. Both groups 1 and 2 contain patients in their ninth decade who were successfully taught to walk with a prosthesis.

Mortality.—*Table III* shows the survival pattern of the patients in the three groups, all of whom have now been followed up for a minimum of 1 year. In the series as a whole the mortality at the end of the fourth postoperative week was 10 out of 41 patients (23 per cent), which at first sight would appear to be unacceptably high. Howard, Chamberlain, and Macpherson (1969) reported a mortality of 14 per cent in their series of through-knee amputations. Martin and others (1967) had a mortality of only 6 per cent in their series of 237 Stokes-Gritti amputations. However, it will be seen that in the present series no fewer than 8 of the 10 deaths were in the palliative operation group (group 3). The mortality within 1 month of operation in those patients for whom there was a real prospect of rehabilitation was only 2 out of 30 patients (6 per cent).

After 6 months 5 of the original 20 patients in group 2 had died. In group 1 only 1 patient had died by this time, whereas, by contrast, in group 3 only 1 patient was still alive.

This analysis emphasizes the importance of separating out the purely palliative amputations when discussing mortality. Clearly, in any series of cases the overall figures will depend on the proportion of patients who fall into this category.

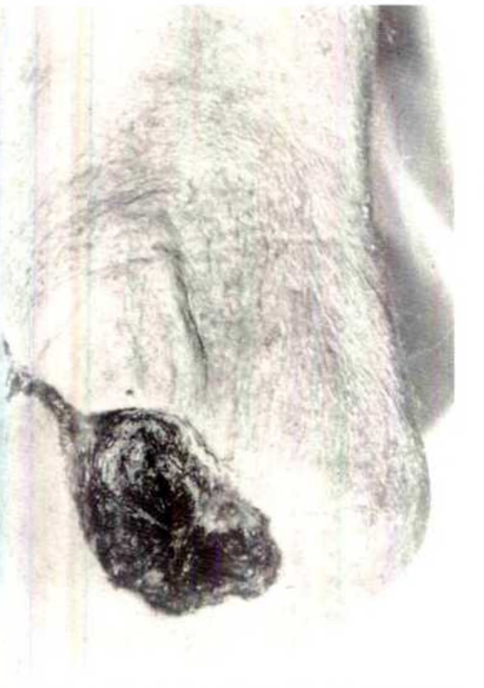

FIG. 5.—Necrosis of the anterior flap with slough over the femoral condyle.

Healing.—In view of the poor reputation that this procedure has acquired for primary healing (Taylor, 1967), particular attention has been paid to this aspect of the present study.

Taking the series as a whole, out of the 43 amputations performed, 2 patients died before healing could properly be assessed. Of the remaining 41 amputations, 26 (64 per cent) healed by primary intention, and 8 (19 per cent) healed after delay due to either wound infection or necrosis at the suture-line. In 7 cases the stump failed to heal, necessitating conversion to an above-knee amputation. Thus, a satisfactory outcome was achieved in 34 out of 41 through-knee amputations, i.e., a success rate of 83 per cent.

This is almost identical with the experience of Howard and others (1969), who found that of their 80 through-knee amputations, 65 ultimately healed—a success rate of 81 per cent. Although these results are inferior to the 91 per cent success rate of ultimate healing reported by Martin and others (1967) for the Stokes-Gritti procedure, they certainly cannot be regarded as unacceptably low.

When failure of healing occurred this was due in every case to full-thickness necrosis of a portion of the anterior skin-flap together with the underlying capsule, leaving the condyle of the femur exposed (*Fig.* 5). This complication led to conversion to an above-knee amputation except in 1 patient. Here the situation was dealt with by removal of the exposed portion of the condyle down to cancellous bone. After an interval of 3 weeks a sufficiently healthy bed of granulation tissue had formed on the bone to permit a split-skin graft to be applied successfully (*Fig.* 6). We believe that this technique may lead to a high rate of stump salvage where localized flap necrosis has occurred.

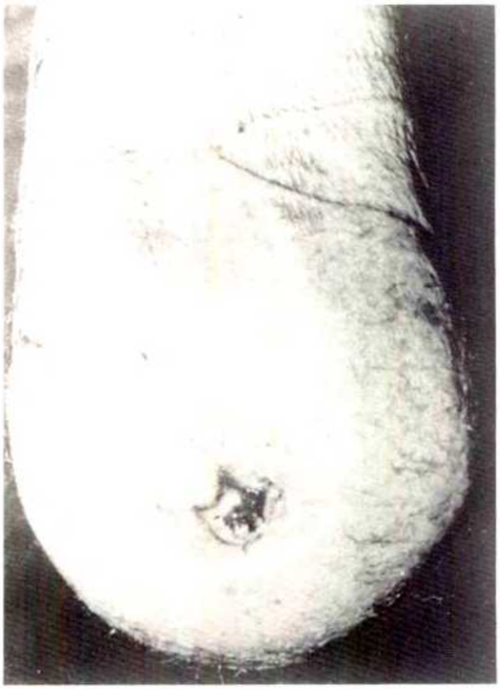

FIG. 6.—The stump has been salvaged by excising the slough and the underlying condyle. A second-stage Thiersch graft has yielded 80 per cent cover.

Table IV.—INCIDENCE OF HEALING IN THE THREE GROUPS OF PATIENTS STUDIED

GROUP	NO. OF AMPUTATIONS	PRIMARY HEALING	DELAYED HEALING	FAILED HEALING
1	10	10	0	0
2	21*	10	6	5
3	10†	6	2	2

* Two patients in group 2 had bilateral amputations, and 1 unilateral amputee died before healing could be assessed.

† One patient in group 3 died before healing could be assessed.

An analysis of the three groups of patients is presented in *Table IV*. The most striking feature is the 100 per cent primary healing rate achieved in group 1, contrasting with the 48 per cent primary healing in group 2. It will be recalled that the patients in group 2 were those who for different reasons were not thought fit for premeasurement at the limb-fitting centre. An analysis of these reasons in relation to healing in this group is given in *Table V*.

From this it will be seen that whereas the cases of *total* failure to heal appear to be unrelated to the preoperative condition, the cases of *delayed* healing were, with 1 exception, confined to those patients whose general condition was such as to make survival after operation uncertain. Eight patients came into this category, and of these, no fewer than 5 showed delayed healing. Two of these were in gross cardiac failure, 1 was hemiplegic on the side of the amputation, 1 was a senile diabetic, and 1 had widespread atherosclerosis with a failed aorto-iliac graft. *It should be noted that despite these disabilities every one of these patients was eventually fitted with a walking pylon and was successfully rehabilitated.* Indeed, although this group showed the highest incidence of delayed healing, the ultimate success rate was 78 per cent.

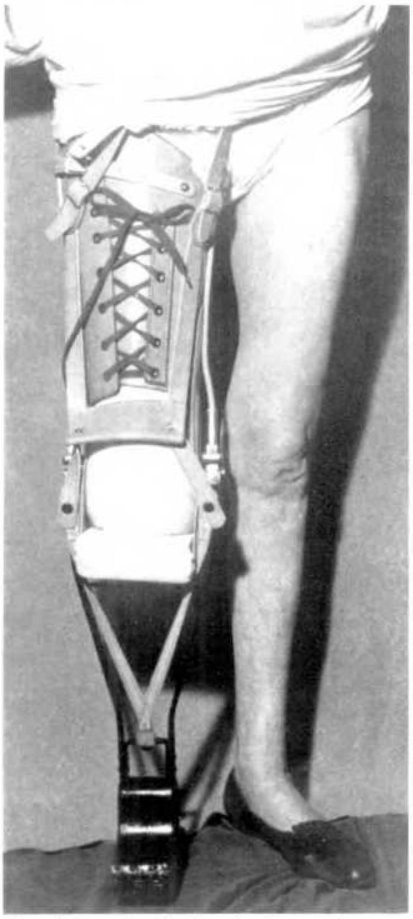

FIG. 7.—A walking pylon fitted on the fourteenth postoperative day.

Table V.—INCIDENCE OF HEALING IN THE PATIENTS WHO WERE THOUGHT UNFIT FOR PREOPERATIVE MEASUREMENT FOR THEIR PROSTHESIS (GROUP 2)

REASON FOR NO PREOPERATIVE MEASUREMENT	NO. OF AMPUTATIONS	PRIMARY HEALING	DELAYED HEALING	FAILED HEALING
a. Poor general condition making survival of operation uncertain	8	2	5	1
b. Severe rest pain leading to urgent amputation	6	4	0	2
c. Failure of recent vascular reconstruction	2	0	1	1
d. Doubt that amputation stump would survive	4	3	0	1

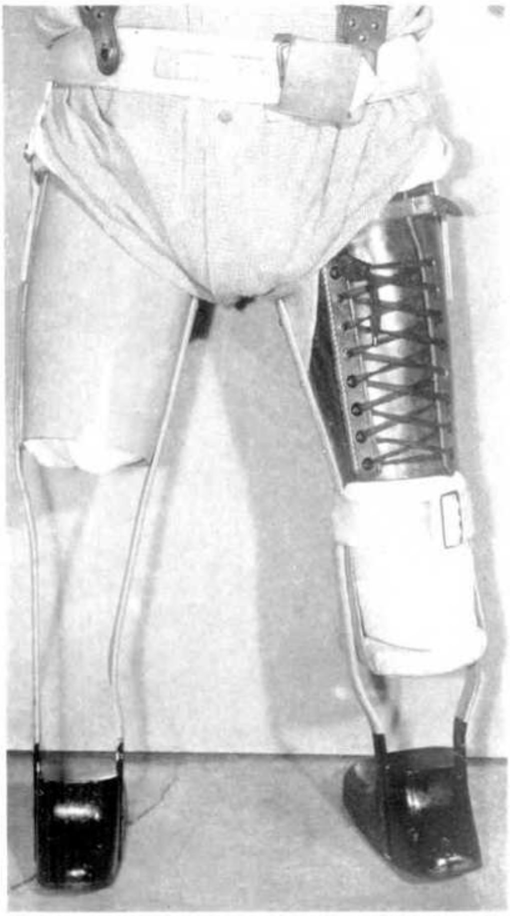

FIG. 8.—A bilateral amputee with short rocker pylons. Note the extra leverage given by the through-knee disarticulation compared with the mid-thigh amputation on the right side.

Rehabilitation.—One of the most important features of the through-knee amputation is the ease with which elderly patients learn to use a walking pylon (Harris, 1967).

The pylon (*Fig.* 7) is designed so that nearly all of the patient's weight is taken on the ischium. The end of the amputation stump rests with only slight pressure on a Sorbo-pad. Where preoperative measurement has been carried out it is usual to start walking training on the fourteenth day after amputation. This is continued until the patient is able to walk with two sticks confidently and without assistance. In addition, he should be able to walk both up and down stairs holding the hand-rail in one hand and a stick in the other. Some patients require the fitting of an additional hand-rail in their homes to give added security.

Even bilateral amputees can achieve a remarkable degree of independent mobility when fitted with short rocker pylons (Vitali, 1966). The patient in *Fig.* 8 is now 81 years old and has had an above-knee amputation of the right leg and a through-knee amputation of the left leg. With bilateral above-knee stumps he would be virtually immobilized. With the extra leverage on the left side he is entirely independent in his home and garden.

Table VI.—THE MEAN TIME FROM AMPUTATION TO FITTING OF A PYLON FOR PATIENTS IN GROUPS 1 AND 2 SURVIVING MORE THAN 6 MONTHS

GROUP	NO. OF PATIENTS SURVIVING 6 MONTHS	NO. WITH SUCCESSFUL UNILATERAL AMPUTATION	MEAN TIME FROM AMPUTATION TO FITTING OF PYLON (days)
1	9	9	14
2	15	11	52

Table VII.—MEAN TIME FROM FITTING OF A PYLON TO FITTING OF AN ARTIFICIAL LIMB IN GROUPS 1 AND 2

GROUP	NO. OF PATIENTS FITTED WITH AN ARTIFICIAL LIMB	MEAN TIME FROM FITTING OF PYLON TO FITTING OF ARTIFICIAL LIMB (weeks)	NO. OF PATIENTS FITTED WITH PERMANENT PYLON
1	8	28	1
2	6	36	5

Wherever possible, as soon as the stump has taken up its final contour and the patient has become sufficiently expert in the use of the pylon, he is fitted with a final prosthesis (*Fig.* 2). This differs from the pylon in several important respects. It is of a lighter construction and the thigh corset is accurately moulded to the stump to prevent rotation in use. Weight-bearing is now for the first time taken fully on the end of the stump, which is well adapted to bear this load. Murdoch (1967) has estimated that the total weight-bearing area here is of the order of 125 sq. cm. The knee mechanism may be of the locking or free-swinging variety. Most patients prefer the added security of the knee-lock, but some, especially the younger patients, learn to use a free-swinging prosthesis extremely well. The major disadvantage of these prostheses is that the joint mechanism must lie outside the limb if it is to be at the same level as the opposite knee. This disadvantage is, however, far outweighed, at least in male patients, by the ease of using it when compared with the difficulty of managing an above-knee prosthesis.

From *Table VI* it will be seen that in group 1 all the 9 patients who survived more than 6 months were fitted with their first pylon and commenced walking training at a mean time interval of only 14 days from the amputation. The mean total time from amputation to discharge in this group was 30 days, and it seems unlikely that this period can be significantly reduced. Even when immediate postoperative fitting of a prosthesis has been practised, the reported time from amputation to completion of walking training is 28 days (Vitali and Redhead, 1967).

In group 2, of the 15 survivors at 6 months, 2 were primary failures requiring conversion to above-knee amputations and 2 were bilateral amputees. In the remaining 11 unilateral amputees the mean interval from amputation to the commencement of walking training was 52 days. Analysis of the data showed that this time interval was the same whether the wound healed by primary intention or was delayed. It seems that the general factors rendering these patients unfit for premeasurement were also largely responsible for the long interval before postoperative measurements could be carried out.

The difference in the capacity for rehabilitation between these two groups is also illustrated by the relative numbers who were ultimately fitted with a prosthesis of the type shown in *Fig.* 2. *Table VII* indicates that 8 of the 9 survivors in group 1 were successfully fitted with this type of artificial limb, with a mean time interval of 28 weeks from the fitting of the first pylon. In group 2 only 6 of the 11 survivors were fitted with such a limb, the mean time interval from the first pylon being 36 weeks, i.e., 2 months longer than for group 1 patients. The remaining 5 patients in group 2 were fitted with a permanent walking pylon.

DISCUSSION

Although our method of subdivision into three groups may seem arbitrary, it has essentially achieved the aim of separating out for special consideration those patients with an exceptionally favourable outlook (group 1) and those with no prospect of rehabilitation (group 3).

The purpose of the operation in the latter group is entirely one of palliation in an otherwise hopeless situation, and the criteria of success are therefore more limited than in the other two groups. In group 3 only two factors are of real importance: primary mortality and the rate of healing. In fact only 1 patient died within 1 week of amputation in group 3, which was regarded as an acceptable primary mortality, but the extremely poor general state of these patients is emphasized by the subsequent survival figures (*Table III*). Six months after amputation only 1 patient out of 11 was still alive, and by 12 months all these patients had died.

In the other two groups the primary mortality of 2 out of 30 patients was considered satisfactory. At 6 months 24 patients were still alive, and there was only 1 further death in the subsequent 6 months. In other words, nearly 80 per cent of those patients for whom rehabilitation was possible survived for more than 12 months. This emphasizes the need for a programme of walking training which is both swift and effective. Perhaps the greatest advantage of the through-knee disarticulation procedure is the speed and quality of rehabilitation that it permits, even in the very elderly (Harris, 1967; Howard and others, 1969). Of the 28 patients in groups 1 and 2 who survived more than 1 month after amputation, all were taught to walk on a pylon. This is a very satisfactory result when it is considered that both groups included octogenarians, and in group 2 there were 2 patients who were hemiplegic on the side of the amputation. Moreover, we found that of the 20 unilateral amputees who survived more than 6 months, 14 were subsequently fitted with an artificial limb. The remaining 6 were given a permanent walking pylon. The important point is that all these patients were fitted with a useful prosthesis on which they could walk without assistance.

The high rate of successful rehabilitation after the through-knee disarticulation procedure is noted by other authors. Vitali and Redhead (1967) achieved a 92 per cent success rate in this respect. With the Stokes-Gritti amputation, on the other hand, the results appear to be inferior. Middleton and Webster (1962) and Lishman (1965) achieved approximately 70 per cent success with walking on either a pylon or an artificial limb, whereas Martin and others (1967) report only a 55 per cent rehabilitation rate in their series of 230 patients.

In the present series the outstanding difference between groups 1 and 2 is in the time interval from amputation to the commencement of walking training. However, these figures must be interpreted with care. It is not suggested that had the patients in group 2 been premeasured, their rate of rehabilitation would have been similar to that in group 1. Although a better performance may have been achieved in some individuals, in the majority of patients in group 2 the factors rendering them unsuitable for preoperative measurement were also largely responsible for the more prolonged postoperative course that they followed.

What is certain, however, is that a policy of *post-operative* measurement in all the cases would have unnecessarily prolonged the duration of hospital treatment of those patients who fell into group 1. Even the most favourable case would not have been fit to travel to the limb-fitting centre until at least the seventh post-amputation day, and many would have been delayed for a considerably longer period than this.

The importance of the excellent results obtained in group 1 is that they set a standard by which the data from group 2 may be judged. In particular, we wish to emphasize the great value of preoperative measurement whenever possible. Apart from the saving of time, which is considerable, this policy has the effect of creating a more positive approach to the operation. To know in advance the date on which the first walking pylon is to be fitted sets a definite target towards which both patient and staff can be encouraged to work.

Finally, the question of healing must be considered. The fact that every patient in group 1 healed by primary intention suggests that there is no inherent defect in this form of amputation with the technique described. It has also been noted that although group 2 patients showed a high incidence (6 out of 16 amputations) of delayed healing, it appeared that other factors were at least as important in determining the time between amputation and the commencement of walking training.

Taking the series as a whole, failure of healing due to full-thickness necrosis of part of the anterior flap occurred in 7 out of 41 amputations, an incidence of 17 per cent. This is considerably lower than the reported incidence of failure in the standard below-knee amputation for atherosclerotic gangrene (Dale and Capps, 1959), but is inferior to the healing record of the Stokes-Gritti procedure. However, with the technique described for dealing with localized flap necrosis, it is hoped that more cases of failed healing in the through-knee disarticulation will be salvaged.

Acknowledgements.—We should like to thank Dr. E. E. Harris and his colleagues at the Limb Fitting Centre, Roehampton, for the advice and the unfailing assistance that we have received in the fitting, training, and rehabilitation of all our patients.

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BILIARY-PRESSURE STUDIES DURING CHOLECYSTECTOMY

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SUMMARY

A method of manometric choledochography is described by which three types of choledochal pressure/filling curves could be obtained in patients undergoing cholecystectomy. This work provides evidence that biliary pressures are mainly a function of the choledochal sphincter in man and are largely independent of duodenal muscular activity. Reflux of contrast medium into the pancreatic duct is not associated with either obstructive pathology of the lower choledochus or biliary hypertension.

BILIARY manometry has been extensively utilized as an ancillary procedure to choledochography in the operative investigation of extrahepatic biliary disease. However, no accurate information is available on the pressure dynamics of the radiologically normal common bile-duct in man, and such data as exist on the subject have largely been derived from animal experimentation (Elman and McMaster, 1926; Lueth, 1931; Parry, Hallenbeck, and Grindlay, 1955). It is not possible to extrapolate these experimental findings to man because of the anatomical differences of the periampullary region that exist between the various species (Didio and Anderson, 1968). There is considerable controversy as to whether the biliary pressures in man are a function of the choledochal sphincter or duodenal muscular activity. Some workers (Lueth, 1931; Bergh and Layme, 1940; Long, 1942) maintain that the choledochal sphincter is capable of independent activity and is responsible for the pressure changes in the choledochus, whilst others (Burget, 1925; Elman and McMaster, 1926; Potter and Mann, 1926) consider that the choledochal pressure is largely dependent on duodenal muscular activity.

A method of operative manometric choledochography is described which allows an accurate measurement of dynamic pressure changes in the common bile-duct before, during, and after the injection of radio-opaque medium. It has been applied to the investigation of choledochal pressures in cases with a radiologically normal common bile-duct.

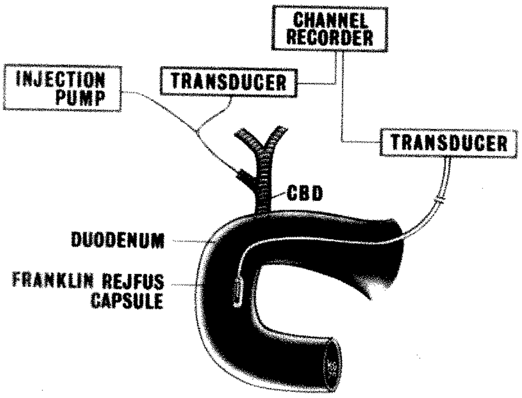

FIG. 1.—The apparatus used.

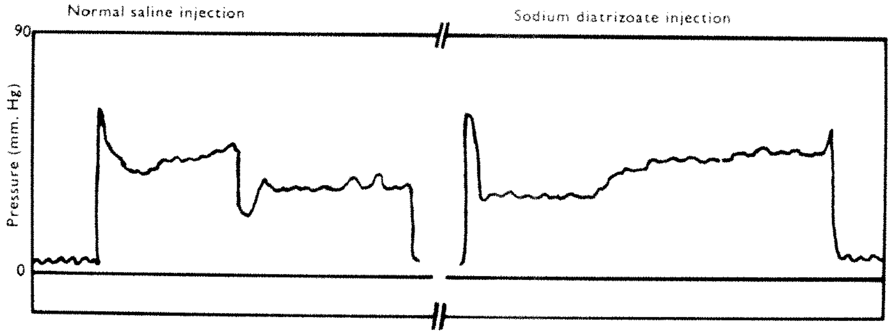

FIG. 2.—Choledochal pressure/filling curves using a constant-flow pump.

MATERIALS AND METHODS

Thirty-two patients undergoing cholecystectomy were studied. The age-range was 28–72 years. No drugs were administered for 10 hours before operation in all but 2 patients. The latter received atropine, 0·6 mg., 1 hour before surgery. Anaesthesia was carried out with thiopentone, nitrous oxide, and oxygen, a combination which has no effect on biliary pressures (Mallet-Guy, 1952). Muscle relaxation was achieved with D-tubocurarine. Each patient had an operative choledochogram using an electrically driven pump. This injected sodium diatrizoate, 40 per cent, at a constant rate of 6 ml. per minute through a Portex cannula inserted into the common bile-duct via the cystic duct (*Fig.* 1). The pressure exerted by the pump varied with the resistance to flow in the tubing but it averaged 25 mm. Hg. The system incorporated a side-tube leading to a pressure transducer which was connected to a multichannel recorder. Simultaneous duodenal pressure tracings were also recorded using a Franklin-Rejfus tube introduced nasogastrically, through which was threaded a Portex pressure line tubing. This was attached to another pressure transducer connected to the same recorder. Continuous visual monitoring of the biliary tree during the period of injection of dye was effected by means of a Siemens image intensifier.

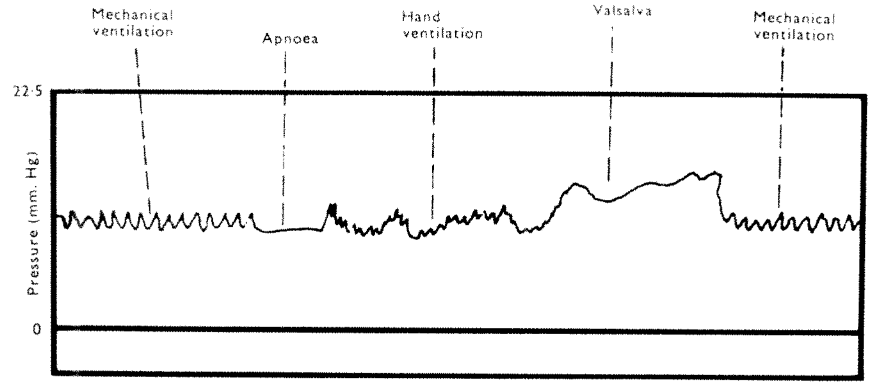

FIG. 3.—Changes in biliary pressure with alterations in ventilation.

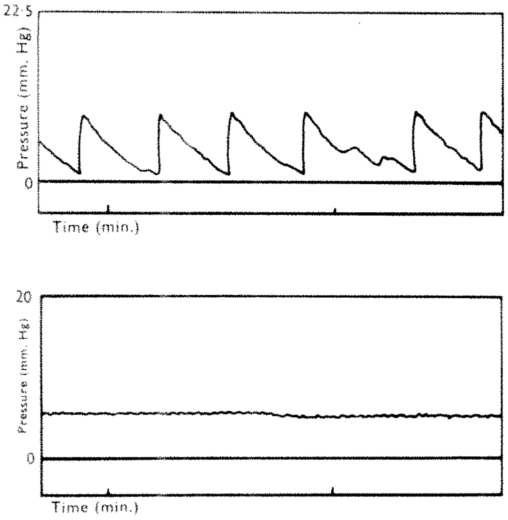

FIG. 4.—Changes in resting choledochal (above) and duodenal (below) pressures.

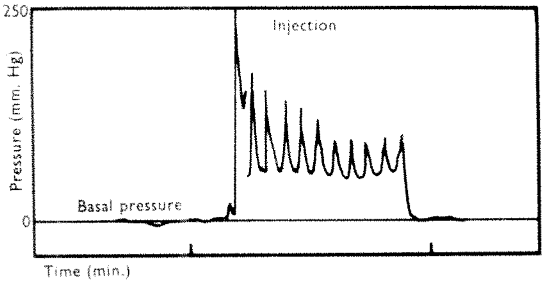

FIG. 6.—A type-1 (normal) choledochal pressure/filling curve.

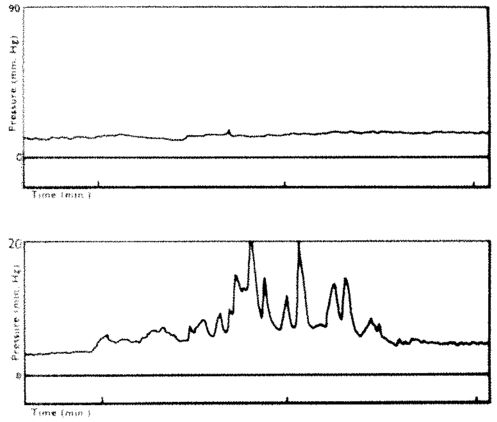

FIG. 5.—Choledochal (above) and duodenal (below) pressure tracings during pentazocine-induced segmental duodenal activity.

Table I.—BASAL CHOLEDOCHAL PRESSURES IN 30 CASES WITH A RADIOLOGICALLY NORMAL OPERATIVE CHOLEDOCHOGRAM

TYPE OF CASE	NO. OF CASES	COMMON BILE-DUCT PRESSURE (mm. Hg)
With good gall-bladder function at cholecystography	17	5·9 ± 3·3
With poor or absent gall-bladder function at cholecystography	13	6·3 ± 2·17
Total	30	6·1 ± 4·3

FINDINGS

Injection of methane iodine compounds into the biliary tree is said to cause biliary hypertension as these compounds are mucosal irritants (Mallet-Guy, 1952). However, choledochal pressure monitoring during injection with isotonic saline at the rate of 6 ml. per minute gives a very similar pressure/filling curve to that obtained during sodium diatrizoate injection at the same rate (*Fig.* 2).

It can also be argued that the introduction of the common bile-duct cannula through the cystic duct would result in an artificially high common bile-duct pressure as a result of the sudden exclusion of the gall-bladder reservoir effect from the extrahepatic biliary system. However, statistical analysis (t-test) showed no significant difference ($P > 0{\cdot}8$) in the basal choledochal pressure measured by this method between cases with good gall-bladder function and cases with poor or absent gall-bladder function at oral cholecystography (*Table I*).

Resting Pressures.—The average choledochal resting pressure was 6·1 ± 4·3 mm. Hg. Cases with good gall-bladder function at oral cholecystography had a mean resting common bile-duct pressure of 5·9 ± 3·3 mm. Hg. The mean resting choledochal

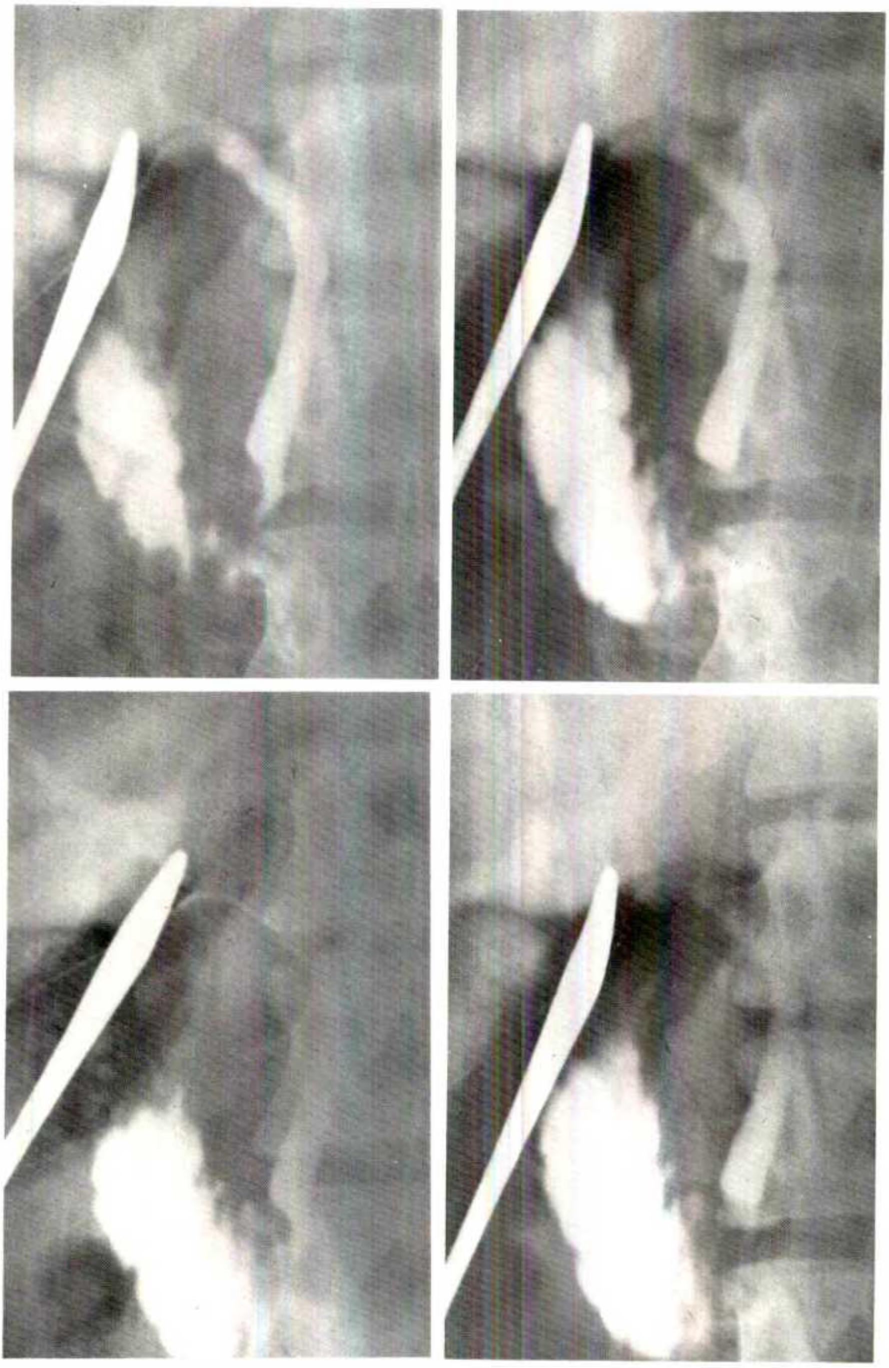

FIG. 7.—Contractions of the lower 2·5 cm. of the common bile-duct in a case showing a type-1 pressure/filling curve.

pressure in cases with poor or total absence of gall-bladder function was 6·3 ± 2·17 mm. Hg.

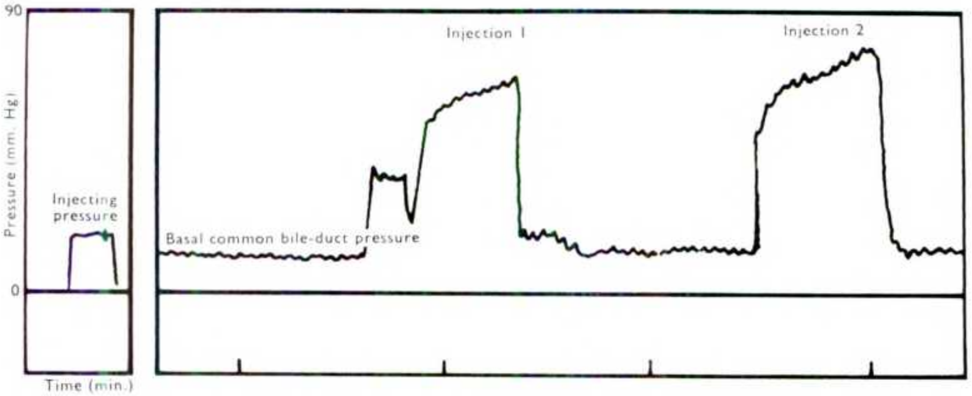

FIG. 8.—A type-2 (hypertonic) choledochal pressure/filling curve.

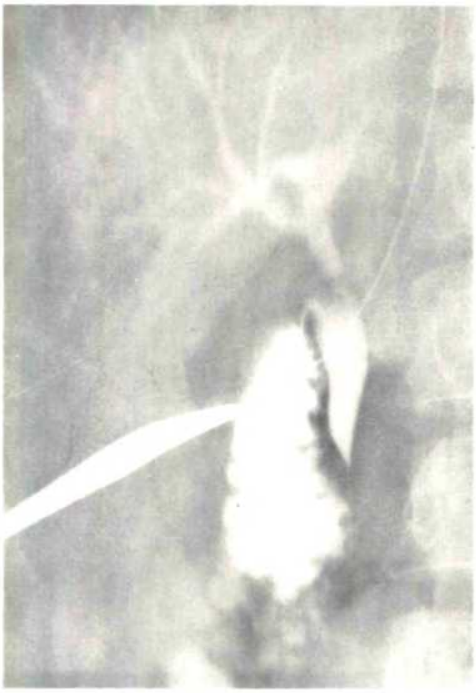

FIG. 9.—Choledochogram from a case showing a type-2 pressure/filling curve.

The resting choledochus exhibited pressure waves of an average amplitude of 2·2 mm. Hg coincident with the downward movement of the diaphragm and liver during respiration. These pressure waves were regular during mechanical ventilation, they disappeared during periods of apnoea, and were extremely variable during hand ventilation (*Fig.* 3). The choledochal pressure showed a steady rise during the Valsalva manœuvre.

The common bile-duct also exhibited pressure-wave activity independent of respiration and heart-beat. These pressure waves, noted in five tracings, were of a mean amplitude of 5·8 mm. Hg, they occurred at irregular intervals, and were not accompanied by any significant changes in either intra-duodenal pressure or duodenal muscular activity (*Fig.* 4). There was no correlation between the resting pressure in the common bile-duct and the mean duodenal pressure or muscular activity. Moreover, the choledochal pressure showed no appreciable alteration during periods of intense duodenal peristalsis induced by pentazocine, 15 mg. i.v. (*Fig.* 5).

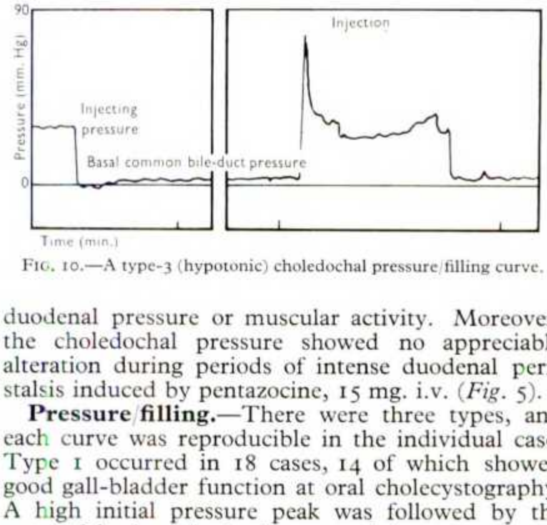

FIG. 10.—A type-3 (hypotonic) choledochal pressure/filling curve.

Pressure/filling.—There were three types, and each curve was reproducible in the individual case. Type 1 occurred in 18 cases, 14 of which showed good gall-bladder function at oral cholecystography. A high initial pressure peak was followed by the entry of dye into the duodenum and the appearance of pressure waves, averaging 10–15 per minute (*Fig.* 6). These were coincident with contractions of the lower 2 cm. of the common bile-duct (*Fig.* 7); the contractions spread from below upwards and relaxed in the reverse direction. The upper parts of the choledochus dilated passively when the lower muscular portion was contracted. After injection the common bile-duct pressure returned to the pre-injection level in all but 2 cases.

Type 2 was obtained in 7 cases, 5 of which showed poor or absent gall-bladder function at oral cholecystography. With injection the choledochal pressure showed a steady rise until the end of injection, there being no wave activity apart from that due to respiration (*Fig.* 8). Dye entered the duodenum in a steady trickle and at a later stage than in type-1 cases. During injection the lumen of the lower 2 cm. of the choledochus showed no change in calibre and the duct was dilated above this lower segment (*Fig.* 9). After injection 5 cases showed a residual pressure in the common bile-duct which lasted for periods up to

1 minute. This residual pressure could be lowered to, or below, the pre-injection level by propantheline bromide, 15 mg. i.v.

Type-3 filling/pressure curve was obtained in 7 cases. Six of these showed complete non-function at cholecystography. With injection there was a momentary rise in the common bile-duct pressure and early entry of dye into the duodenum, after which the pressure in the choledochus approximated to the pump pressure, indicating that the choledochal sphincter was offering little or no resistance to the flow of Hypaque into the duodenum. The choledochal pressure returned to the resting level immediately after injection (*Fig*. 10). Dye entered the duodenum in a constant flow, and the lower end of the common bile-duct remained patent throughout the period of injection without any radiologically visible contractions (*Fig*. 11). In some of these cases the common hepatic and the more proximal bile-ducts could not be visualized radiologically unless the rate of injection of dye was doubled to 12 ml. per minute.

Pancreatic Reflux.—Reflux of sodium diatrizoate into the pancreatic duct was observed in 7 cases. It was associated with a low resting choledochal pressure (mean, 2·3 mm. Hg; range, 0–6·0 mm. Hg). In 5 cases it occurred during injection but after the entry of dye into the duodenum. Three of these showed a type-3 pressure/filling curve, with early and rapid entry of dye into the duodenum (*Fig*. 12). In the other 2 cases pancreatic reflux occurred after the injection of dye at a time when the duodenum showed gross segmental activity (*Fig*. 13). One of these patients had chronic pancreatitis. Drugs which induce spasm of the choledochal sphincter, such as morphine, codeine, and pethidine, raised the choledochal pressure but did not precipitate reflux. On the other hand, pancreatic reflux occurred after the intravenous injection of propantheline bromide.

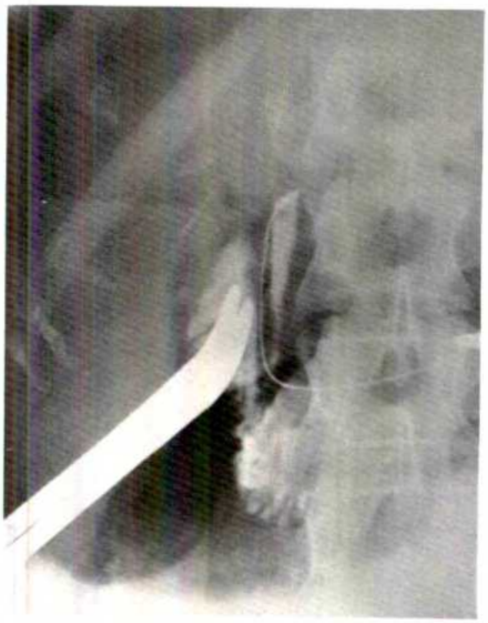

FIG. 11.—Choledochogram from a case with a type-3 pressure/filling curve.

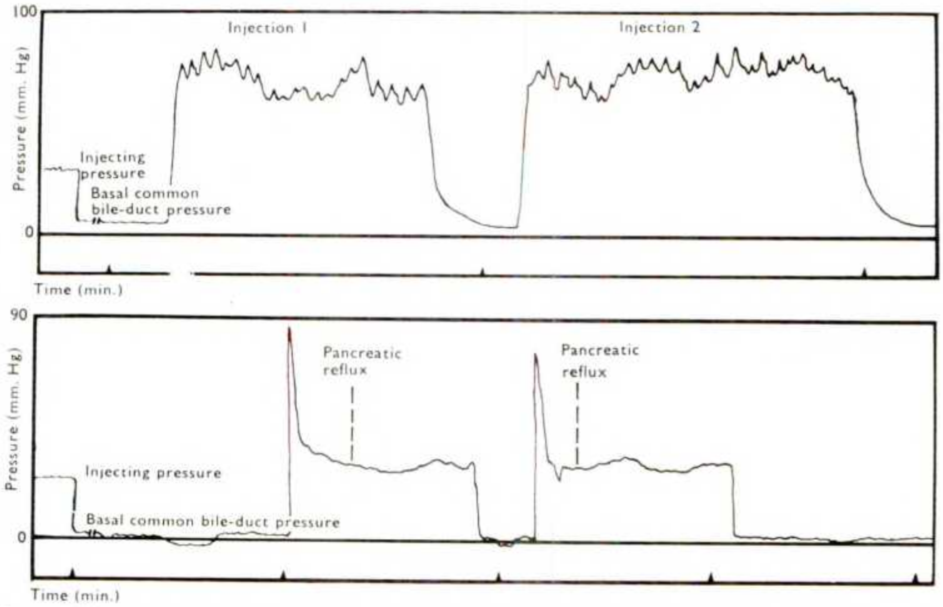

FIG. 12.—Pressure/filling curve in a case showing pancreatic reflux during injection of dye (below), compared with a normal choledochal pressure/filling curve (above).

DISCUSSION

The choledochal sphincter contains both intrinsic (circular and longitudinal) and extrinsic (duodenal) musculature. In man extrinsic musculature is less well developed than the intrinsic component (Didio and Anderson, 1968). According to Nuboer (1929), the choledochal sphincter acts both as a closing mechanism as well as an ejaculatory muscle, a view which is quite different from that of the majority of authors.

A great controversy has raged as to whether the resistance to drainage of both pancreatic and biliary outflows is dependent on sphincteric action or duodenal muscular activity or both. In the present authors' opinion the varying results may be accounted for by the varying experimental situations and species types used in these studies.

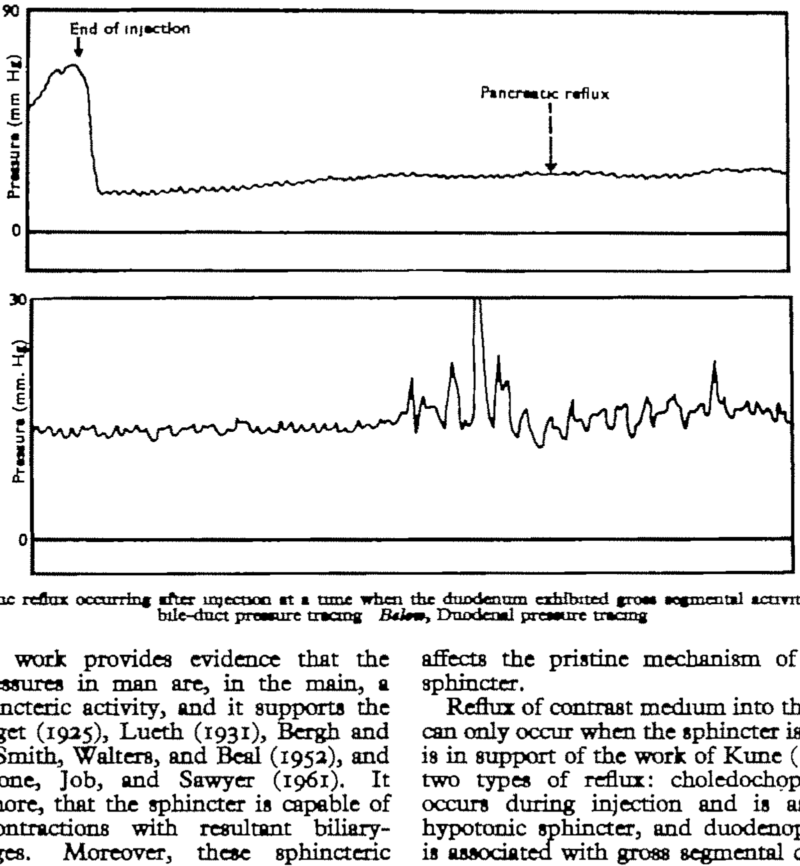

FIG. 13.—Pancreatic reflux occurring after injection at a time when the duodenum exhibited gross segmental activity *Above*, Common bile-duct pressure tracing *Below*, Duodenal pressure tracing

This present work provides evidence that the choledochal pressures in man are, in the main, a product of sphincteric activity, and it supports the findings of Burget (1925), Lueth (1931), Bergh and Layme (1940), Smith, Walters, and Beal (1952), and Daniels, McGlone, Job, and Sawyer (1961). It shows, furthermore, that the sphincter is capable of independent contractions with resultant biliary-pressure changes. Moreover, these sphincteric contractions are independent of duodenal muscular activity. Similar findings have been reported by Caroli, Porcher, Pequingnot, and Delattre (1960) and Nebesar, Pollard, and Potsaid (1966). However, Wyatt (1967, 1969) has produced experimental evidence in dogs to show that gastric peristalsis is related to changes of resistance at the sphincter, and disconnexion of the stomach from the duodenum, as occurs with Polya gastrectomy, results in changes in the dynamics of bile-flow. Unfortunately, gastric motility was not monitored in this study.

Cases showing a type-1 pressure/filling curve are the commonest and would seem to represent the normal situation. They show the existence of a physiologically active muscular portion of the distal common bile-duct. It follows from this and from the anatomical work of Hand (1963) that transduodenal sphincterotomy cannot divide the whole extent of the choledochal sphincter and is, therefore, incomplete.

Cases with a type-2 pressure/filling curve are examples of muscular hypertonia of the choledochal sphincter. They are associated with poor gall-bladder function at oral cholecystography, and can be distinguished from organic narrowing of the peri-ampullary region by intravenous injection of propantheline bromide.

Type-3 cases provide manometric evidence for the existence of hypotonia of the choledochal sphincter. They too are associated with poor gall-bladder function. It would seem that gall-bladder disease affects the pristine mechanism of the choledochal sphincter.

Reflux of contrast medium into the pancreatic duct can only occur when the sphincter is relaxed, and this is in support of the work of Kune (1970). There are two types of reflux: choledochopancreatic, which occurs during injection and is associated with a hypotonic sphincter, and duodenopancreatic, which is associated with gross segmental duodenal activity. One of the patients exhibiting the latter phenomenon had chronic pancreatitis, and this may be of significance as both Muller-Wieland (1963) and Anderson (1968) have reported abnormal duodenal motility in patients with chronic pancreatitis.

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TWELVE-HOUR LIVER PRESERVATION IN THE PIG USING HYPOTHERMIA AND HYPERBARIC OXYGEN

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SUMMARY

In an attempt to prolong successful storage of the pig liver beyond the 6–8 hours previously described from this laboratory, the addition of cell-membrane-stabilizing drugs to the preserving solution and the use of a potassium-rich solution were investigated. Using simple hypothermia alone, 10- and 12-hour storage was unsuccessful. Using the previously described hypothermic technique, but with the addition of hyperbaric oxygen at 3 atmospheres absolute (A.T.A.), consistently successful 12-hour preservation was achieved.

A PREREQUISITE for any clinical liver transplantation programme is a simple and reliable method of organ preservation. Under favourable circumstances most liver transplants within a city can be completed within 6 hours (Calne, 1969; Orr, Charlesworth, Mallick, Jones, Harris, Jones, Keen, McIver, Testa, and Turnberg, 1969). Recent reports from various centres indicate that simple cooling provides adequate protection for this duration (Slapak, Baddeley, Wexler, Saravis, Sise, Garcia, Giourard, and McDermott, 1970; Abouna, Koo, Howanitz, Ancarani, and Porter, 1971; Hadjiyannakis, Calne, Marshall, and Davis, 1971; Mieny and Myburgh, 1971; Spilg, Uys, Hickman, Saunders, and Terblanche, 1971). Occasionally, however, preservation for a longer period is necessary (Starzl and Putnam, 1969). At present this can only be achieved by complicated perfusion systems (Brettschneider, Daloze, Huguet, Porter, Groth, Kashiwagi, Hutchison, and Starzl, 1968; Belzer, May, Berry, and Lee, 1970). The present study was undertaken to investigate simpler methods to prolong liver preservation for 12 hours.

MATERIALS AND METHODS

Large White, Landrace, or cross Large White × Landrace pigs of both sexes obtained from local farmers and weighing between 27 and 36 kg. were used. The donor and the recipient were matched for weight approximation with a preferred weight difference of no more than 5 kg. between the donor and the recipient. Some transplants were between litter-mates, while others were between unrelated animals.

Table I.—COMPOSITION OF THE PRESERVING SOLUTIONS

Solution II
400 ml. A.C.D. fresh-frozen pig plasma*
80 ml. 5 per cent dextrose water
20 ml. 4·2 per cent sodium bicarbonate
10 mg. heparin
1 MU. Penicillin G
1 g. streptomycin

Solution III
400 ml. A.C.D. fresh-frozen pig plasma
80 ml. 5 per cent dextrose water
20 ml. 4·2 per cent sodium bicarbonate
50 mg. chlorpromazine
50 mg. phenoxybenzamine
100 mg. hydrocortisone
1 g. magnesium sulphate (50 per cent w./v.)
10 mg. heparin
1 MU. Penicillin G
1 g. streptomycin

Solution IV
400 ml. kidney-preserving solution†
20 ml. 50 per cent dextrose
3 g. magnesium sulphate (50 per cent w./v.)
10 mg. phenoxybenzamine
1 MU. Penicillin G
1 g. streptomycin

A.C.D., Acid citrate dextrose.

* Preparation of plasma: A fully grown pig was anaesthetized and under sterile conditions a catheter was inserted into the femoral artery. Heparin, 2 mg. per kg., was given intravenously and the animal was exsanguinated. The blood was collected into sterile A.C.D. bottles and centrifuged at 1800 r.p.m. to pack the red cells. The supernatant plasma was drawn off aseptically and stored in a deep freeze at −20 to 40° C. Prior to use the plasma was thawed in a water-bath at 37° C. and then refrigerated at 4° C.

† Saphar Laboratories, Johannesburg. Each 100 ml. of kidney-preserving solution contains:—

Potassium acid phosphate	205 mg.
Potassium phosphate dibasic, $3H_2O$	970 mg.
Potassium chloride	112 mg.
Sodium bicarbonate	84 mg.
Procaine HCl	10 mg.
Heparin	500 U.

The donors were starved for 24 hours preoperatively. They were anaesthetized without premedication with halothane, nitrous oxide, and oxygen, and a large-bore stomach tube was passed to decompress the stomach. Through a midline incision extending between the xiphisternum and the pubis the liver was skeletonized. Heparin, 1 mg. per 2 kg., was then given intravenously and the donor was exsanguinated via an arteriotomy in the abdominal aorta. Without grouping or cross-matching, this blood was used for transfusion in the recipient animal. Following a warm ischaemic interval of 5–10 minutes, rapid core cooling of the liver was achieved by intraportal infusion with 3 litres of solution I (3 litres Tis-U-sol, 90 ml. Rheomacrodex 10 per cent w./v. in dextrose) at 4° C. with a hydrostatic pressure of 60 cm. using gravity drainage from a drip stand. The hepatectomy was completed during the period of cooling. Thereafter the cold liver was placed in a sterile plastic bag containing 1 litre normal saline at 4° C. and the liver was perfused via both the portal vein and hepatic artery with 500 ml. of a preserving solution (*Table I*) run in from a drip stand over a period of 20 minutes. For simple hypothermic storage the bag with the liver completely immersed in the preserving solution was sealed and surrounded by ice to maintain the temperature at 8–12° C. or was placed in an unpressurized hyperbaric chamber in a cold room at a temperature of 2–5° C. When hypothermic storage was combined with hyperbaric oxygen the bag containing the liver was left untied, placed in a portable hyperbaric chamber (Ackerman and Barnard, 1966), pressurized to 3 atmospheres absolute (A.T.A.) with pure oxygen, and stored in a cold room at 2–5° C.

Table II.—LENGTH OF SURVIVAL AND CAUSE OF DEATH IN PIGS UNDERGOING LIVER TRANSPLANTATION USING LIVERS WHICH HAD BEEN PRESERVED BY DIFFERENT TECHNIQUES

GROUP	PRESERVING SOLUTION	TEMPERATURE (° C.)	HYPERBARIC OXYGEN (A.T.A.)	ISCHAEMIC TIME (hours)	SURVIVAL TIME	CAUSE OF DEATH
A (3 experiments)	II	8–12	—	10	3 d. 2 hr. 7 mth.	Ascites Bleeding Alive
B (3 experiments)	III	8–12	—	10	28 hr. 4 hr. 5 hr.	Bleeding Bleeding Bleeding
C (3 experiments)	IV	8–12	—	10	2 hr. 2 hr. 2 hr.	Bleeding Bleeding Bleeding
D (3 experiments)	II	8–12	—	12	9 hr. — 8 hr.	Bleeding Bleeding Bleeding
E (3 experiments)	II	2–5	—	12	— — 6 hr.	Bleeding Bleeding Bleeding
F (5 experiments)	II	2–5	3	12	20 d. 40 d. 5 d. 10 d. 3 d.	Subphrenic abscess Strangulated incisional hernia Pulmonary embolus Rejection Bleeding

The recipient operation was similar to that described by Terblanche, Peacock, Bowes, and Hobbs (1968) except that only a splenojugular shunt was used to by-pass the portal circulation. Biliary drainage was by a direct bile-duct to bile-duct anastomosis (Calne, Yoffa, White, and Maginn, 1968; Dent, Uys, Hickman, Saunders, and Terblanche, 1971). A gastroduodenostomy without vagotomy was performed to eliminate gastric ulceration (unpublished data). Intra-operative fluids totalled between 1500 and 1800 ml., of which 1 litre was donor blood. Ten mg. vitamin K_1 and 20 ml. 50 per cent dextrose were given intravenously as soon as the liver was revascularized with portal blood. Postoperatively the recipient animal was transferred to a warm cage, maintained on intravenous fluids for 72 hours, and thereafter was fed a standard pig diet. Intravenous antibiotics (1 MU. Penicillin G, 0·5 g. streptomycin, and 1 g. chloramphenicol) were given for 10 days. No immunosuppressive agents were administered because of the low-grade rejection seen in pigs after liver transplantation (Calne, White, Yoffa, Binns, Maginn, Herbertson, Millard, Molina, and Davis, 1967; Terblanche, Peacock, Hobbs, Hunt, Bowes, Tierris, Palmer, and Blecher, 1968; Garnier, Clot, and Chomette, 1970).

RESULTS

The results are set out in *Table II.*

Group A: 10 Hours' Preservation with Solution II at 8–12° C.—Only 1 of the 3 animals survived and was still alive 7 months after transplantation. The animal which died 3 days postoperatively had massive ascites. The third animal died shortly after completing the operation from a generalized bleeding diathesis.

Group B: 10 Hours' Preservation with Solution III at 8–12° C.—All 3 animals died within 28 hours of completing the operation. Notable postoperative features in this group were a prolonged apnoea requiring assisted respiration, severe hypoglycaemia not readily responding to intravenous glucose, and gross histological disruption of the liver parenchyma.

Group C: 10 Hours' Preservation with Solution IV at 8–12° C.—All 3 animals survived the operation, woke up promptly after discontinuation of the anaesthetic, but died shortly afterwards from a generalized bleeding diathesis.

Group D: 12 Hours' Preservation with Solution II at 8–12° C.—One animal died shortly after complete revascularization of the liver from a generalized bleeding diathesis. The remaining 2 animals died 8–9 hours postoperatively from the same complication.

Group E: 12 Hours' Preservation with Solution II at 2–5° C.—Two animals died after revascularization of the liver but before completing the whole operation. The third animal died 6 hours postoperatively. All 3 deaths were due to a generalized bleeding diathesis.

Group F: 12 Hours' Preservation with Solution II at 2–5° C. with Hyperbaric Oxygen at 3 A.T.A.—This combination resulted in 4 consecutively successful experiments. In the only failure a leak in the chamber resulted in incomplete pressurization (1·5 A.T.A.). The postoperative behaviour of the survivors was similar to animals undergoing immediate liver transplantation without storage. The biochemistry (*Fig.* 1), however, showed increased elevation of the serum bilirubin, serum glutamic oxalo-acetic transaminase, and alkaline phosphatase, suggesting a more severe degree of ischaemic damage. These parameters returned to normal values within 4 days, demonstrating the remarkable regenerative ability of the hepatocyte. Serum-protein estimations were similar to those for non-stored livers.

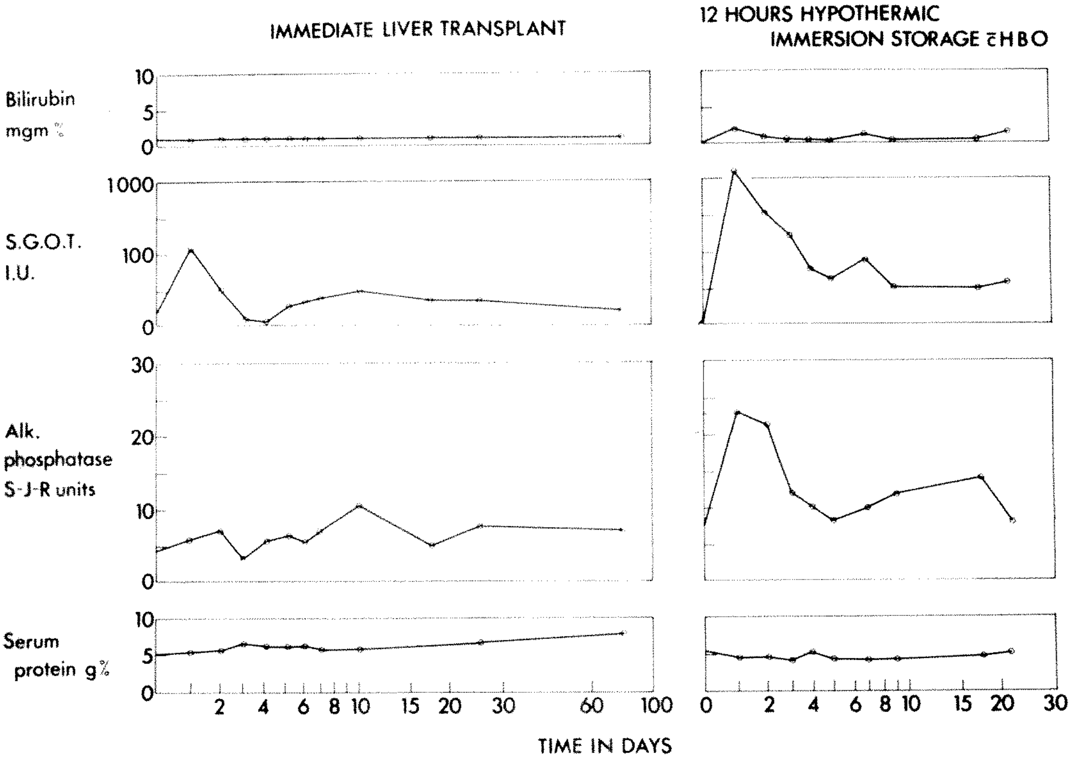

FIG. 1.—Comparative liver function in pigs following a typical immediate liver allograft and a liver allograft which had been preserved for 12 hours (group F).

DISCUSSION

Studies by Starzl, Kaupp, Brock, Lazarus, and Johnson (1960) established that cooling the canine liver with a balanced salt solution to a core temperature below 10° C. gave protection for up to 90 minutes of ischaemia. Later Schalm (1968), using the same species and a preserving solution of homologous plasma, bicarbonate, dextrose, procaine, and hydrocortisone at 4° C., extended this period to 3·5 hours with life-sustaining function. This observation and the reports of prolonged preservation of other organs by altering the constituents of the preserving media (Collins, Bravo-Schugarman, and Terasaki, 1969; Manax and Lillehei, 1969) supported the thesis that whilst hypothermia itself was an important factor in organ preservation the composition of the preserving solution assumed equal importance (Humphries, 1967). The inadequacies of the dog liver in experimental transplantation has led investigators to turn to other animals such as the pig or primates. Recently Abouna and others (1971), Hadjiyannakis and others (1971), and Spilg and others (1971), using three basically different preserving solutions, reported successful preservation of the pig liver for 6 hours. Slapak and others (1970) and Mieny and Myburgh (1971) preserved primate livers for similar periods using a balanced salt solution; Mieny and Myburgh (1971) even obtained a 50 per cent survival following 20 hours of cold ischaemia. These reports stress the importance of species differences as well as that of the composition of the preserving media. This is confirmed in the present series of experiments by the failure of the addition of cell-membrane-stabilizing drugs or the use of a potassium- and magnesium-rich solution to extend liver preservation beyond the 8-hour period achieved previously in our laboratory with solution II (Spilg and others, 1971). Reducing the temperature from 8–12 to 2–5° C. also failed to prolong the period of successful preservation.

The failure of other investigators (Kestens, Mikaeloff, Haxhe, Dureau, Alexandre, Rassat, Cuilleret, Hassoun, Dubernard, Descotes, and Morelle, 1966; Hobbs, Hunt, Palmer, Badrick, Morris, Mitra, Peacock, Immelman, and Riddell, 1968; Belzer and others, 1970) to prolong liver preservation significantly by continuous hypothermic perfusion stimulated the present investigation of combining simple hypothermia with hyperbaric oxygen. In 1964 Manax, Bloch, Longerbeam, and Lillehei published their first report on the technique and results of hypothermia and hyperbaric oxygen in the preservation of whole organs, and they clearly demonstrated the advantages of this combination over either of the two modalities used separately. Since then many other workers have confirmed this observation for the heart (Bloch, Manax, Eyal, and Lillehei, 1964), kidney (Lempert, Blumenstock, and Carter, 1965; Ackerman and Barnard, 1966), and lungs (Blumenstock, Lempert, and Margado, 1965). There is only one report in the literature of the combination of hypothermia and hyperbaric oxygen in liver preservation. Brettschneider and others (1968) unsuccessfully preserved 3 dog livers for 24 hours using this method of storage, but achieved occasional success when continuous perfusion was added.

In the present study the pig liver was successfully preserved for 12 hours in 4 out of 5 experiments using hypothermia at 2–5° C. and hyperbaric oxygen at 3 A.T.A. These organs were capable of immediately supporting life in a hepatectomized recipient for a minimum period of 4 days with biochemical evidence of satisfactory liver function. Further experimental work is required to determine the maximum duration of storage possible by this combination. These results using a relatively simple method are comparable to those previously described using more sophisticated and complex techniques.

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CHOLEDOCHODUODENOSTOMY*

A REAPPRAISAL OF ITS INDICATIONS BASED ON A STUDY OF 64 PATIENTS

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SUMMARY

The indications for choledochoduodenostomy in 64 patients are discussed and compared with those in other series from the literature. The essential indications are the presence of a dilated common bile-duct with calculous disease or associated pathology at the lower end of the common bile-duct, particularly in the elderly and poor-risk patients. It is a safe procedure with few complications provided that a stoma of 2·5 cm. or more is made.

SPRENGEL performed the first successful choledochoduodenostomy in 1891 and the operation has become well established on the continent of Europe (Finsterer, 1952; Mallet-Guy and Descotes, 1955). In Britain, however, it has only recently gained in popularity since Hosford drew attention to its merits in 1957, and it has been slow to win acceptance in the United States of America since the first paper on the subject by Sanders in 1946. It has been increasingly realized that the theoretical objections to the operation have not been experienced in practice, provided that it is properly performed (Capper, 1961; Madden, Chun, Kandalaft, and Parekh, 1970).

There is a wide variation in the indications for choledochoduodenostomy, some surgeons using it as the routine sequel to exploration of the common bile-duct, whether dilated or not (Magarey, 1966), whereas others consider it should only be used if no other alternative is possible (Smith, 1964). A critical reappraisal is needed and this paper discusses the indications for the operation in 64 patients in the light of other published series.

OPERATIVE TECHNIQUE AND COMPLICATIONS

A side-to-side anastomosis was performed in all except 1 patient, with a longitudinal incision in the common bile-duct and a longitudinal or transverse incision in the duodenum. In all cases the common bile-duct was dilated and the stoma was always over 2 cm. in diameter. The anastomosis was performed with a single layer of interrupted 00 chromic catgut, occasionally with 00 silk reinforcement externally as required. There were no operative deaths, but 2 patients had a bile leak which ceased spontaneously. Two patients had a single episode of cholangitis within 1 month of discharge from hospital, with no subsequent trouble over a 3-year and a 6-month follow-up period respectively. Barner (1966) reports a similar experience.

DETAILS OF PATIENTS IN THE PRESENT SERIES

Fifty patients were operated on for benign disease. The male to female ratio was 1 : 2 and the age range was 38–82 years, with an average of 66 years. Fifty per cent of the patients were over 70 years of age, 22 per cent being over 80 years. Only 18 per cent were younger than 50 years. During the same period, 14 patients underwent operation for malignant obstruction of the common bile-duct.

Table I.—INDICATIONS FOR OPERATION IN 50 PATIENTS WITH BENIGN DISEASE

Indication for Operation	*No. of Patients*
Dilated C.B.D.* with impacted stones, sludge, etc.	13
Dilated C.B.D. with recurrent stones	16
Dilated C.B.D. with stenosis of sphincter	7
Dilated C.B.D. with no obvious cause	6
Dilated C.B.D. with chronic pancreatitis	6
Dilated C.B.D. and recent acute pancreatitis	2
	50

* C.B.D.: common bile-duct.

Table II.—COMPARISON OF INDICATIONS FOR BENIGN DISEASE IN THE PRESENT SERIES WITH THOSE IN OTHER SERIES

INDICATION	PRESENT SERIES		CAPPER (1961)		MADDEN AND OTHERS (1970)	
	No.	Per cent	No.	Per cent	No.	Per cent
Dilated C.B.D. with impacted stones, sludge, etc.	13 } 29	58	57 } 79	69	44	53
Dilated C.B.D. with recurrent stones	16		22			
Dilated C.B.D. with stenosis of sphincter; no stones	7	14	—	—	14	17
Dilated C.B.D. with no obvious cause	6	12	8	7	4	5
Relapsing or chronic pancreatitis with C.B.D. stones	—	—	10	9	—	—
Chronic pancreatitis without C.B.D. stones	6	12	4	3	20	24
Recent acute pancreatitis with C.B.D. stones	—	—	1	1	—	—
Recent acute pancreatitis without C.B.D. stones	2	4	4	3	—	—
Miscellaneous	—	—	9	8	1	1
Total	50	100	115	100	83	100

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* This term implies 'external' choledochoduodenostomy as opposed to transduodenal or 'internal' choledochoduodenostomy (sphincterotomy or sphincteroplasty).

INDICATIONS FOR CHOLEDOCHODUODENOSTOMY

It is unlikely that a decision to employ this procedure is made preoperatively, because the indications only become apparent at laparotomy, and usually after carrying out peroperative cholangiography and choledochotomy with removal of free stones, sludge, etc.

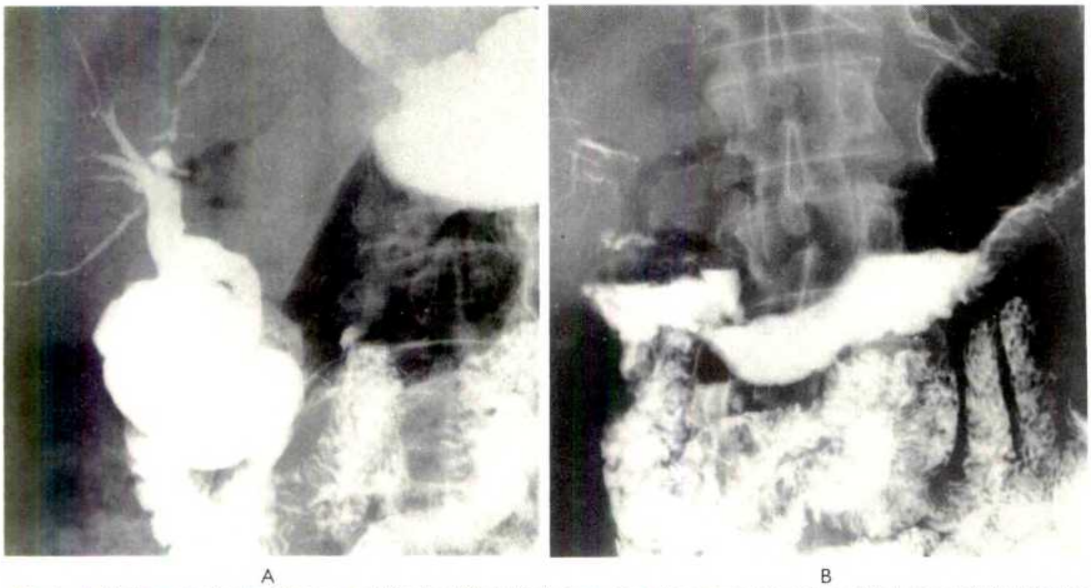


FIG. 1.—A, Radiograph showing the common bile-duct filled with barium. Note the convex obstruction of the lower end which has been unchanged since the original operation 3 years before. B, A few minutes later, showing the emptying of the duct including most of the lower portion.

Table III.—AVERAGE LENGTH OF TIME BETWEEN FIRST OPERATION AND CHOLEDOCHODUODENOSTOMY

PREVIOUS OPERATION	NO. OF CASES	AVERAGE TIME BETWEEN OPERATIONS
Cholecystectomy alone	9	11 years
Cholecystectomy and exploration of C.B.D.		
Residual stones	2	2½ months
Recurrent stones	5	5 years

Table I gives the indications for choledochoduodenostomy with benign disease in this series, and *Table II* compares these with two other series (Capper, 1961; Madden and others, 1970), in which the similarities will be noted.

1. Dilated Common Bile-duct.—The procedure should be performed only on finding a dilated common bile-duct, where the overriding consideration is the presence of some obstruction at the lower end of the duct (*see* (3) and (4) below), usually detected by palpation or 'on-table' cholangiography.

A wide dilated duct allows the necessary wide stoma to be constructed. A duct with a normal calibre does not indicate choledochoduodenostomy and an attempt at this results in a narrow stoma, postoperative problems, and a bad name for a valuable procedure in a surgeon's repertoire.

2. Age and General Condition of the Patient.—If the age and condition of the patient are weighed against the degree of difficulty and the risk of morbidity and mortality of a transduodenal exploration with sphincterotomy or sphincteroplasty, the surgeon may then judge that a choledochoduodenostomy is the quickest and safest alternative.

3. Obstructive Pathology at the Lower End of the Common Bile-duct at the First Operation.—

a. An impacted stone or stone in a false diverticulum adjacent to the sphincter of Oddi.

b. The presence of sticky biliary sludge and mucus.

c. Thickened wall of the common duct and some evidence of cholangitis, e.g., 'red-hot duct' (Rains, 1959).

d. Narrowing of the lower end of the duct as demonstrated by cholangiography or on careful exploration with a sound or dilator.

e. Thickening of the head of the pancreas owing to chronic pancreatitis or as a sequel to acute pancreatitis.

f. Discrete lump in the head of the pancreas—possibly a neoplasm or a stone.

4. Obstructive Pathology at the Lower End of the Common Bile-duct at a Second Operation.—This is usually due to recurrent stones in the duct. Indeed, in the present series, 16 of the 29 patients with stones in the common bile-duct had undergone a previous operation. Nine had had a cholecystectomy without exploration of the common bile-duct, whereas 7 had had a previous exploration of the common bile-duct, in 2 of whom the second operation was within 3 months of the first, which strongly suggests that the stones were residual rather than recurrent. *Table III* shows the average length of time between the first and second operations in each group. It will be seen that in those who had cholecystectomy alone the average time was 11 years.

The following case illustrates the danger of *not* performing choledochoduodenostomy when a recurrence of stones could be predicted from the findings at the first operation.

CASE REPORT

A 57-year-old female had undergone a cholecystectomy and exploration of the common bile-duct when no stones had been found in the gall-bladder but two large stones had been present in the dilated common bile-duct. Cholecystectomy had been performed. The sphincter of Oddi had become narrowed and therefore it had been dilated, the bile-duct being closed around a T-tube after removal of the stones.

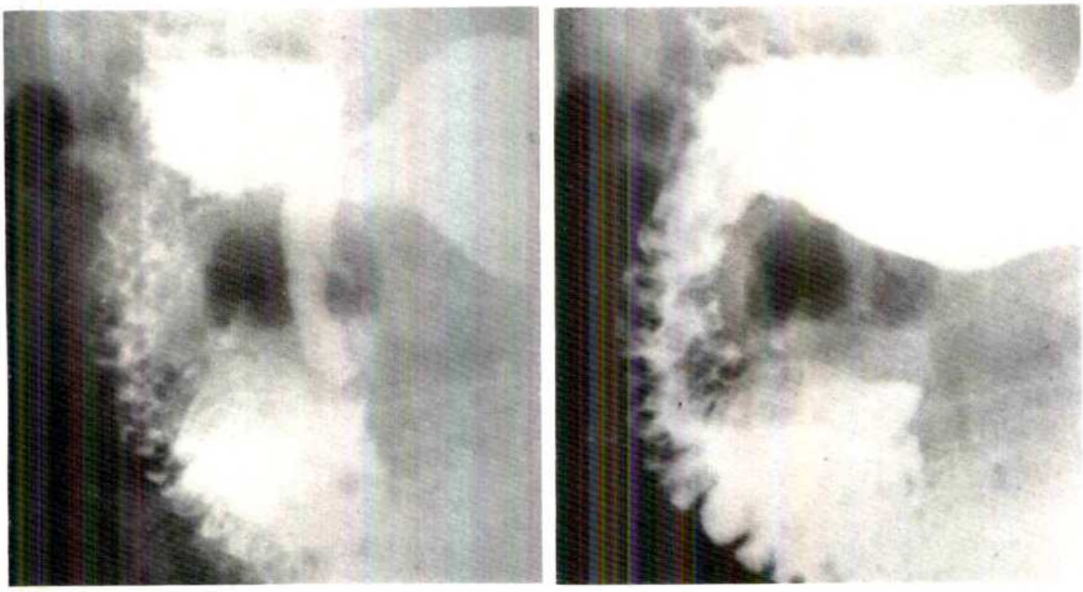


FIG. 2.—A, Radiograph 1 year after choledochoduodenostomy, showing the lower end of the duct filled with barium. B, Thirty seconds later, showing the duct emptying up into the duodenal cap.

The patient was admitted to Charing Cross Hospital 2 years later with suppurative cholangitis and Gram-negative septicaemia. At operation the dilated common bile-duct contained small stones and sludge. A choledochoduodenostomy was performed and the patient made a satisfactory postoperative recovery. This nearly lethal recurrence could have been avoided by choledochoduodenostomy at the original operation.

MALIGNANT OBSTRUCTION

The aim of any operation in this situation is to provide a satisfactory by-pass for the bile as far from the obstructing carcinoma as possible. The normal operation for inoperable carcinoma of the pancreas is a cholecystojejunostomy with either a Roux-en-Y or a loop with entero-anastomosis. Choledochojejunostomy or choledochoduodenostomy may be used in only two situations: (*a*) when the gall-bladder has previously been removed, and (*b*) when the cystic duct enters the common bile-duct low down and thus is likely to be obstructed before an anastomosis higher up the duct.

CRITICISMS OF CHOLEDOCHODUODENOSTOMY

1. That there is a Danger of Cholangitis due to Reflux of Duodenal Contents into the Bile-duct.—This seems to be a theoretical rather than a practical objection, provided that the stoma is more than 2 cm. and preferably 3 cm. in diameter (Johnson and Stevens, 1969). Madden and others (1970), in a collected series from the literature over the period from 1946 to 1968, give the incidence of cholangitis as 0·4 per cent of 1255 operations. In addition, they anastomosed the bile-duct to the unprepared colon of dogs and provided that there was no stomal obstruction cholangitis did not occur, despite the reflux of faecal contents into the biliary tract.

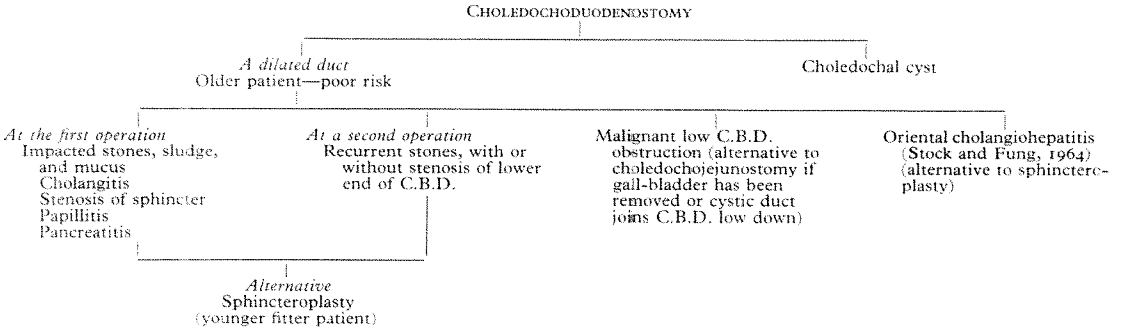
2. That the Blind Part of the Common Bile-duct below the Anastomosis becomes filled with Vegetable Debris, leading to Choledochitis and Possible Pancreatitis (Smith, 1964).—Stock and Fung (1964) and Madden and others (1970) point out that this is a rare occurrence. *Fig.* 1 shows the rapid emptying of the bile-duct of barium, including most of the lower part of the duct, in a patient who was radiographed 3 years postoperatively. *Fig.* 2 is the radiographs of another patient 1 year after operation, showing the emptying of the lower part of the duct a few seconds after it had filled with barium. On screening, the contrast was seen to empty back up into the duodenum. Despite these observations, it is agreed that there is occasionally recurrent stone formation in the blind segment (Wilson, 1970), but it may give no trouble.

3. That in Some Cases a Lump related to the Lower End of the Bile-duct will remain undiagnosed.—This is a valid criticism which implies that patients with ampullary carcinoma could be denied the chance of cure by a pancreaticoduodenectomy (Whipple's operation). Clearly, a circumscribed lump in the head of the pancreas related to the duct is best explored by incision via a duodenotomy (Rains, 1969). In the relatively younger and fitter patient with such a tumour, major excision can be undertaken. In the elderly unfit patient the duodenotomy, if suitably placed, can be used for making the choledochoduodenostomy.

SPHINCTEROPLASTY VERSUS CHOLEDOCHODUODENOSTOMY

Acute pancreatitis is a potentially serious complication of sphincteroplasty, and Farrar, Painter, and Betz (1969) give the mortality of the operation as 5–10 per cent. Keighley, Johnson, and Stevens (1969), in a small series, found that 56 per cent of patients who underwent sphincterotomy or dilatation of the sphincter had significantly raised postoperative serum amylase levels, whereas none of those who underwent choledochoduodenostomy had a raised level. Once postoperative pancreatitis has occurred the mortality is as high as 77 per cent (Thompson, Howard, and Vowles, 1957).

Table IV.—SUMMARY OF INDICATIONS FOR CHOLEDOCHODUODENOSTOMY


CHOLEDOCHODUODENOSTOMY
A dilated duct
Older patient—poor risk
Choledochal cyst
At the first operation
Impacted stones, sludge, and mucus
Cholangitis
Stenosis of sphincter
Papillitis
Pancreatitis
At a second operation
Recurrent stones, with or without stenosis of lower end of C.B.D.
Malignant low C.B.D. obstruction (alternative to choledochojejunostomy if gall-bladder has been removed or cystic duct joins C.B.D. low down)
Oriental cholangiohepatitis (Stock and Fung, 1964) (alternative to sphincteroplasty)
Alternative
Sphincteroplasty
(younger fitter patient)

There is also little doubt that dilatation of a stenosed sphincter or simple sphincterotomy is followed by a high incidence of restenosis. In practice, once it has been decided that decompression of the common bile-duct is required if a stone has been removed transduodenally or the sphincter has been inspected by this route, a carefully performed sphincteroplasty with mucosa-to-mucosa suture is the natural procedure. If, as in the majority of cases, the common bile-duct is explored from above the easiest and safest procedure is to perform a choledochoduodenostomy using the extended choledochotomy incision.

CONCLUSIONS

Choledochoduodenostomy is particularly suitable for the elderly patient where the minimum operative procedure is required for an unresolved and supposedly benign problem at the lower end of the common bile-duct, provided that the bile-duct is dilated and a stoma 2·5 cm. or more in size can be achieved.

In malignant lower bile-duct obstruction this operation should be limited to patients in whom the gall-bladder has previously been removed, or where the cystic duct joins the common bile-duct low down.

Choledochoduodenostomy is also useful in the treatment of choledochal cyst and oriental cholangiohepatitis. The indications are summarized in *Table IV*.

The incidence of complications is very small, but it is likely to increase if the operation is performed for inadequate indications, and it is obviously undesirable to produce a biliary by-pass unless this is really necessary.

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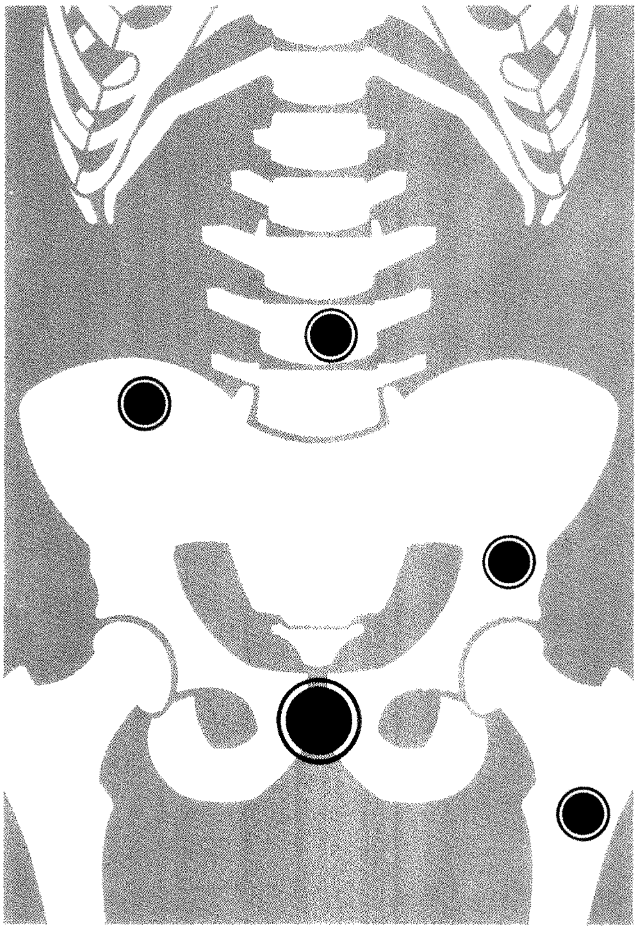

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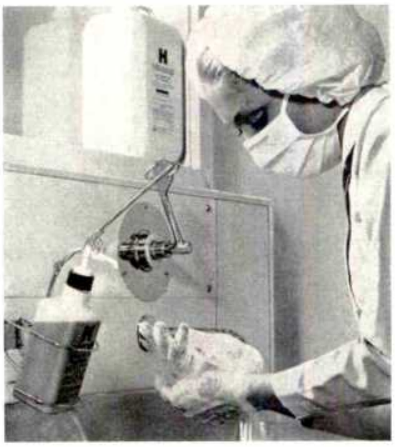

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THE TREATMENT OF ACHALASIA BY CARDIOMYOTOMY

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SUMMARY

The results of treatment in 27 cases of achalasia carried out in the Tehidy Thoracic Surgical Unit are reviewed. The value of air insufflation of the oesophagus to assist in the division of the muscle and to ensure that the mucosa is not damaged is stressed. The advantages of early operation using a modified Heller's procedure are shown, and the results demonstrate that a poor outcome is most common in cases with a long history and that usually these cases have been treated by conservative measures.

HELLER'S procedure is safe and satisfactory, and should be considered as the primary treatment for achalasia because results are better when it is done early in the course of the disease. Inflation of the lower oesophagus by air is a great help in the division of muscle-fibres during operation.

The failure of cardiomyotomy shows as persistent dysphagia, and this may be due to either incomplete myotomy or secondary stricture formation following hiatus hernia. Great care should be taken to avoid both complications because reoperation is difficult and unsatisfactory.

In the series of 27 cases presented here the patients in the second half of the series had a repair of the right crus carried out when there was any hint of a lax oesophageal hiatus. It is thought that this additional procedure accompanying cardiomyotomy is worth while in all cases.

The symptoms, oesophagoscopic findings, and radiological appearances of achalasia of the oesophagus are well known. The pathogenesis has been extensively studied, but there is still little agreement regarding the choice of treatment. For this reason every report concerning this problem is worth while.

MATERIALS AND METHODS

Patients reviewed.—The present survey is based on a series of 27 patients with achalasia who were operated on between the years 1954 and 1969. All the patients were followed up, and the follow-up period of 25 of the cases was at least 1½ years and in some cases as long as 15 years. Two cases have been excluded from this series because they have been operated on too recently. There was a slight preponderance of women over men—16 to 11—which is of no significance. The age of the patients at the time of surgery was between 12 and 66 years; 15 per cent were less than 21 years old, half were between 21 and 44, and 35 per cent of the patients were more than 51 years of age. The average age was 37 years.

Symptoms.—Dysphagia and regurgitation were constant symptoms, and the degree of both varied. Dysphagia was usually the main complaint, and although in many cases it was severe, in some the diagnosis was first established because of other symptoms, mainly pulmonary. Some of the patients had had symptom-free intervals of many years' duration which were interrupted by bouts of progressive dysphagia. Dysphagia was aggravated in some cases by psychic stress. It was found that patients with long-standing disease often acquired some special manœuvres to allow food to pass into the stomach. These tricks varied from a simple Valsalva manœuvre to drinking large quantities of water before or after meals.

The pain was variously described as a heavy feeling causing distension and discomfort, as burning or acute in character, or sometimes as blunt or aching. When pain occurred it was usually retrosternal, but in some cases it was epigastric. It was referred to meals, but was not relieved by regurgitation or by antacids. Loss of weight was in some cases rapid and severe, and in some long-standing cases malnutrition was clearly evident. In younger patients a feature was failure to gain weight rather than a loss of weight. In 6 cases pulmonary complications such as aspiration bronchitis and bronchopneumonia were evident, clinically and radiologically.

The duration of symptoms prior to surgery varied between 1 year and 20 years, 80 per cent of the patients having had symptoms for 2 years or more before operation and 46 per cent for more than 5 years.

Diagnosis.—This was based on history, clinical examination, barium studies, and oesophagoscopy. In 3 cases, however, it was not possible to exclude completely the possibility of malignancy. Five patients had been treated extensively before admission to the unit, 4 having had repeated dilatations in hospital and self-bouginage at home. The fifth patient had had a cardiomyotomy performed through the right chest.

Operation.—It was considered that the treatment of achalasia should be surgical rather than conservative. Before operation the patients were given a liquid diet for 4–10 days, in some cases it being necessary to use parenteral feeding. The oesophagus was washed out repeatedly with sodium bicarbonate solution, and antibiotics were given as and if required after oesophagoscopy.

In all the cases a modified Heller's operation (6)* was performed through a left thoracotomy. After exposure of the oesophagus a longitudinal incision was made through the muscle coats of the oesophagus and stomach, the myotomy being extended for some 4–7 cm. on the oesophageal side of the oesophagogastric junction and approximately 2 cm. on the gastric side. It was found that distension of the oesophagus with compressed air via an intra-oesophageal tube introduced by the anaesthetist facilitated the procedure. Damage to the mucosa was most likely to occur at the oesophagogastric junction, and where it did occur the damaged mucosa was repaired with 0000 silk using atraumatic sutures.

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* Reference, *see* p. 284.

Care was taken not to cut the oblique fibre bundles at the gastro-oesophageal junction in the hope that this would prevent gastro-oesophageal reflux (2, 13, 20, 64). After the myotomy had been completed the muscle was separated from the mucosa for about one-third of the circumference of the oesophagus. The mucosa bulged freely into the wound and this was further facilitated by distending the area with compressed air through an oesophageal tube. This also showed whether the mucosa was airtight and, if there was any further doubt, saline solution was poured into the chest to cover the mucosa while air was passed into the stomach.

In the first 7 years of the study no attempt was made to reapproximate the limbs of the right crus behind the oesophagus, except when the hiatus had been found widely opened. In the past 7 years it has been routine procedure to bring down the lower part of the oesophagus below the diaphragm and to suture the right crus behind the oesophagus (4) to prevent postoperative herniation and gastro-oesophageal reflux (7, 18, 21, 24, 25, 35, 46, 60, 64). No other procedure, such as fundoplication or repair of the phreno-oesophageal ligament, has been used.

For the first 24 hours postoperatively, fluids were given intravenously. The patients were then given fluids by mouth and after 24 hours the amounts were increased. On the third postoperative day patients were given semi-solids, and solid food was allowed after 7–10 days.

Complications following Surgery.—There were no postoperative deaths. In 1 case perforation of the oesophagus occurred 24 hours after surgery, although during the operation the mucosa was proved to be airtight. Perforation probably happened because of devascularization of the mucosa owing to too extensive dissection of the muscle. Immediate reoperation and suture were performed and the patient recovered. In 2 cases left lower-lobe atelectasis occurred postoperatively, but this cleared rapidly with intensive physiotherapy.

RESULTS

Following discharge the patients were seen at 1 month, then at 3-monthly intervals for the first year, half-yearly during the second year, and subsequently at yearly intervals. Barium swallow was carried out and repeated as necessary. During the barium swallow the presence of gastro-oesophageal reflux was looked for especially. Cases where symptoms recurred were readmitted to the unit for further assessment. Follow-up results have been considered for 25 cases, and the results have been classified into four categories (*Table I*).

Table I.—THE RESULTS OF CARDIOMYOTOMY

Group	*No. of Cases*	*Percentage of Cases*
Excellent	9	80
Good	9	
Satisfactory	2	
Bad	5	20
Total	25	

1. Excellent.—Patients in this group had no symptoms in the follow-up period. They all gained weight (as much as 19·5 kg. in 1 case), and the oesophagus on barium swallow appeared less wide than before operation.

2. Good.—This group was without symptoms, but radiological examination showed that the oesophagus was still dilated, often being as wide as before operation. The patients included in this group had neither dysphagia nor regurgitation and all had gained weight, but they did occasionally complain of retrosternal discomfort. Most were subjectively well satisfied and felt enormously improved by surgery.

3. Satisfactory.—These patients had occasional, minimal dysphagia, the symptoms being transient with food passing rather slowly down into the stomach. They could, however, eat all foods, whereas before operation most of them had only been able to have semi-solids and fluids and had required frequent bouginage.

These three categories of patients—excellent, good, and satisfactory—account for the majority of the patients of the series. Five cases come under the final category.

4. Bad.—In this group operation did not cure the symptoms of dysphagia, regurgitation, or pain, or surgery caused new complications. Five cases are included in this group.

Case 1.—For 1 year after cardiomyotomy this patient experienced considerable improvement but, after this, symptoms of reflux oesophagitis became manifest and dysphagia reappeared. A barium swallow was carried out and an oesophageal stricture was seen. Although a hiatus hernia was not proved by barium meal, we are now convinced of its existence and further surgery is to be carried out.

Case 2.—This patient developed dysphagia and regurgitation 5 years after what had appeared to be successful cardiomyotomy. Barium swallow was carried out and a hiatus hernia was seen with oesophageal reflux.

Case 3.—This woman was found to have a mucosal perforation 24 hours after cardiomyotomy. The chest was reopened and the perforation was repaired. During her postoperative convalescence the patient developed an oesophageal stricture. Three years after the original Heller's operation cardioplasty was performed, and was followed by reflux oesophagitis and recurrent oesophageal stenosis. One year later a partial oesophagogastrectomy and pyloroplasty were carried out. The patient died of bilateral bronchopneumonia in the postoperative period 5 years after her cardiomyotomy.

Case 4.—This patient had a cardiomyotomy via a right thoracotomy performed elsewhere. The operation was carried out at the same time that a right lower lobectomy for bronchiectasis was performed. The results were satisfactory for the first 9 years. At the end of this period the symptoms of achalasia manifested themselves again and a second cardiomyotomy was performed through the left chest in the Tehidy Thoracic Surgical Unit. For 5 months after the second operation the patient was asymptomatic, but after this time increasing dysphagia recurred, accompanied by heartburn and retrosternal pain. A further barium swallow and oesophagoscopy showed an oesophageal stricture to be present. The oesophagus remained distended and it was clear that the sigmoid deformity and kinking of the terminal thoracic oesophagus had become worse than ever. A laparotomy was carried out and the sigmoid bulge was pulled down into the abdomen and fixed there. This procedure resulted in considerable improvement, but the patient still had some dysphagia and occasional retrosternal pain. Fourteen months ago partial oesophagogastrostomy with vagotomy and pyloroplasty were carried out, with, to date, excellent results.

Case 5.—This patient developed dysphagia within a week of undergoing cardiomyotomy. His symptoms were similar to those which he had had before operation. Repeated radiological examinations have shown neither reflux nor the appearance of hiatus hernia, but the oesophagus remains the same size with marked narrowing of the terminal oesophagus and muscle spasm. Failure to control the symptoms in this patient was almost certainly due to incomplete myotomy.

In these 5 cases the causes of failure were incomplete cardiomyotomy in 1 case, the occurrence of hiatus hernia with reflux oesophagitis in 2 cases, reflux oesophagitis probably due to unsuccessful bilateral cardiomyotomy where a massive sigmoid loop existed in 1 case, and cicatricial stenosis as a result of mucosal perforation in the fifth case. In 3 cases, therefore—and this is to be expected from our experience with hiatus hernia—incompetence has been followed by reflux oesophagitis and secondary stenosis. Two patients in this series had postoperative reflux oesophagitis and stenosis because the lax oesophageal hiatus was not recognized and dealt with at operation.

DISCUSSION

The Choice of Treatment.—There is no satisfactory conservative medical treatment for achalasia. The surgical treatment which has been recommended has varied from endoscopic dilatations to oesophagogastric resection. Those who prefer conservative measures consider that the results are no worse than those of surgery, such as the Heller procedure. However, if dilatation is to be successful it is necessary to disrupt muscle-fibres, and such measures might result in perforation of the oesophageal wall. Successive dilatations tend to become more and more difficult, and when the oesophagus is grossly enlarged and sigmoid, dilatation becomes extremely difficult. We consider the only operation of value in the treatment of achalasia is a modified Heller procedure (single cardiomyotomy). Such operations as cardioplasty or oesophagogastric anastomosis can cause reflux oesophagitis (9, 14, 31, 50, 52, 64). Cardiomyotomy is a safe procedure—in most series the mortality is nil—and it is possible to divide all the muscle-fibres under direct vision.

For many years the conviction prevailed that surgery should be kept for cases of failure of dilatation (5, 11, 27, 30, 31, 32, 36, 37, 40, 41, 42, 45, 46, 48, 56, 57, 61, 62), but now increasing numbers of surgeons recognize surgery as a primary treatment for achalasia (2, 8, 17, 19, 22, 23, 25, 26, 28, 33, 34, 39, 49, 55, 58, 59, 60, 63). In the present series the results were better when cardiomyotomy was performed on patients with short histories. *Fig.* 1 shows the results obtained compared with the length of symptoms prior to surgery. Although the series is small it is obvious that bad results have occurred almost entirely in those patients with a long-standing history. This is an argument in favour of early surgery.

Finally, another advantage of surgical treatment is the early recognition of carcinoma occurring in a patient with achalasia. The incidence of carcinoma in mega-oesophagus is much higher than in the normal population (2, 10, 15, 22, 25, 29, 38, 39). In 1969 Just-Viera and Haight (38) collected 167 such cases from the literature. Ellis (22) stated that the incidence of carcinoma of mega-oesophagus in patients with achalasia was 19 per cent, and Belsey (10) mentioned a figure of 7·3 per cent. However, Ellis and others (25) from the Mayo Clinic could find no cases in 240 patients. If stasis is a precipitating factor it seems reasonable to eliminate this factor as early as possible.

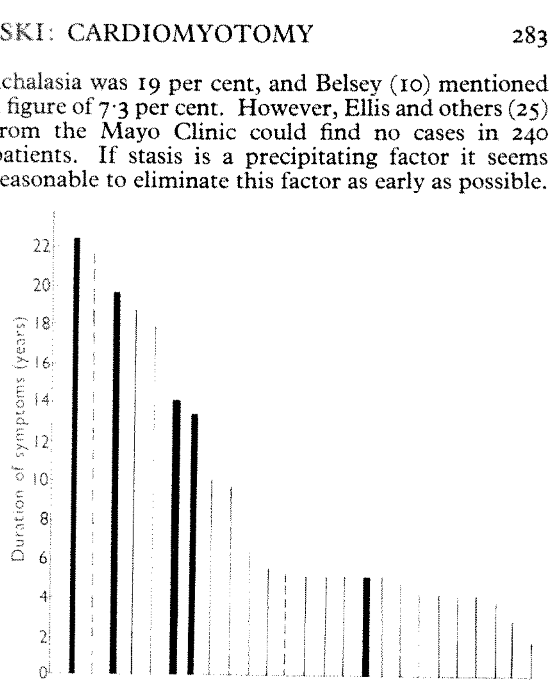

FIG. 1.—The results of myotomy compared with the duration of symptoms. ▬, Bad results. - - -, Satisfactory results. ——, Excellent and good results.

Whereas cardiomyotomy is certainly the best and almost certainly the most widely accepted operation for achalasia, there is some doubt whether it is of value in all cases (8, 16, 22, 33, 43, 47), as can be seen from the following quotes: 'In gross oesophagectasia . . . cardiomyotomy is only of limited value' (Ellis in (22)); 'the Heller principle is the best available except in extremely advanced cases' (Barlow in (7)); 'no satisfactory form of treatment has been found for the patient with the grossly dilated oesophagus, the distal end of which is kinked' (Le Roux and Wright in (41)); 'the myotomy technique has limited value in the patient with stenotic scarring from advanced stages of the disease. In these instances distal oesophageal resection with interposition of either jejunum or colon should probably be considered' (Root and Wangensteen in (52)). This raises the problem that if the Heller procedure is not carried out in advanced cases the only alternative is partial oesophagogastrectomy with oesophagogastroanastomosis or jejunal or colon transplant (3, 7, 15, 51, 53). Although all these operations have been proposed they are not generally accepted (8, 12, 26, 33, 49, 55). Adams (3) and Camara-Lopez (15) have different views. The latter believes that the operation for achalasia should not only relieve dysphagia but also should prevent the possibility of carcinoma. By 1963 he had performed some 80 oesophagogastrectomies with a 6 per cent mortality and good late results. Adams (3) produced 26 similarly treated cases. We believe that oesophagogastrectomy cannot be accepted as the primary treatment for achalasia and should be reserved only for failures after cardiomyotomy. In extreme cases of mega-oesophagus it may be wise to proceed to temporary gastrostomy (44) to enable proper preparation of the patient and gullet (10). The bad results achieved by cardiomyotomy in the long-standing advanced cases of achalasia suggest that surgery should be performed early without preliminary conservative treatment.

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THE RESULTS OF FUNDOPLICATION FOR THE RELIEF OF OESOPHAGEAL REFLUX DUE TO HIATUS HERNIA

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SUMMARY

Fundoplication has been performed in 25 patients suffering from symptoms or complications due to oesophageal reflux associated with hiatus hernia. There was no peri-operative mortality and only 1 failure to relieve symptoms of reflux. The procedure is benign and is well tolerated if it is performed without splenectomy.

IT is generally believed that the main symptoms and pathological sequelae of sliding hiatus hernia are due to gastro-oesophageal reflux. In the operation of fundoplication, as described by Nissen (1961), the fundus of the stomach is freed and wrapped around the oesophagogastric junction in the form of a cuff. This maintains an acute angle of entry from the oesophagus to the stomach, with the object of restoring competent valvular action at the cardia. The present trial was stimulated by the encouraging short-term results reported by Smiddy and Ross (1964).

MATERIALS AND METHODS

Twenty-five patients are included in this study and all had radiological evidence of sliding hiatus hernia with free reflux. Surgical treatment was advised only when the symptoms resisted medical management, or when necessary for the relief of blood-loss, spasm, or impending stricture of the oesophagus. There were no other criteria of selection and no other method of repair of hiatus hernia was used during the 7-year period of trial, commencing in 1964. Ages ranged from 36 to 88 years, with 4 patients aged over 70 years. The sex distribution was equal. Two of the operations were performed as emergencies for acute haematemesis. Vagotomy and pyloroplasty were performed in addition to fundoplication in 14 patients: in 4 because of the presence of chronic duodenal ulceration, and in the other 10 because either excessive gastric secretion was deemed to be present on the basis of the pentagastrin test, or there was radiological evidence of hypertrophy of the duodenal mucosa, or irritability of the duodenal cap. Cholecystectomy was performed in addition to fundal plication in 2 patients because of coincident chronic cholecystitis with cholelithiasis.

Technique.—Oesophagoscopy usually preceded laparotomy, which was always effected through a high left paramedian incision. To obtain better access to the duodenum or biliary tract, downward extension was made if necessary, crossing the midline above and to the right of the umbilicus. Exposure of the hiatus was improved by raising the head of the table and tilting the right side down. The triangular ligament was divided and the left lobe of the liver was folded on itself and retracted. In the first 10 operations elective splenectomy was performed as a means of mobilization of the fundus, but, later, great care was taken not to disturb or injure the spleen in any way. The fundus of the stomach was usually freed by incising the peritoneal reflection from its upper border to the diaphragm, starting medially near the oesophagus and working laterally and downwards, dividing and ligating the attachments of the stomach to the spleen. The upper part of the lesser omentum was then divided, starting above at the right border of the oesophagus and extending downwards 7–8 cm. Sometimes it was necessary to divide and ligate the ascending branch, or main trunk, of the left gastric artery. Mobilization from above was occasionally difficult, especially if the fundus was small and inaccessible owing to obesity or to depth of the chest. It was then expedient to open into the lesser sac below the level of the lower pole of the spleen and to free the fundus from this point upwards.

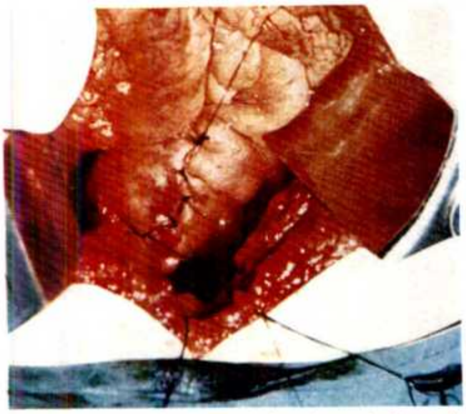

FIG. 1.—Showing the fundus encircling the terminal oesophagus and secured by black silk sutures.

The completely free fundus was pushed, by finger, behind and to the right of the oesophagus, and then drawn forward and around to the left as far as it would go with gentle traction exerted through dissecting forceps. The free anterior border of the fundus was secured in this position to the stomach lying behind it by interrupted seromuscular sutures of black silk placed at 5-mm. intervals. In this way a cylindrical or slightly conical cuff was made to envelop the whole oesophagogastric junction and the lower part of the abdominal oesophagus. This cylinder was usually 7–8 cm. long, 4–5 cm. in diameter, and composed on all sides of two full thicknesses of stomach wall (*Fig.* 1). A large-bore stomach tube was occasionally passed before the fundus was rotated. This formed a pivot about which the fundus could turn but was not essential. A finger passed upwards within the cylinder of stomach and alongside the oesophagus was aware of gentle elastic compression from all sides.

No attempt was made to narrow the hiatus or to perform any other form of repair or fixation.

RESULTS

All the patients remained under surveillance for periods which varied at the time of review from 18 months to 7 years, except for 1 who died of natural causes after 4 years of complete freedom from symptoms of oesophageal reflux.

Serious postoperative complications occurred in 3 of the 10 patients in whom elective splenectomy had been performed. These were left subphrenic abscess, empyema thoracis, and pneumonia respectively.

Diarrhoea with colicky abdominal pain troubled 3 patients for periods of 6–12 months following operation. These 3 were amongst the 14 in whom truncal vagotomy and pyloroplasty had been performed. Dysphagia with a large bolus of food was reported by 3 patients, but this gradually disappeared without treatment 1–3 months after operation.

Results have been assessed on the basis of a modified Visick grading (Goligher, Pulvertaft, de Dombal, Conyers, Duthie, Feather, Latchmore, Shoesmith, Smiddy, and Wilson-Peppter, 1968). Twenty-two patients classed as Grade I were completely relieved of all symptoms. One patient classed as Grade II was pleased with the results, although admitting on direct questioning to mild intermittent symptoms of reflux. One patient classed as Grade III believes the operation was worth while although he was still troubled by dysphagia secondary to oesophageal stricture, which was well established at the time of operation and still requires dilatation at yearly intervals.

One 44-year-old man classed as Grade IV submitted to fundoplication with splenectomy and truncal vagotomy with pyloroplasty, in November, 1965. There was then a 2-year history of severe epigastric and retrosternal pain after meals with distressing heartburn. Barium meal showed a chronic duodenal ulcer with a sliding hiatus hernia and free oesophageal reflux. Operation was followed by good symptomatic relief for 18 months. The previous symptoms then recurred in a milder form and have persisted intermittently since. Barium meal has shown the recurrence of slight reflux and a small chronic duodenal ulcer. The Hollander test suggests that vagotomy has not been complete. The patient's general condition has, however, improved and the offer of further surgical treatment has been refused. For many years this man has suffered domestic discord and poor eating habits.

The effect of operation on individual symptoms, as defined by Edwards, Phillips, and Rowlands (1964), is shown in *Table I*, where it can be seen that a high success rate has been achieved in the present series.

Barium-meal examination was performed before and after operation in all patients. In 20 patients there was no sign of reflux following surgery and 18 of these have remained completely symptom-free. Of the other 2 patients without radiological reflux, 1 was classed as Visick Grade II and the other as Visick Grade III. The latter's symptoms, as have been mentioned, are due to established oesophageal stricture. There was radiological evidence of slight reflux in 5 patients. Four of these have remained entirely symptom-free, but the other, who also has a chronic duodenal ulcer, claims to have benefited very little from fundoplication with vagotomy and has been classed as Visick Grade IV.

Table I.—THE EFFECT OF OPERATION ON INDIVIDUAL SYMPTOMS

SYMPTOM	RELIEVED	NOT RELIEVED	NOT PRESENT PREOPERATIVELY
Reflux pain	23	1	1
Heartburn	23	1	1
Regurgitation	20	0	5
Vomiting	10	1	14
Dysphagia	5	2	18
Excessive belching	7	10	8
Haematemesis	2	0	23

In 3 patients approximately one-third of the cylindrical mass formed by plication was seen to herniate through the hiatus during barium-meal examination, but there were no associated symptoms or signs of reflux.

DISCUSSION

The advances in the surgical treatment of hiatus hernia which have followed the realization of the significance of oesophageal reflux, as well as better understanding of the factors which normally prevent reflux, have been well described by Collis (1970) and Mustard (1970). The importance of the oesophagogastric angle has been emphasized, and the results of the present trial, in which the procedure of fundoplication has been used alone without any other attempt at fixation or closure of the hiatus, confirm that effective valvular action at the cardia can be restored by maintenance of an acute angle of entry from the oesophagus. Fundoplication not only restores the angle necessary for flap-valve action but also provides a seat for this valve, the firmness of which increases as pressure within the stomach rises.

The diameter of the mass formed by fundoplication depends on the size of the fundus and the thickness of its wall. In most cases the mass appears to be too big to pass through the hiatus, but when the hiatus is wide and the fundus small there is no apparent impediment to herniation, and radiological evidence that this could occur was found in 3 patients. The fact that herniation was not accompanied by symptoms or signs of reflux demonstrates again the paramount importance of an effective valve at the cardia.

The length of follow-up, which has been complete for periods of 18 months to 7 years, is probably adequate as it is known that recurrent symptoms usually appear fairly soon after operation (Tanner and Hardy, 1970). Fundoplication has given entirely satisfactory symptomatic relief to 23 out of 25 patients. Failure in 1 patient is attributed to an established oesophageal stricture, and although dilatation at yearly intervals is still required there is radiological evidence that the operation has succeeded in stopping further reflux. Without fundoplication, repeated dilatation might well have been followed by extension and exacerbation of the stricture (Barrett, 1960).

The patient for whom the operation has been an almost complete failure had a chronic duodenal ulcer as well as a hiatus hernia with free reflux, and this combination presents a difficult problem. It is particularly unfortunate that vagotomy proved to be incomplete as it is likely that persistent symptoms are due to continued activity of the ulcer. Other patients in whom radiology shows reduction without complete abolition of reflux have usually had good symptomatic relief in our experience, as well as in that of Edwards and others (1964).

Table II.—A COMPARISON OF THE RESULTS OBTAINED IN THE PRESENT SERIES WITH THOSE OBTAINED IN SERIES USING OTHER METHODS OF TREATMENT

	EDWARDS AND OTHERS (1964)	MUSTARD (1970)	TANNER AND HARDY (1970)	PRESENT SERIES (fundoplication)
No. of patients	63	87	41	25
Percentage of patients of Visick Grades I and II	77	78	81	92
Percentage of patients free of reflux pain and heartburn	90	91	54	95
Percentage of patients with post-operative radiological reflux	63	21	Not stated	20

An attempt has been made to compare the results of the present series with those obtained from other methods, as described by Edwards and others (1964), Mustard (1970), and Tanner and Hardy (1970). The need for such a comparison has been considered sufficient to outweigh the risk of fallacies owing to the different numbers involved or unknown variables, but it should be noted that Tanner and Hardy (1970) have excluded patients with peptic ulcer, cholelithiasis, or other abdominal abnormality. Otherwise the basic criteria of selection appear to be the same in each series. It would appear from *Table II* that fundoplication has given comparatively favourable results both in respect of the proportion of Visick Grades I and II as well as in the relief of the predominant symptoms of reflux and the low incidence of post-operative radiological evidence of reflux.

The postoperative complications which have followed fundoplication are believed to be mainly due to other procedures performed at the same time, particularly splenectomy and vagotomy with pyloroplasty. The latter is now omitted unless there is definite evidence of chronic duodenal ulceration. The most serious complications of subphrenic abscess, empyema, and pneumonia occurred in 3 of the first 10 operations, and in these elective splenectomy had been performed as a means of mobilizing the fundus, as described by Smiddy and Ross (1964). Our unfortunate experience with iatrogenic splenectomy has been shared by Devlin, Evans, and Birkhead (1969). From the time this danger was appreciated, great care has been taken to avoid injury to the spleen, and the last 15 operations have been satisfactorily performed without splenectomy. The simple expedient of starting mobilization of the fundus from below has proved most helpful in difficult cases. Fundoplication performed in this way is the most benign of upper abdominal operations, and, by comparison, is much better tolerated by frail or elderly patients than either cholecystectomy or vagotomy with pyloroplasty. Furthermore, when performed in conjunction with the above procedures, fundoplication has caused no recognizable additional stress or complication. Fundoplication by abdominal incision is far less traumatic than repair of hiatus hernia by the thoracic or abdominothoracic route, and it has the advantage of compatibility with other abdominal procedures which are often necessary in these patients.

On the basis of our experience we would agree with Franklin (1969) that Nissen's procedure of fundoplication has not always received the recognition it deserves.

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PERFORATED DUODENAL ULCER IN CHILDHOOD

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SUMMARY

Perforation of an acute duodenal ulcer in an infant and a child, both with other illness, is reported. Surgical management in both cases was successful. The importance of awareness of this complication is stressed and the cause, presentation, and management are discussed.

PERFORATED peptic ulcer in infants and children occurs so infrequently that it is not usually considered in the differential diagnosis of the acute abdomen (Rubell, Leix, and Clelland, 1952). In the literature 118 cases of perforated duodenal ulcer in neonates (under 1 month), infants (1 month–2 years), and children (2–15 years) have been reported, and of these, only 50 survived. Raffensperger and Greengard (1966), in a series of 80 patients with peptic ulcer, reported 23 with perforated duodenal ulcer, and of these, 80 per cent died. In two series an incidence of 1 and 1·5 per cent for perforated peptic ulcer was found at autopsy of infants dying from other causes. Two children with perforated duodenal ulcer who were treated successfully are reported in this paper.

CASE REPORTS

Case 1.—M. P., aged 1 year 11 months, was admitted with a 4-day history of vomiting and reluctance to feed. Two days before admission he had passed several loose, greenish bowel motions. Following admission his condition deteriorated, his vomitus became faeculent, and he was treated by intravenous infusion and nasogastric suction. A radiograph showed the presence of a pneumoperitoneum and he was transferred to the Paediatric Surgical Unit.

On examination the patient was lethargic and flushed but apyrexial. His pulse-rate was 108 per minute and his blood-pressure was 115/70. The abdomen was soft but deep palpation in all areas was resented. Bowel-sounds were present. At laparotomy a perforated acute ulcer was found on the anterior aspect of the first part of the duodenum. The perforation was closed in two layers with chromic catgut and the peritoneum was drained. The postoperative course was uneventful and the child made a full recovery.

Six weeks after admission the gastric acid secretion of the patient was assessed. In the first hour after pentagastrin, 52 ml. of gastric secretion were obtained, giving a total acid response of 4·5 mEq. The result of gastrin assay was within the normal limit for an adult, but we do not know the normal range for a child.

Case 2.—J. R., a 9-year-old boy, was admitted to hospital seriously ill with pneumococcal meningitis. Despite treatment his conscious level deteriorated and he developed generalized convulsions followed by respiratory arrest. He was transferred to the Assisted Ventilation Unit. His conscious level had not altered after 2 days of ventilation, and a tracheostomy was carried out. On the third day he vomited small amounts of coffee-ground material. On the fifth day his conscious level had improved and he was able to recognize his father. A routine chest radioagraph at that time showed a pneumoperitoneum.

On examination the patient's temperature was 37·8° C., his pulse-rate was 120 per minute, and blood-pressure was 120/70. There was slight abdominal distension with generalized guarding but no rigidity. Laparotomy was carried out under general anaesthesia. A 2-mm. perforation of an acute anterior duodenal ulcer was found with slight bilious soiling of the peritoneum. The perforation was closed by simple suture with an omental overlay. A vacuum drain was placed below each hemidiaphragm. The patient's postoperative recovery was uneventful, the tracheostomy tube being removed the following day and a light diet being commenced 2 days postoperatively. At follow-up examination he has had no symptoms of duodenal ulceration. Gastric acid secretion and gastrin assay were not carried out.

DISCUSSION

Perforation may complicate acute or chronic duodenal ulceration. Acute ulcer in the neonate may develop with prematurity, anoxia, abdominal distension, or hyperacidity. It has been suggested that anoxia may be associated with selective shunting of blood leaving relatively ischaemic areas in the gastrointestinal tract (Lloyd, 1969). Acute ulceration in the infant and child may be secondary to stress, such as lesions of the central nervous system (Cushing's ulcer), sepsis, burns, malnutrition, trauma, steroid therapy, and major surgery. *Case* 2 exemplified this, but in *Case* 1 the accompanying illness would have been associated with considerably less stress.

Chronic duodenal ulcer is more common in the older child and resembles the adult pattern where an ulcer diathesis is presumed. Adverse emotional factors may be present, and Muggia and Spiro (1959) stressed lack of security as an aetiological factor. Proctor (1925) stated that 2 per cent of adults with a peptic ulcer give a history dating back to childhood. Goldberg (1957) and Milliken (1965) reported gastric hypersecretion in 1 of 10 cases and in 5 of 15 cases respectively. Both, however, felt that gastric analysis in the child was unreliable.

In the neonate and infant the clinical findings after perforation of an acute duodenal ulcer may be those of an acute abdomen, but the signs may be masked, especially in the presence of other illness. The diagnosis is frequently overlooked because of its rarity. An abdominal radiograph in the lateral or erect position is of value, as a pneumoperitoneum in the neonate may be due to a perforated ulcer (Muggia and Spiro, 1959).

In the healthy child abdominal signs of perforation become more reliable and the diagnosis may be confirmed radiologically. Gastrografin may be helpful in the localization of the site of perforation.

Both the children in this paper presented in an atypical manner, the abdomens being soft and bowel-sounds present. A pneumoperitoneum was shown radiologically in each case.

Perforation may complicate chronic peptic ulceration in the older child. Evidence of a chronic ulcer may be difficult to establish. Symptoms are frequently atypical. The pain may be referred to the umbilical region, may be unrelated to meals, may last only a few minutes, and may not be present at night. Some children have undergone elective appendicectomy. The condition more closely resembles that of the adult as the age approaches 15 years.

The neonate and infant are at particular risk from abdominal sepsis. Successful surgery in the neonate depends on early diagnosis, intensive care in the pre- and postoperative periods and expert anaesthesia. Ten out of 21 infants and neonates reported in the literature survived after surgery but none survived without operation. In all age-groups closure of the perforation is carried out with care not to obstruct the lumen and using an omental plug. The acute duodenal ulcer in young children rarely recurs after treatment of the presenting problem (Schuster and Gross, 1963).

The principle of simple closure is usually followed in perforation of chronic duodenal ulcer. A history of previous complications may indicate definitive surgery. Consideration in choice of operation must then be given to the extra nutritional demands of the growing child, so that gastric anatomy and physiology are altered as little as possible (Gross, 1953). Swenson (1962) reported that vagotomy in children causes more gastro-intestinal dysfunction than in adults, but Raffensperger and Greengard (1966) did not confirm this in their series of 11 cases.

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TUBERCULOSIS OF THE GALL-BLADDER

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SUMMARY

Three female patients with tuberculous cholecystitis are reported. They had symptoms of cholecystopathy of varying duration. No jaundice was recorded. Cholecystograms disclosed non-functioning gall-bladders in 2 cases and a functioning gall-bladder with two stones in the other case. At cholecystectomy, cholelithiasis was found in all the patients, and in addition 1 of them showed tuberculous peritonitis. Microscopic examination showed tuberculous changes in the gall-bladders. Postoperative tuberculostatic treatment was given. The presence of stones is believed to have been of importance for the development of the tuberculous infection in the present cases.

Although the frequency of cholecystitis has increased during the past decades (Kettler, 1958), the incidence of gall-bladder tuberculosis is still very low (Schöndube, 1956). This may be due to a failure to recognize the condition, or to a special resistance of the gall-bladder to the tubercle bacillus (Rankin and Massie, 1926). Farkas (1960) has concluded that only about 50 of the hundreds of thousands of gall-bladders that have been examined microscopically have shown a tuberculous inflammation. We have been able to find only 41 cases of tuberculous cholecystitis who have undergone surgery reported in the literature up to 1970 (Weitz, 1955; Leng-Lévy, David-Chaussé, Martin, Lagoarde, and Herné, 1965; Vojtisek and Zrustova, 1965; Rybkowski, 1966; Krejczy and Krejczy, 1967; Gonzales, Donoso, and Chamorro, 1967; Mlynek and Engel, 1968). Because of this, reports of new cases may still be of interest. The present communication is an account of 3 cases with tuberculosis and stones in the gall-bladder who underwent surgery.

CASE REPORTS

Case 1.—A 50-year-old woman who had had pulmonary tuberculosis 25 years previously presented with a 15-year history of typical biliary symptoms. On two occasions the urine had been bile-stained and the stools had been decolorized. She had never been icteric. A peroral cholecystogram 9 months previously had shown a non-functioning gall-bladder.

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At cholecystectomy extensive adhesions were found around the gall-bladder. The gall-bladder had a thickened wall and contained about fifty stones with diameters of 3–10 mm. Operative cholangiograms were normal. No signs of peritoneal tuberculosis were observed.

Microscopic examination of the extirpated gall-bladder showed an atrophic and partly ulcerated mucosa, moderate hyperplasia of the muscular coat, and marked fibrosis. Granulomas of varying size occurred mainly in the fibrous portions. They were composed of epithelioid cells, with an admixture of Langhans' giant cells, peripheral lymphocytes, and occasional central caseous necroses (*Fig.* 1). These alterations made the diagnosis of tuberculosis probable.

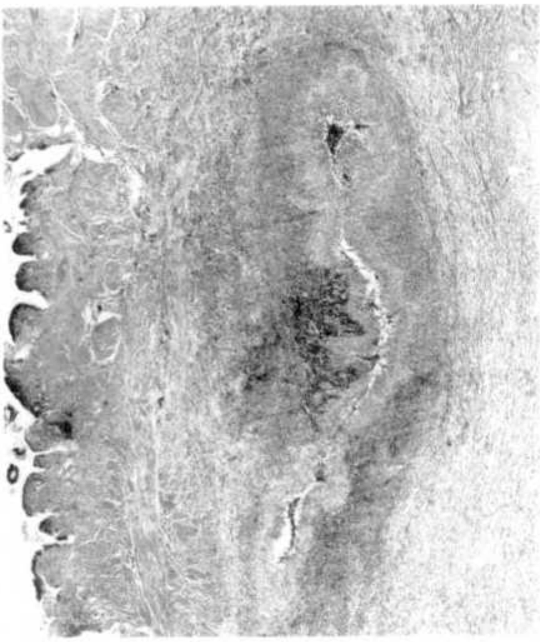
FIG. 1.—*Case* 1. Photomicrograph of the gall-bladder showing fibrous thickening of the wall and a large tubercle with central necrosis.

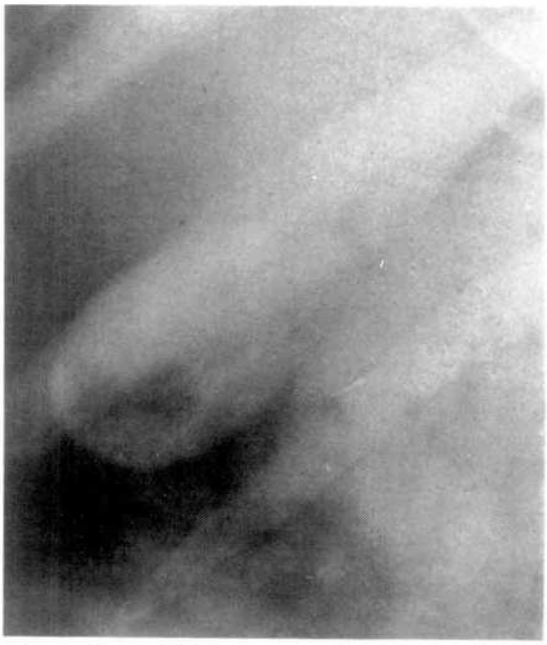
FIG. 2.—*Case* 2. Oral cholecystogram demonstrating a functioning gall-bladder with two radio-opaque stones.

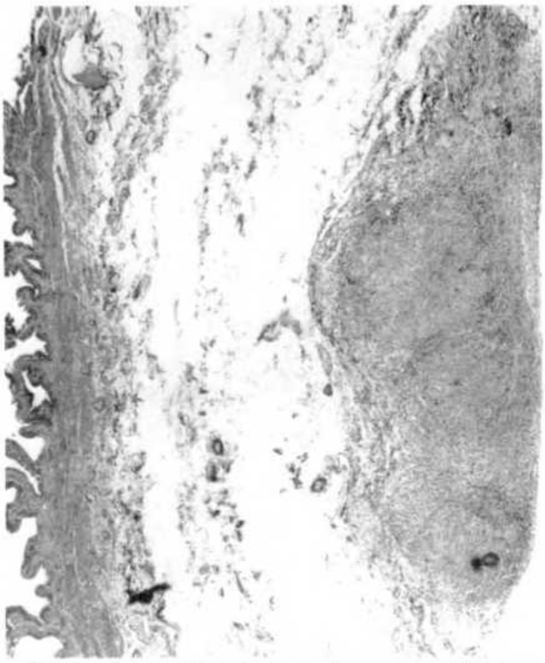
FIG. 3.—*Case* 2. Photomicrograph showing the gall-bladder with preserved mucosa (left) and a large tubercle with an occasional giant cell in the serous layer.

Direct microscopy of sputum as well as guinea-pig inoculation of sputum, gastric lavage, and urine were negative. Pulmonary radiographs showed no active tuberculous foci. Postoperatively the patient received tuberculostatic treatment. At repeated control investigations no complications have been recorded.

Case 2.—A 54-year-old woman had a 1-year history of cholecystopathy. Jaundice had not been present, but she had had periods of diarrhoea. A peroral cholecystogram 2 weeks before the operation showed two stones in a functioning gall-bladder (*Fig.* 2).

Cholecystectomy was performed and 3 litres of yellowish fluid were found in the peritoneal cavity. Small yellowish-white knots, which seemed to be of a tuberculous nature, were widely disseminated over the peritoneal surfaces. Around the gall-bladder there were numerous adhesions, and the gall-bladder itself exhibited a thickened wall and contained two stones. Operative cholangiograms were normal. Microscopic examination of the gall-bladder showed numerous, small, epithelioid granulomas with associated Langhans' giant cells and lymphocytes, mainly in the serous layer (*Fig.* 3). Postoperatively, tuberculostatic treatment was instituted. The subsequent course has been uneventful.

Case 3.—A 59-year-old woman who had previously had good health was seen with fever, an elevated sedimentation rate, and pains in the upper right quadrant. No jaundice was recorded. A peroral cholecystogram showed a non-functioning gall-bladder.

Cholecystectomy was performed and numerous adhesions were seen around the gall-bladder which also had a thickened wall with scattered necrotic portions. About forty stones with diameters of 5–15 mm. were found in the gall-bladder. Operative cholangiograms were normal. Microscopic examination of the extirpated gall-bladder showed hyperplasia of the muscular layer, extensive fibrosis, and caseous necroses surrounded by epithelioid cells with intermingled giant cells of Langhans' type and peripheral infiltrates of lymphocytes (*Fig.* 4). The alterations were mainly confined to the fibrous portions. The microscopic changes indicated tuberculosis. Direct microscopy of gastric lavage as well as guinea-pig inoculation of gastric lavage and urine were negative. After operation tuberculostatic treatment was given. The patient remains in good health at the present time.

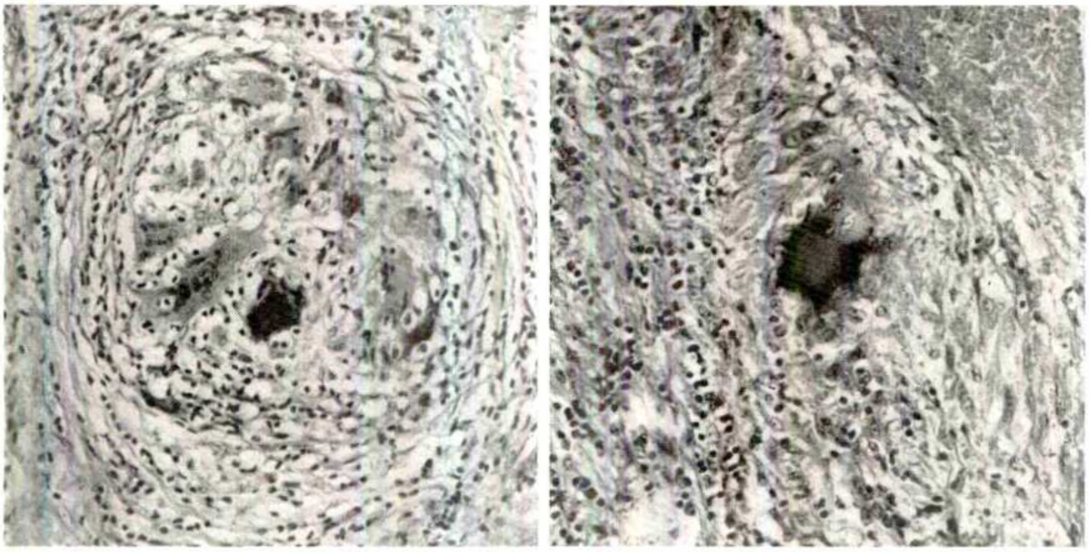

FIG. 4.—*Case* 3. A, Portion of the gall-bladder showing a tubercle composed of central epithelioid cells and giant cells with more peripherally localized lymphocytes and fibroblasts. B, Portion of another tubercle demonstrating necrotic material, epithelioid cells, a giant cell, lymphocytes, and fibroblasts.

DISCUSSION

Simmonds (1908) differentiated between an acute form of tuberculous cholecystitis, which is caused by an infection through the biliary passages, and a chronic type, which is caused by secondary infection of a gall-bladder that has already been damaged by non-specific inflammation. Weitz (1955) has proposed the following classification of tuberculosis of the gall-bladder:—

1. Miliary tuberculosis in children with ulcerating tubercles in the gall-bladder.
2. Gall-bladder tuberculosis in association with severe general tuberculosis.
3. Tuberculosis limited to the gall-bladder, often discovered accidentally at microscopic examination of extirpated gall-bladders.
4. Gall-bladder involvement in association with tuberculosis in other peritoneal organs.

According to this classification *Cases* 1 and 3 of the present study belong to group 3, whereas *Case* 2 belongs to group 4. There are only two previous reports of patients belonging to the latter group (Latronche, 1911; Pohl, 1949). The cholecystograms from *Case* 2 showed stones in a functioning gall-bladder. Such a finding does not seem to have been reported previously in cases of tuberculosis of the gall-bladder. The preserved function may be due to the fact that the inflammatory process mainly involved the serosa.

The symptoms in our cases were similar to those encountered in patients with non-specific cholecystitis. No jaundice was recorded. This conforms with the findings of Vallejo (1950), who stated that pain after meals, nausea, diarrhoea, and fever are common symptoms, and that jaundice is infrequent in cases of tuberculosis of the gall-bladder. Alterations in the biliary tracts seem to occur only seldom in cases of tuberculous cholecystitis. Autio, Virtanen, and Antila (1963) have, however, reported changes in the biliary tracts in a patient with tuberculous infection of the gall-bladder.

There are several possible routes by which tuberculous infection may reach the gall-bladder. Haematogenic or lymphogenic dissemination from neighbouring or distant organs may occur (Rankin and Massie, 1926; Vojtisek and Zrustova, 1965). Another possibility is infection by direct extension from neighbouring foci (Pohl, 1949; Weitz, 1955). An ascending or descending canalicular infection via the biliary passages has been suggested by Simmonds (1908) and Ajello (1940). The possibility of an ascending canalicular dissemination has, however, been denied by others (Rankin and Massie, 1926; Elfving, 1949; Weitz, 1955; Remmele and Lennert, 1957). Kettler (1958) has proposed that the absence of tubercles from the mucosa indicates a haemato- or lymphogenic spread of the infection, whereas tubercles mainly localized in the mucosa denote canalicular dissemination. Wohlgemuth, Herrmann, and Vogel (1960) found involvement of the ducts of Luschka in gall-bladder tuberculosis, which was believed to indicate infection from the gall-bladder lumen.

In 2 of the present cases (*Cases* 1 and 3) the histological changes were mainly absent from the gall-bladder mucosa, which might denote that the infection was carried by the lymph or blood from some other focus. In *Case* 2 the microscopic alterations were mainly confined to the serous layer of the gall-bladder and there were tubercles scattered over the peritoneal surfaces, which might indicate dissemination via the peritoneal cavity to the gall-bladder.

It is not quite clear whether tuberculous infection can occur in the absence of changes in the biliary tracts and gall-bladder. Fraenckel and Krause (1918) reported tuberculous manifestations in gall-bladders without previous disease. However, it has been suggested that the intact gall-bladder has a special resistance to tuberculous infection. The factor or factors responsible for this resistance are not clearly known. It has been suggested that anti-tuberculous activity is present in salivary and pancreatic secretions (Hirsch, 1955). Autio and others (1963) have reported that pure bile contains bile acids in concentrations high enough to inhibit the growth of the tubercle bacillus, which might contribute to the resistance. They also suggested that cystic-duct obstruction leads to the disappearance of bile acids from the gall-bladder and to a lowered resistance against tuberculous infection.

Experimental evidence emphasizes the importance of previous damage for the development of tuberculous cholecystitis. Delitalia (1935) tried to evoke tuberculosis of the gall-bladder by intravenous injection of tubercle bacilli in rabbits. This was not possible when the gall-bladder was normal. Only after experimental induction of cholelithiasis were tuberculous manifestations of the gall-bladder obtained.

Clinical studies denote that stones may be of pathogenetic significance for the development of tuberculosis in the gall-bladder. Of the 44 cases of tuberculosis of the gall-bladder (the present 3 cases have been added to those reported in the literature), only 2 seem to have been acalculous. One patient reported by Vallejo (1950) showed an obstruction of the cystic duct caused by a 'granulomatous whitish mass'. In another case reported by Rankin and Massie (1926) there was no information about any obstruction, but this possibility remains since the gall-bladder was filled with 'caseous material'. The frequency of gall-stones in these 44 cases seems to be approximately the same as in non-specific cholecystitis. In acute cholecystitis stones occur in about 95 per cent of cases (Glenn and Mannix, 1956).

Common-duct stones were found in 5 of the 44 cases (11 per cent), which denotes that the frequency of choledocholithiasis is about the same in non-specific as in specific cholecystitis. Two of these 5 cases had stones in the common duct but not in the gall-bladder (White, 1932; Peruzzo and Zannini, 1952).

It is well known that stones are important pathogenetic factors for non-specific cholecystitis. Spontaneous delivery of concrements may be involved in the formation of acalculous cholecystitis (Andersson, Bergdahl, and Boquist, 1971). We believe that the presence of stones with associated non-specific inflammatory alterations may also play a prominent role in the development of tuberculosis of the gall-bladder. In *Case* 1 there was a 15-year history and in *Case* 2 a 1-year history of cholecystopathy. Fibrous thickening of the gall-bladder wall occurred in *Cases* 1 and 3, denoting the existence of chronic inflammatory alterations. Cholelithiasis which was present in all of our cases is believed to have induced inflammatory changes of varying severity that diminished the resistance of the gall-bladder to the tuberculous infection.

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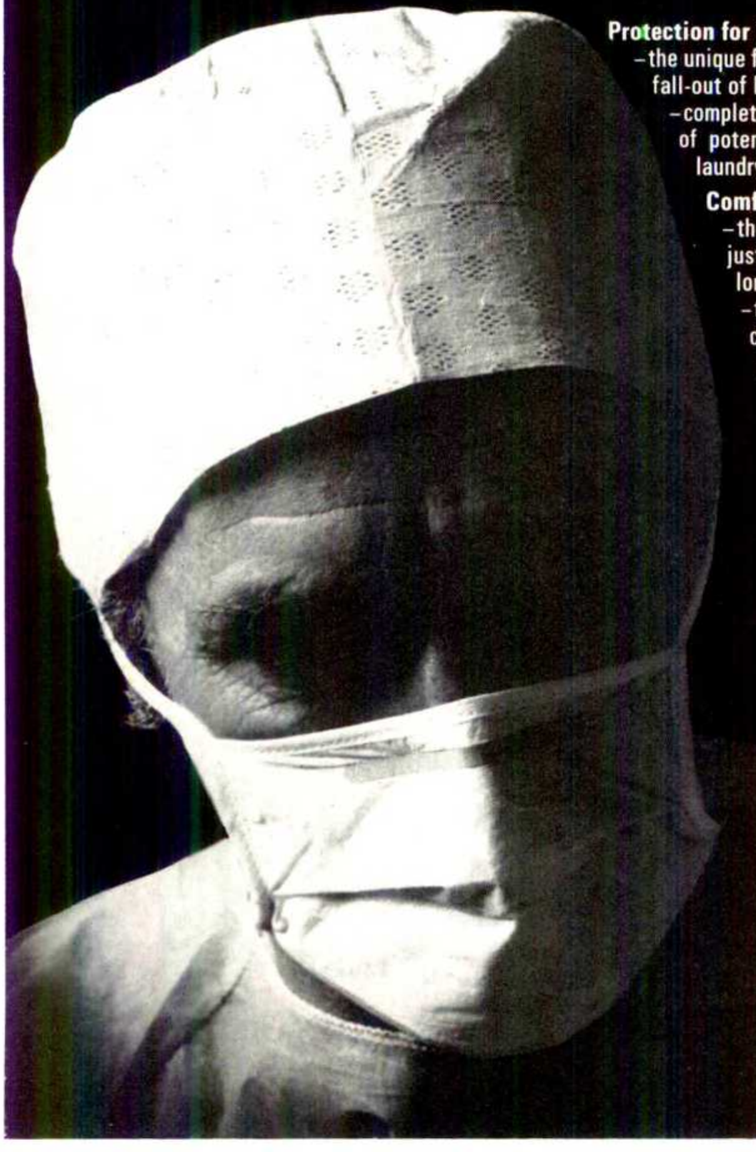

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DRAINAGE FOLLOWING CHOLECYSTECTOMY

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SUMMARY

The effect of intraperitoneal drainage and incidental appendicectomy has been studied in 309 patients who had undergone routine cholecystectomy.

Patients who did not have drainage fared better than those in which drains were used. There was an increase in postoperative morbidity when the drain was left in position for more than 48 hours. But when the drain was removed during the first 48 hours the results obtained were the same as for cases in whom no drain was used. Incidental appendicectomy while carrying out cholecystectomy did not affect the morbidity or mortality of the operation.

It is concluded that in the absence of bile leakage, drains from the hepatorenal space should be removed within 48 hours, and incidental appendicectomy should be carried out when it can be performed with ease and without undue manipulation.

In recent retrospective studies that have included 1000 or more patients the mortality following cholecystectomy has been found to vary between 0·6 and 3·8 per cent (MacVicar, McNair, Wilken, and Bruce, 1967; Meyer, Capos, and Mittlepunkt, 1967; Holm, Edmunds, and Baker, 1968; Magee and MacDuffee, 1968; Seltzer, Steiger, and Rosato, 1970). MacVicar and others (1967) noted in their review of 2043 operations for benign conditions of the gall-bladder and common bile-duct that the majority of the 77 deaths (3·8 per cent) were associated with leakage of bile, and they concluded that prevention and early treatment of this complication would reduce the mortality. They also observed that deterioration in the condition of these patients occurred shortly after the operation, usually within the first 48 hours. Their study supported the routine use of intraperitoneal drainage after cholecystectomy to allow the escape of bile from (*a*) an insecurely tied cystic duct, (*b*) a small accessory bile-duct cut and unrecognized at operation, or (*c*) a damaged biliary duct.

Drainage, however, is associated with a small but significant morbidity that includes the introduction of infection and the formation of incisional herniae. Also, a syndrome of fever and pain in the right upper quadrant of the abdomen has been described by Myers (1962) and termed 'drain fever'. This occurred in 5·3 per cent of his cases following manipulation of a drain that had been present for more than 48 hours. The pain persisted for 1–3 days and subsided with the fever, although daily rises of temperature of up to 38° C. occasionally persisted for as long as 2 weeks. It has also been suggested that the surgeon may rely completely on a drain to indicate a biliary leak and, because of this false security, may miss the signs of a hidden collection of bile.

The length of time for which drainage is advised in the absence of bile leakage varies, Myers (1962) recommending less than 48 hours, Maingot (1964) 2–3 days, and George (1964) 4–5 days. To add to the confusion it has been estimated that 16 per cent of surgeons do not routinely drain after cholecystectomy but rely on the physical signs to indicate biliary leakage (Lazarus, Baum, and Briedenbach, 1954). Dreese (1963) reported a series of 667 simple cholecystectomies in which drainage had been omitted in 230 cases. His cases had to satisfy strict criteria when no drainage was used. These included no spillage of purulent material during the operation, absence of bleeding or biliary ooze from the gall-bladder fossa, double ligation of the cystic duct, and tying of the cystic artery under direct vision. Only 1 patient required secondary drainage and there were no deaths in the series.

A survey was carried out by the Public Health Laboratory Service (1960) to estimate the incidence of sepsis following surgical operations and found it to be as high as 20·6 per cent following cholecystectomy. This figure was among the highest for general surgical operations and may be the result of several factors, including spillage of infected bile, the presence of a drain, and incidental appendicectomy. Komarn and Kaufman (1963) found a higher incidence of wound infection when appendicectomy was carried out with cholecystectomy and concluded: 'transection of a faecal-containing organ in an otherwise clean operation violated established surgical principles'. This conclusion was not supported by either Lowery and Lenhardt (1962) or Bogart and Sebesta (1969), who found that appendicectomy did not affect the incidence of wound infection in their series of cholecystectomies. Unfortunately, none of these studies took into account the presence or absence of intraperitoneal drainage.

Our study was carried out to assess the place of intraperitoneal drainage as a routine practice following cholecystectomy with and without incidental appendicectomy.

MATERIALS AND METHODS

The operations included in this study were carried out at two hospitals in the same city. At one hospital it was the policy never to use intraperitoneal drainage after simple cholecystectomy but to rely on physical signs to diagnose biliary leakage. At the second hospital this was not the policy and drains were inserted for periods that varied according to the whims of individual surgeons. Surgical registrars rotated between the two hospitals and adopted the policy of drainage of each hospital accordingly. This produced two random groups of patients on whom the effects of drainage could be compared.

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All routine cholecystectomies carried out at these two hospitals during the 5-year period 1965–9 were included in this study. Cases where exploration of the common bile-duct or any other surgical procedure, except appendicectomy, was carried out were excluded. Also excluded were operations for carcinoma of the gall-bladder.

A total of 309 cases were reviewed and included in the study; 170 had been drained and 139 not drained.

Table I.—THE GROUPS OF PATIENTS STUDIED

Group	*No. of Patients*
Drainage with appendicectomy	34
Drainage without appendicectomy	136
No drainage and appendicectomy	62
No drainage or appendicectomy	77
Total	309

Twenty-six per cent of the patients in both groups were male and the average ages for the groups with and without drainage were 54·3 years (range, 15–89 years) and 53·3 years (range, 23–80 years) respectively.

These two groups were further subdivided according to whether or not appendicectomy had been carried out at the time of the cholecystectomy (*Table I*).

The operations were carried out by 28 different surgeons who used either corrugated-rubber strips, rubber tubes, or Penrose wick drains. No significant difference was found between the results obtained for the various drains.

Four criteria were studied in each group and were compared statistically:—

1. Mortality.
2. Incidence of infection and biliary peritonitis.
3. Duration of the postoperative pyrexia. This was calculated as the period immediately after operation that the temperature remained above 38° C.
4. Length of postoperative stay in hospital.

RESULTS

1. Mortality.—Two patients (0·65 per cent) died during the postoperative period, 1 from a pulmonary embolus and the other from septicaemia (infecting organism, *Clostridium welchii*). Both died on the third postoperative day and were not included in the rest of this study.

2. Infection and Biliary Peritonitis.—There were 13 cases (7·8 per cent) of wound infection in the group of patients with drains, and 2 cases (1·4 per cent) of wound infection in the group without drains. It is interesting to note that in only 3 of these cases, all in the group with drainage, was incidental appendicectomy carried out.

Two patients, both in the group with drainage, developed a subhepatic abscess, and each required a further operation to drain the collection of pus. Two other patients required second operations: 1 for bleeding which in spite of the presence of a corrugated-rubber drain was concealed for 48 hours, and the other for a collection of 300 ml. bile which also failed to escape along a corrugated-rubber drain. The diagnosis of a collection of bile was made clinically on the third postoperative day and the patient made a satisfactory recovery after a second operation to drain it.

3. Postoperative Pyrexia.—The temperature remained above 38° C. for a significantly longer period when a drain was present (*Table II*), and the duration of postoperative pyrexia was not affected by carrying out an appendicectomy with the cholecystectomy (*Table III*).

Table II.—COMPARISON OF THE DURATION OF POSTOPERATIVE PYREXIA AND STAY IN HOSPITAL IN PATIENTS WITH AND WITHOUT DRAINAGE

GROUP OF PATIENTS	NO. OF PATIENTS	POSTOPERATIVE PYREXIA (hours)		POSTOPERATIVE STAY IN HOSPITAL (days)	
		Mean ± S.E.	*P*	Mean ± S.E.	*P*
Total with drainage Total without drainage	168 139	97·7 ± 5·0 72·0 ± 4·8	< 0·001	12·00 ± 0·41 10·30 ± 0·27	< 0·01
Drainage without appendicectomy No drainage or appendicectomy	135 77	94·1 ± 5·3 68·6 ± 5·8	< 0·01	11·94 ± 0·48 10·62 ± 0·40	0·05
Drainage with appendicectomy No drainage with appendicectomy	33 62	112·1 ± 6·5 75·1 ± 7·0	< 0·01	12·21 ± 0·82 9·65 ± 0·31	< 0·001

The effect of the period of drainage was assessed by comparing the duration of postoperative pyrexia when the drain was removed within 48 hours with (*a*) the group without drainage and (*b*) when the drain remained for more than 48 hours (*Table IV*). No difference was found between the group without drainage and patients in whom the drain was removed within 48 hours. However, there were significant differences between those patients in whom the drains were left for more than 48 hours and the other two groups.

In our study 7 patients (4·3 per cent) complained of pain at the drain site associated with a pyrexia after manipulation of the drain. Each drain had been left in position 48 hours or more.

4. Length of Postoperative Stay in Hospital.—The same comparisons were made as were carried out for postoperative pyrexia. The patients with drains remained in hospital for a significantly longer period than those without drains (*Table II*). When the effect of appendicectomy was considered, varying results were obtained (*Table III*). No difference was found between the groups with drainage, but in the groups without drainage patients who had incidental appendicectomy had a shorter postoperative stay in hospital.

Patients in whom the drain had been left in position for more than 48 hours had significantly longer postoperative stays in hospital than either the patients without drainage or those drained for less than 48 hours (*Table IV*). No difference was found between these latter two groups.

The results of individual surgeons for both postoperative pyrexia and length of stay in hospital were compared statistically. No significant differences in distribution were found (*Table V*).

Table III.—EFFECT OF APPENDICECTOMY ON THE DURATION OF POSTOPERATIVE PYREXIA AND STAY IN HOSPITAL FOLLOWING CHOLECYSTECTOMY

GROUP OF PATIENTS	NO. OF PATIENTS	POSTOPERATIVE PYREXIA (hours)		POSTOPERATIVE STAY IN HOSPITAL (days)	
		Mean ± S.E.	*P*	Mean ± S.E.	*P*
Drainage with appendicectomy	33	112·1 ± 6·5	>0·10	12·21 ± 0·82	>0·70
Drainage without appendicectomy	135	94·1 ± 5·3		11·94 ± 0·48	
No drainage with appendicectomy	62	75·1 ± 7·0	>0·40	9·65 ± 0·31	<0·05
No drainage or appendicectomy	77	68·6 ± 5·8		10·62 ± 0·40	

Table IV.—EFFECT OF THE PERIOD OF DRAINAGE FOLLOWING CHOLECYSTECTOMY ON THE DURATION OF POSTOPERATIVE PYREXIA AND STAY IN HOSPITAL

GROUP OF PATIENTS	NO. OF PATIENTS	POSTOPERATIVE PYREXIA (hours)		POSTOPERATIVE STAY IN HOSPITAL (days)	
		Mean ± S.E.	*P*	Mean ± S.E.	*P*
Drainage for less than 48 hours	44	78·5 ± 8·2	<0·02	10·16 ± 0·39	<0·01
Drainage for more than 48 hours	124	104·4 ± 6·0		12·63 ± 0·51	
Drainage for less than 48 hours	44	78·5 ± 8·2	>0·40	10·16 ± 0·39	>0·70
Total without drainage	139	72·0 ± 4·8		10·30 ± 0·27	
Drainage for more than 48 hours	124	104·4 ± 6·0	<0·001	12·63 ± 0·51	<0·001
Total without drainage	139	72·0 ± 4·8		10·30 ± 0·27	

Table V.—COMPARISON OF THE RESULTS OBTAINED FOR DIFFERENT SURGEONS IN THE STUDY

GROUP OF PATIENTS	POSTOPERATIVE PYREXIA		POSTOPERATIVE STAY IN HOSPITAL	
	χ^2	*P*	χ^2	*P*
Drainage and appendicectomy	13·80	>0·05	3·59	>0·50
Drainage without appendicectomy	2·20	>0·99	3·59	>0·98
No drainage with appendicectomy	2·74	>0·70	1·60	>0·90
No drainage or appendicectomy	1·25	>0·95	1·52	>0·95

DISCUSSION

Drainage of the hepatorenal space after simple cholecystectomy is advised by the majority of authors to allow bile that might leak from the biliary tract and produce peritonitis to escape. When this complication occurs there is a significant increase in the postoperative mortality and morbidity. In our study the presence of a drain was associated with an increased incidence of wound infection and significantly longer periods of postoperative pyrexia and stay in hospital when compared with a group of patients in whom no drain was used. This increase in postoperative morbidity was independent of the type of drain used. The better results for the group without drainage may be the result of several factors. These include the more meticulous technique used by a surgeon who knows that he will not have a drain to warn him of biliary leakage or blood-loss—complications that are usually the result of technical errors. Also drains, particularly when made of rubber, are an irritant in the tissues and may predispose to infection. However, if in the absence of bile leakage the drains were removed within 48 hours, results no different from those of the group without drainage were obtained.

As this is a retrospective study, other factors have to be considered before conclusions can be made from the results. Drains may have been left in position for longer than 48 hours because signs or symptoms of infection were present and a more cautious approach to the removal of the drain was indicated. Careful examination of the notes revealed no leakage of bile or excessive loss of serous fluid from any of the drains which were left for longer than 48 hours, and no obvious reason for their continued presence was found. Also, if evidence of infection had been present in this group, then similar evidence would have been found in the group of patients without drainage if the infection had not been due to the presence of the drain itself.

Although the two groups of patients were treated at separate hospitals the majority were operated upon by the same surgeons using the same basic techniques. The hospitals received patients from the same geographical districts and social classes, so that these factors could not have accounted for any of the differences observed. Other factors exist that may have affected the length of postoperative stay at the two hospitals. These include the pressure on beds and the availability of convalescent facilities, neither of which could be accurately assessed in this study.

However, the findings in this study are particularly relevant when considered with the findings of Myers (1962) and MacVicar and others (1967). MacVicar and others (1967) found that deterioration in the condition of a patient as a result of bile leakage following cholecystectomy usually occurred during the first 48 hours. Myers (1962) described a syndrome of pain and fever occurring in approximately 5·3 per cent of patients following manipulation of a drain that had been present for 48 hours or more. A similar syndrome was observed in 4·3 per cent of our patients. Therefore, when no bile is escaping there is no indication for leaving the drain in position for longer than 48 hours. By that time it will have served its purpose and its presence for a further period will only produce an increase in postoperative morbidity.

It is of interest that the 4 cases in our series requiring second operations for intraperitoneal collections had been drained during the initial procedure. One of the 2 patients who developed a subhepatic abscess had been drained with a tube drain and the other with a corrugated-rubber strip. Both the patients who formed collections of bile and blood had been drained with corrugated-rubber strips, and in neither case was the condition recognized until the patient had developed symptoms. The reliability of corrugated-rubber strips for intraperitoneal drainage is therefore open to doubt.

In this study the practice of carrying out an appendicectomy at the time of the cholecystectomy did not affect the postoperative morbidity. Komarn and Kaufman (1963) claimed that it increased the incidence of wound infection, but the results obtained by Lowery and Lenhardt (1962) and Bogart and Sebesta (1969) did not support this conclusion. Incidental appendicectomy was advocated by Lowery and Lenhardt (1962) and Bogart and Sebesta (1969), as they found histological evidence of either active or chronic disease existing in 28·4 per cent and 35·9 per cent of the appendices removed respectively. None of these papers took into account the effect of drainage which we found to affect the morbidity, but in our study, which takes drainage into account, no adverse effects were found when incidental appendicectomy was carried out. In fact, patients who had appendicectomy and cholecystectomy without drainage had shorter postoperative stays in hospital. On analysis of this group it was found that 4 of the patients who had not had appendicectomies had longer stays in hospital than usual: 2 because of deep-vein thrombosis and 2 because of pneumonia. Our study supports incidental appendicectomy when it can be carried out with complete ease and without undue manipulation.

Acknowledgements.—We wish to express our thanks to Mr. K. P. S. Caldwell, Mr. H. Dendy Moore, Mr. K. D. J. Vowles, and Mr. C. Shaldon for permission to study their patients.

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ANTERIOR DISLOCATION OF THE HIP AND DIASTASIS OF THE CONTRALATERAL SACRO-ILIAC JOINT—THE REAR-SEAT PASSENGER'S INJURY?

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SUMMARY

A mechanism of injury is described to account for the combination of anterior dislocation of the hip and diastasis of the contralateral sacro-iliac joint occurring in rear-seat car passengers. Two cases are described and discussed in relation to precipitating factors and how the injury may be prevented.

THE association between comminuted fracture of the patella and posterior dislocation of the ipsilateral hip in 'dashboard' injuries has long been recognized as a hazard to front-seat passengers in cars which are involved in head-on collisions.

Two recent cases of anterior dislocation of the hip occurring in rear-seat passengers have indicated the manner in which the injury was produced. In 1 of these cases the dislocation was associated with diastasis of the contralateral sacro-iliac joint, suggesting that the injuries are connected and produced by the same forces.

CASE REPORTS

Case 1.—W. P., a 62-year-old man, was seated behind the driver in a small family car which was involved in a

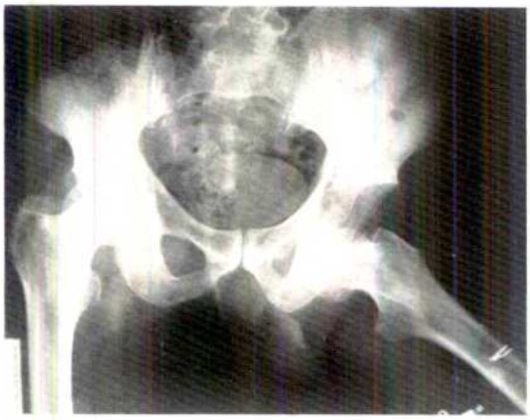

FIG. 1.—*Case* 1. Radiograph of the pelvis and both hips showing anterior dislocation of the left hip.

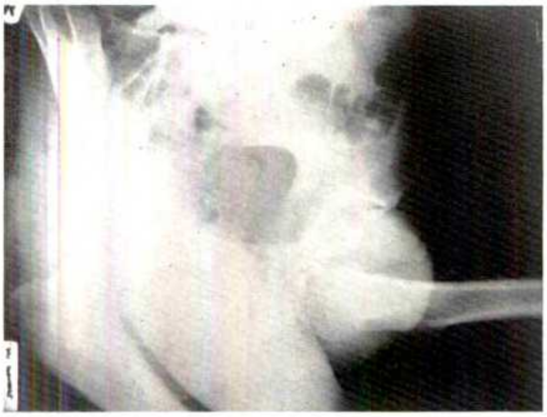

FIG. 2.—*Case* 2. Radiograph of the pelvis and both hips showing anterior dislocation of the left hip with diastasis of the right sacro-iliac joint.

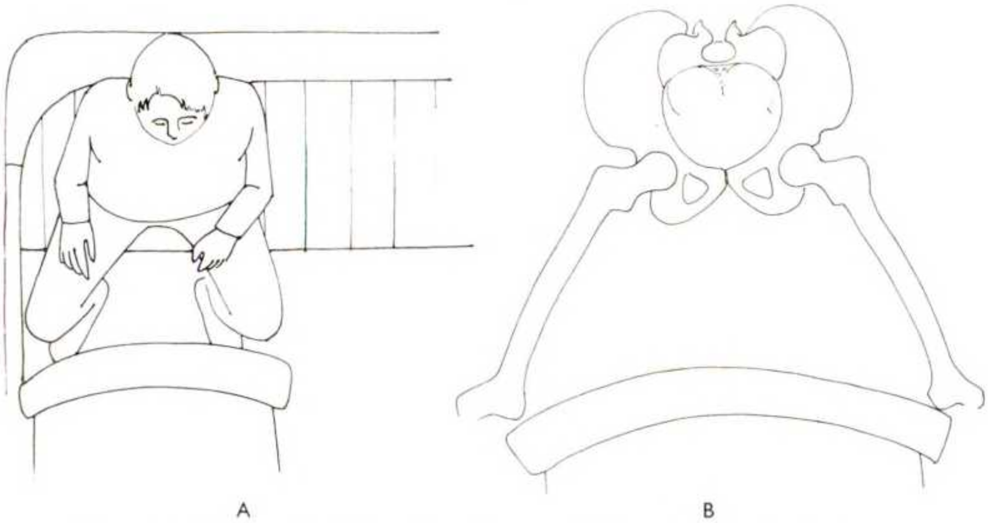

FIG. 3.—A, Position of rear-seat passenger prior to impact. B, Anatomical position prior to impact.

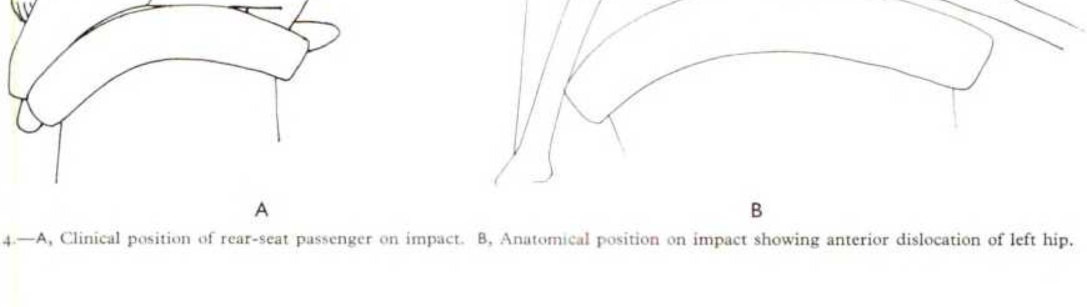

FIG. 4.—A, Clinical position of rear-seat passenger on impact. B, Anatomical position on impact showing anterior dislocation of left hip.

head-on collision. The force of the impact threw him forward against the back of the driver's seat and he sustained an anterior dislocation of the left hip (*Fig.* 1). This dislocation was subsequently reduced and, after a period of immobilization on traction, the patient made a full and uncomplicated recovery.

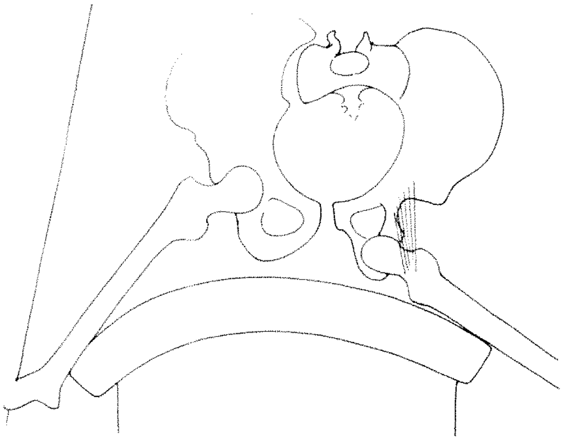

FIG. 5.—Anterior dislocation of the left hip with separation of the contralateral sacro-iliac joint.

Case 2.—W. J., a 19-year-old man, was sitting behind the driver in a saloon car when it was involved in a high-speed, head-on collision with another vehicle. He was thrown forward against the driver's seat and sustained an anterior dislocation of the left hip and a diastasis of the right sacro-iliac joint (*Fig.* 2). The dislocation was reduced under general anaesthesia and the pelvic separation was treated successfully in a pelvic sling. Subsequent progress was uneventful.

DISCUSSION

Front-seat car passengers tend to sit with their knees together and their hips flexed at a right-angle. This is the optimum position from which to sustain a posterior dislocation of the hip on forcible impact of the knee against the dashboard. The impact also produces a comminuted fracture of the patella in many cases.

Rear-seat car passengers tend to sit with knees and hips flexed to a right-angle but with their hips in abduction and slight external rotation (*Fig.* 3). When such a passenger is subjected to sudden deceleration he is thrown forward against the front seat. The leg nearest the side of the car becomes wedged between the front seat and that side of the vehicle, thus becoming fixed and relatively safe from injury. However, the leg nearest the centre of the car has freedom of movement and is subjected to an abducting and externally rotating force, which produces an anterior dislocation of the hip-joint (*Fig.* 4). If the deceleration is very rapid and results from high-velocity impact, any unspent force remaining after the hip has dislocated will be transmitted through the ligaments of that hip to the pelvis. The innominate bone adjacent to the side of the vehicle is already fixed in the same way as the femur on that side, and separation of the pelvis occurs at that sacro-iliac joint, being the point between its fixed and potentially mobile parts.

In the 2 cases described here both patients were seated behind the driver and in each case the left hip was dislocated. Clearly the same mechanism would apply in the case of a person seated behind an occupied front-passenger seat, but in this case the right hip and the left sacro-iliac joint would be injured.

Other marginal factors affecting the extent of injury are illustrated in the cases described. In *Case* 1 the speed at impact was much less than that in *Case* 2, which may account for the hip alone being affected in the first patient. In both cases the vehicles were fitted with individual front seats which probably contribute to this type of injury.

Should a rear-seat passenger be thrown against an unoccupied front seat it is a matter for conjecture whether his injuries would be severe or whether the seat would itself become deformed by absorbing some of the force of impact. The construction of the vehicle and whether or not the front seats are anchored would have some bearing on the injury pattern.

The only way in which these particular injuries can be prevented is for rear-seat passengers to wear safety belts and thus be prevented from being thrown forward on vehicle impact.

Acknowledgements.—I am grateful to Mr. F. W. Taylor for permission to publish details of patients under his care, and for his help in the preparation of this paper; also to Mrs. I. Blincow for the drawings and Mrs. B. M. Wilson for secretarial help.

SURGICAL RESEARCH SOCIETY

A meeting of the Surgical Research Society was held in the Medical School, St. Bartholomew's Hospital, London, on 7 and 8 January, 1972, with Professor R. B. Welbourn (President of the Surgical Research Society) in the Chair. The following papers were presented:—

1. Effects of Expanding Intracranial Lesions on Cerebral Blood-flow: J. D. Miller, A. E. Stanek, and T. W. Langfitt (W. B. Jennett), Pennsylvania, and Department of Neurosurgery, University of Glasgow.

Maintenance of cerebral blood-flow (C.B.F.) during increased intracranial pressure (I.C.P.), produced experimentally by the infusion of cerebrospinal fluid (C.S.F.), depends on the preservation of autoregulation (A.R.) of the C.B.F. to changes of mean arterial pressure (M.A.P.) (Miller et al., 1971).

To produce a more relevant model of increased I.C.P., extradural balloons were inflated in 13 anaesthetized ventilated dogs in which the C.B.F., M.A.P., and I.C.P. were continuously measured; the arterial blood-gases and body temperature were controlled.

In all dogs A.R. was first tested by reducing the M.A.P.; after the return of M.A.P. to the control level the I.C.P. was increased by balloon inflation. The balloon was then deflated and the sequence was repeated.

With intact A.R. a fall in the M.A.P. of 23·4 ± 3·2 (S.E.) mm. Hg caused no change in the C.B.F.; a succeeding increase in the I.C.P. from 9·4 ± 1·0 to 27·2 ± 1·3 mm. Hg did not alter the C.B.F. When A.R. was impaired, an M.A.P. decrease of 23·4 ± 1·7 mm. Hg reduced the C.B.F. by 5·9 ± 0·7 ml. per min.; increasing the I.C.P. from 10·7 ± 1·5 to 29·4 ± 1·7 mm. Hg now reduced the C.B.F. by 5·1 ± 0·7 ml. per min. These changes were significant ($P < 0{\cdot}001$).

It is concluded that if the A.R. is intact in most of the brain the initial increase in I.C.P. due to an expanding intracranial mass will not reduce the total C.B.F.; if the A.R. is impaired, however, the C.B.F. will fall as soon as the I.C.P. increases.

Miller, J. D., Stanek, A. E., and Langfitt, T. W. (1971), *Fedn Proc. Fedn Am. Socs exp. Biol.*, **30**, 263.

2. Catgut—An Analysis and Immunological Study in Rabbits: I. Capperauld (H. L. Duthie), Ethicon Research Unit, Kent.

Catgut hypersensitivity has been reported, both clinically and experimentally (Hopps, 1944). An analysis of catgut coupled with immunological testing in rabbits was performed.

Plain and chromic catgut was made into solution by autoclaving at 20 lb. per in.^{2} for 24 hours. Each solubilized catgut was separated into six component fractions by high-voltage electrophoresis. Individual components were eluted and a quantitative analysis of the twenty-one amino-acids in each component was carried out. Methionine was found to be absent, and its absence was confirmed by cyanogen bromide extraction.

Immunological tests (Timpl et al., 1968) were carried out in rabbits using the extracted components of solubilized plain and chromic catgut. Samples were dissolved in water and emulsified with Freund's complete adjuvant. This was injected into rabbits on days 1, 15, and 30. Serum was obtained on day 37 and precipitation tests were performed against all the original component 'antigens'. These tests proved negative.

Hypersensitivity to plain or chromic gamma-irradiated catgut was not demonstrated in rabbits in this investigation.

Hopps, H. C. (1944), *Archs Surg. Chicago*, **48**, 438, 445, 450.

Timpl, R., Wolff, I., Wick, H., Furthmay, H., and Steffen, C. (1968), *J. Immun.*, **101**, 725.

3. Evaluation of Mammary Thermography: B. E. Nathan, J. I. Burn, and D. MacErlean, Royal Postgraduate Medical School, London.

Recent interest in mammary thermography has been stimulated by its potential in identifying asymptomatic disorders of the breast. We have assessed its value in the differential diagnosis of 359 patients with established mammary symptoms. Patients in whom a confident clinical diagnosis of cancer had been made were not included.

The thermograms were interpreted as being 'normal' or 'abnormal', as judged by well-defined localized areas of heat or clear inequality between the two breasts. There were 164 patients with normal thermograms and 195 (54 per cent) with abnormal thermograms.

Of the 164 patients with normal thermograms, 116 had no confirmed organic lesion, 7 had malignant disease, and 41 had benign lesions (29 per cent false negatives). Of the 195 patients with abnormal thermograms, 27 had malignant disease, 53 had benign lesions, and 115 had no confirmed organic lesion (58 per cent false positives).

Sixty-nine of the patients with benign organic lesions had localized mammary dysplasia (fibro-adenosis, cystic disease). Forty (58 per cent) of these had abnormal thermograms, the remainder being normal. Seven (20 per cent) of the 34 patients with cancer had normal thermograms.

We conclude that mammary thermography is of no practical value in the differential diagnosis of symptomatic mammary disease.

4. Skin Organisms beyond the Reach of Disinfectants: S. Selwyn (H. Ellis), Westminster Medical School, London.

Skin bacteria are regarded usually to be confined to the epidermal surface and therefore accessible to thorough disinfection (Marples, 1969). This view is based on the results of insensitive and mainly qualitative tests that can detect only those organisms that are indeed accessible to disinfectants. The fallacy is revealed by a quantitative technique using skin biopsies. Unprepared and disinfected skin areas are excised at routine operations. Bacteria are counted both by microculture of frozen sections and in suspensions from biopsies agitated in Triton X-100.

On abdominal skin mean counts of accessible organisms in 35 patients were 30,000 per cm.^{2}, reducing by 95·5 per cent after disinfection with alcoholic iodine. Other disinfectants proved less efficient. However, approximately one-fifth of the total microflora was beyond the reach of even the most vigorous sampling methods and could be seen surviving in frozen sections cultured from doubly disinfected biopsies. Moreover, skin areas rich in sebum have a 'protected' flora that is often larger than the accessible flora. Comparable findings were obtained in parallel experiments using less sensitive tape-stripping methods and studies on the restoration of numbers in occluded skin areas after disinfection.

Marples, M. (1969), *Br. J. Derm.*, **81**, suppl., **1**, 2.

5. A Trial of Two Different Régimes of Subcutaneous Heparin in the Prophylaxis of Deep-vein Thrombosis: L. P. LE QUESNE, J. BRAMBLE, I. C. GORDON-SMITH, D. GRUNDY, and J. NEWCOMBE, The Middlesex and Central Middlesex Hospitals, London.

Sharnoff (1966) claimed that small doses of subcutaneous heparin, insufficient to cause prolonged anticoagulation, given subcutaneously before and after operation could diminish the incidence of pulmonary embolism. Kakkar et al. (1971) produced strong evidence that such treatment significantly reduced the incidence of postoperative deep-vein thrombosis (D.V.T.).

The majority of postoperative D.V.T. start within 24 hours of operation. It may be that the major benefit from prophylactic heparin treatment accrues in the first 24-hour period after operation. To test this hypothesis and to confirm the observations of Kakkar et al. (1971) a trial is in progress on patients undergoing abdominal operations, allocated randomly to three groups: group I, no heparin (controls); group II, heparin, 5000 I.U. subcutaneously, 1 hour preoperatively and 12 and 24 hours later; group III, heparin, 5000 I.U. subcutaneously, 1 hour preoperatively, thereafter 12-hourly for 5 days. D.V.T. was detected by the ^{125}I-fibrinogen technique.

To date 114 patients have been studied. The incidence of D.V.T. was significantly less in both group III (5·9 per cent; $P < 0{\cdot}0005$) and group II (13·2 per cent; $P < 0{\cdot}005$) than in group I (42·9 per cent). No significant difference could be demonstrated between groups II and III, though the numbers so far studied are too small to allow of firm conclusions about the comparable efficacy of these two dosage régimes.

KAKKAR, V. V., FIELD, E. S., NICOLAIDES, A. N., and FLUTE, P. T. (1971), *Lancet*, **2**, 671.
SHARNOFF, J. G. (1966), *Surgery Gynec. Obstet.*, **123**, 303.

6. The Nature of the Reflux Material in Reflux Oesophagitis: E. W. GILLISON, L. M. NYHUS, and K. KUSAKARI (J. D. Hardcastle), Universities of Nottingham and Illinois.

The role of bile in reflux oesophagitis was studied in the Rhesus monkey. The oesophagogastric junction prevents reflux of gastric juice into the oesophagus in the monkey. Reflux could be produced after oesophagogastrectomy when the anastomosis was situated 2 cm. above the diaphragm.

Four groups of monkeys were studied:—

Group I had the reflux procedure alone and their progress was followed by endoscopy for 6 months.

Group II had a bile diversion procedure consisting of pylorectomy, closure of the duodenal stump, and a Roux-en-Y anastomosis. This was followed by the reflux operation 4 weeks later.

Group III had cholecystogastrostomy to produce bile contamination, followed by the reflux operation 4 weeks later.

Group IV differed from group III by having daily depot histamine in bee's wax injections (2 mg. per kg.).

About a third of the control monkeys in group I developed mild oesophagitis. Groups II, III, and IV were evaluated endoscopically at 1 and 3 months. Surviving monkeys were killed at 3 months to check the accuracy of the endoscopy.

At 3 months only 1 out of 7 monkeys in group II had oesophagitis despite daily reflux of pure gastric chyme. All the monkeys in groups III and IV showed oesophagitis, including ulceration and stricture. Administration of depot histamine did not increase the severity of oesophagitis.

The maximal acid outputs were followed in all the groups. The output was not significantly changed in group I over 6 months, but the level fell in the other three groups. Groups III and IV were almost equally achlorhydric after 3 months.

7. Insensible Water Loss in Operative Patients: C. D. BAUMBER, R. G. CLARK, and P. HOWLETT, Department of Surgery, University of Sheffield.

Large increases in insensible water loss have been reported in operative patients. In the operating theatre Coller and Maddock (1932) reported an increase of 500 per cent. In the first few postoperative days insensible water loss increased by more than 100 per cent (Paquin, 1958).

We wish to report a study of insensible water loss before and after operation measured by direct weighing and the use of tritiated water in 10 patients undergoing moderately severe abdominal operations.

The mean preoperative insensible water loss was 0·6 ml. per kg. per hr. The insensible water loss increased significantly during the period of operation to 1·65 ml. per kg. per hr. In those patients receiving intravenous fluids postoperatively the insensible water loss increased to 0·7 ml. per kg. per hr. ($P < 0{\cdot}05$). In those patients receiving restricted oral fluids alone it fell to 0·4 ml. per kg. per hr. ($P < 0{\cdot}01$).

Under modern operating conditions abdominal surgery is not accompanied by the gross increases in insensible water loss previously reported. In the postoperative period insensible water loss is a function of the state of hydration of the patient as well as of the environment.

COLLER, F. A., and MADDOCK, W. G. (1932), *J. Am. med. Ass.*, **99**, 875.
PAQUIN, A. J. (1958), *Ann. Surg.*, **98**, 952.

8. The Effect of a Long-acting Anabolic Steroid on Nitrogen Balance during the Anabolic Phase of Recovery from Abdominal Surgery: D. E. F. TWEEDLE, CHRISTINE WALTON, and I. D. A. JOHNSTON, Department of Surgery, University of Newcastle upon Tyne.

The results of giving anabolic steroids to minimize the catabolic response to trauma are often difficult to interpret owing to variations in the body-weight and the nutritional intake of the patients studied. It has been suggested that anabolic hormones may exert their maximal effect during the anabolic phase of recovery when nitrogen is being retained by the body.

A study was planned to examine the effect of a long-acting anabolic steroid (nandralone decanoate, 50 mg. intramuscularly) on both the catabolic and anabolic phases of recovery from vagotomy and pyloroplasty.

Nitrogen balances were performed for 8 days after operation in 24 men. Patients were allocated randomly to four groups:—

Group I: Low calorie (13 cal. per kg. per 24 hours).
Group II: Low calorie + anabolic steroid.
Group III: High calorie (31 cal. per kg. per 24 hours).
Group IV: High calorie + anabolic steroid.

The total 8-day balances of groups II, III, and IV were improved significantly compared with that of group I ($P < 0{\cdot}05$).

Daily nitrogen balance was improved significantly during both the catabolic phase (days 1–4) and the anabolic phase (days 5–8) in group II compared with group I ($P < 0{\cdot}05$). Nitrogen balance in the high-calorie group was enhanced by anabolic steroids also, but not significantly ($P = 0{\cdot}1$).

The difference between the low-calorie groups represents a sparing of 663 g. of protein tissue in a 70-kg. male when anabolic steroids are given.

9. Haemorrhagic Shock in Afibrinogenaemic Dogs: D. H. Lewis, H. Myrvold, and P. Olsson (N. Matheson), Göteborg and Stockholm.

A double-isotope technique using ^{133}Xe and ^{131}I has been developed for the simultaneous measurement of capillary blood-flow and capillary transport in skeletal muscle. The isotope mixture is injected i.m. (0·1 ml.) and clearances are measured by external detection. Xenon clearance estimates capillary blood-flow, and iodide clearance, at the observed flow level, is an estimate of capillary transport function, calculated from Renkin's (1959) formula for permeability/surface area product (P.S.).

In haemorrhagic shock there is a deficit in capillary transport out of proportion to the existing capillary flow (Appelgren and Lewis, 1971). One possible explanation could be disseminated intravascular coagulation. To investigate this 6 dogs were made afibrinogenaemic with reptilase (Pentapharm A.G./A.B. Bofors), 3·4 mg. per kg. i.v. on 3 successive days. Haemorrhagic shock was induced by bleeding up to 60 per cent of the calculated blood volume and the animals were followed with repeated isotope clearances for up to 10 hours. After 4–5 hours all the dogs had an iodide clearance lower than that expected for the flow value obtained, that is, the same pattern of response as in animals with normal fibrinogen levels.

The results indicate that the observed alteration in the skeletal muscle microcirculation cannot be attributed to intravascular coagulation.

Appelgren, K. L., and Lewis, D. H. (1971), *Eur. Surg. Res.* (in the press).

Renkin, E. M. (1959), *Am. J. Physiol.*, **197**, 1205.

10. The Pathological Basis for Skeletal Scintigraphy: C. S. B. Galasko, Nuffield Orthopaedic Centre, Oxford.

It has been shown previously that skeletal scintigraphy, using ^{18}Fl and the gamma camera, is useful both for the early detection of skeletal metastases (Galasko, 1969) and for the assessment of the response of these metastases to therapy (Galasko and Doyle, 1970). The underlying pathological changes which allow us to use isotopes to study these lesions were investigated.

Ninety-six histological sections obtained at autopsy from 20 patients who had died from malignant disease were examined for the type of bone and the amount of osteoid which was present. Where metastases were present, 27·8 per cent of the total bone was osteoid; in the absence of metastases only 5·2 per cent was osteoid tissue. In the presence of tumour 36·3 per cent of the bone consisted of immature woven bone; where no tumour was present, only 1·9 per cent was woven bone.

Tumour-cell suspensions of the VX2 carcinoma were injected into the tibiae and ilia of experimental rabbits. Autoradiographs obtained after the injection of ^{47}Ca and ^{18}Fl showed that the isotope was localized in the new bone which was laid down in response to the tumour. Where the VX2 carcinoma was successfully treated the remaining bone lost its osteoid reaction and its increased avidity for 'bone-seeking' isotopes.

These studies suggest that the clinical use of isotopes in skeletal metastases depends on the osteoid reaction which the tumour invokes in the invaded bone.

Galasko, C. S. B. (1969), *Br. J. Surg.*, **56**, 757.

— — and Doyle, F. (1970), *Ibid.*, **57**, 859.

11. The Quantitative Colour T.V. Image Analyser—A New Method of Assessing Bone Density: R. A. Dickson, F. Paice, and J. S. Calnan, Royal Postgraduate Medical School, London.

The progress of osteoporosis in rheumatoid disease has been studied by measuring cortical width (Virtama et al., 1968). We have followed its course with a television camera, a colour monitor, and an electronic counter.

The quantitative colour T.V. image analyser, developed by the M.R.C. Cyclotron Unit, converts seven shades of grey in an optical image into seven characteristic colours. Furthermore the image can be analysed numerically in terms of total area, number of intercepts, and number of discrete areas for each colour. The serial radiographs of 20 rheumatoid hands were analysed in this manner, and for each digit the densities of three fields were examined: the metacarpophalangeal joint, the middle two-fourths of the metacarpal, and the middle two-fourths of the proximal phalanx.

Metacarpal density was always greater than that of the corresponding joints and proximal phalanges, irrespective of the stage of the disease. Both bones showed a continuous loss of density at a rate of up to 17 per cent per year. Approximately 75 per cent of the joints showed a similar continuous density loss, but 25 per cent showed increased density and this occurred in joints that had collapsed, subluxed, or grown new bone. Losses in the three fields examined did not appear to be interrelated.

Virtama, P., Helela, T., and Kalliomaki, J. L. (1968), *Acta rheum. scand.*, **14**, 276.

12. Cellular Immunity to Tumour Factors in Human Breast Carcinoma: D. J. Evans, Gillian Simpson, A. Campos, and J. I. Burn, Royal Postgraduate Medical School, London.

The existence of a host defence response in human breast carcinoma has been a matter of controversy.

We have searched for a lymphocyte-mediated response to tumour factors in patients with early breast carcinoma.

In patients with a cellular immunity to an antigen the exposure of the patients' lymphocytes to the antigen results in a small percentage of them undergoing blast transformation. We exposed patients' lymphocytes to homogenates of their own tumours as putative antigens using standard methods of lymphocyte culture and of assessment of response. With this technique twenty breast carcinomas tested showed an entirely negative response, as did a variety of benign lesions and extracts of muscle.

Four tumours gave a positive response. Three of these were medullary carcinomas with a lymphoid stroma. The fourth was an unusual tumour of the type designated adeno-osteoclastoma by Willis (1967). Extracts from these tumours did not produce transformation in the lymphocytes of normal controls.

These preliminary results suggest that there is no lymphocyte-mediated response to the majority of breast carcinomas but that in some carcinomas lymphocytes in the stroma are reacting against tumour antigens.

Willis, R. A. (1967), *Pathology of Tumours*, 4th ed., p. 216. London: Butterworths.

13. The Morbidity of Mastectomy: M. Maureen Roberts, Isobel G. Furnival, and A. P. M. Forrest, Department of Clinical Surgery, University of Edinburgh, and Department of Diagnostic Radiology, The Welsh National School of Medicine, Cardiff.

Few studies of the morbidity of breast surgery have been performed (Eisenberg and Goldenberg, 1969). This we have attempted to assess in 112 women. Eighty-six were included in a randomized trial comparing conservative and radical methods of treatment. Patients in both groups also received radiotherapy if the removed axillary nodes were positive. A further 26 patients had an elective standard Halsted radical mastectomy.

Morbidity was assessed by interview at home, by completion of a questionnaire, and by clinical examination. Particular attention was paid to the social and psychological effects of the operation and to objective measurements of arm oedema and arm movements.

Fifty per cent of all patients admitted anxiety or depression, with no significant variation between the treatment groups. Thirty-six per cent complained of phantom breast sensations and this was most common in premenopausal women. Arm oedema of more than 2 cm. occurred in 15 per cent of women treated by simple mastectomy alone and rose significantly to 46 per cent in those who had had axillary clearance. Arm movement was normal in those treated by simple mastectomy alone, but the incidence of restriction of movement increased significantly (25 per cent) when the axilla had been cleared surgically.

It is concluded that there is important psychological and physical morbidity associated with all operations for primary breast cancer, and that physical morbidity increases with the extent of treatment.

EISENBERG, H. S., and GOLDENBERG, I. S. (1966), in *Clinical Evaluation in Breast Cancer* (ed. HAYWARD, J. L., and BULBROOK, R. D.), p. 93. London: Academic Press.

14. Comparison of the Inhibitory Effects of Lymphocytes from Patients with and without Cancer on the Growth of Human Tumour Cells in Culture: C. W. JAMIESON, St. Mary's Hospital, London.

Apparently unsensitized murine lymphocytes may inhibit the growth of tumour cells in culture (Jamieson and Wallace, 1970). The effect of human lymphocytes on allogenic tumour cells in culture was studied in a large group of patients. Lymphocytes from 90 patients with a variety of cancer and 72 control patients were cultured with HeLa cells using the method of Jamieson et al. (1969). Their inhibitory effect on the growth of these tumour cells in culture was measured over 48 hours.

A great variation was found to exist between patients but the results were reproducible in an individual. The lymphocytes from patients with cancer had a mean inhibitory effect on the growth of HeLa cells which was significantly greater than the mean effect of lymphocytes from patients without cancer ($P < 0{\cdot}001$). This effect was not related to an effect of the serum or general lymphocyte reactivity when measured by lymphocyte transformation studies.

It is not claimed that this difference is related necessarily to tumour-associated antigens, but the increased responsiveness of patients with cancer does not support suggestions that such patients have impaired cell-bound immunity.

JAMIESON, C. W., RUSSIN, D., BENES, E., DEWITT, C. W., and WALLACE, J. H. (1969), *Nature, Lond.*, **222**, 284.

— — and WALLACE, J. H. (1970), *J. Immun.*, **105**, 7.

15. The Vascular Dissemination of Tumour Cells by Manipulation of an Artificially Produced Bowel Tumour in the Rat: D. G. JAGELMAN (H. Ellis), Westminster Hospital, London.

The spread of tumour cells at operation owing to manipulation has been realized for some years but little importance seems to have been attached to it. An experiment was designed to demonstrate whether manipulation of a malignant bowel tumour liberated cancer cells into the circulation.

The Walker 256 tumour was implanted by means of a gelatin capsule into the invaginated caecum in 30 animals. Two weeks following implantation the artificially produced bowel tumour was subjected to trauma at a second laparotomy. Portal vein blood samples were taken before and after trauma to the tumour. The blood samples were spun down and the buffy coat removed. Smears were made on standard laboratory slides and stained with acridine orange to differentiate RNA and DNA. By means of this stain it was possible to differentiate tumour cells from normal blood elements.

In the pre-trauma blood samples 3 out of 30 animals showed malignant cells in the portal venous blood, whereas after trauma 19 blood samples were positive.

It is concluded that after trauma or manipulation of a malignant tumour in this experimental model an increased number of cancer cells are liberated into the blood-stream.

16. Treatment of Patients with Hypotonic Bladder by Radio-implant: S. ALEXANDER and D. ROWAN, Royal Infirmary, Glasgow.

Detrusor hypotonicity associated with difficulty in voiding and high residual and overflow incontinence were evaluated by recording transvesical pressure during 50-ml. filling increments and during attempted micturition.

The radio-implant consisted of two pairs of stainless-steel loop electrodes sited on the bladder fundus connected directly to an implanted receiver stimulator linked by radio-signal to an external transmitter delivering rectangular pulses with a duration of 1 millisecond, a frequency of 20 pulses per second, and an amplitude of 5–10 volts (Bradley et al., 1963; Hald et al., 1967).

The neurological diagnosis of the 8 patients in this series was as follows: multiple sclerosis, 3; stroke, 1; traumatic paraplegia, 1; cervical and lumbar myelopathy, 1; spina bifida, 1; no neurological lesion, 1—or: upper motor neuron, 6; lower motor neuron, 1; normal, 1.

At the operative insertion of the implant the rise in vesical pressure evoked by stimulation was found to be small (2–14 cm. water), whereas application of the stimulus several weeks later evoked a significantly larger rise in vesical pressure (25–60 cm. water).

Four of the 6 patients with upper motor neuron lesions had improved ability to void and 2 of these were restored to continence. The patient with the lower motor neuron lesion had a much improved ability to void and partial restoration of continence. The patient without neurological disease derived no benefit and this was probably related to an abnormal bladder-neck.

BRADLEY, W. E., CHOU, S. N., and FRENCE, L. A. (1963), *J. Neurosurg.*, **20**, 953.

HALD, T., MEIER, W., KHALILI, A., AGRAWAL, G., BENTON, J. G., and KANTROWITZ, A. (1967), *J. Urol.*, **97**, 73.

17. Evaluation of Prostatic Disease by Ultrasound: S. S. MILLER, A. D. CHRISTIE, and G. SMITH, Department of Surgery, University of Aberdeen.

Accurate assessment of prostatic size is of considerable value to the surgeon. With this information it is possible to determine the correct operation for any particular patient whether by open or endoscopic approach.

A new method of evaluation of prostatic enlargement is described, utilizing an ultrasonic scanning technique, which is simple and rapidly performed with no discomfort to the patient.

The benign prostate appears as a smooth, homogeneous structure, approximating to a sphere in outline. Serial transverse sections are taken at different levels to estimate the outline, the largest section is selected, and the volume is calculated from the measured radius.

Twelve patients with prostatic disease were studied using this technique and a comparison was made with clinical and radiographic methods of estimation of prostatic volume. This ultrasonic technique was shown to be superior and to give an extremely accurate estimate of prostatic size as measured at operation.

In the 2 malignant cases studied the prostate appeared as a non-homogeneous structure with an irregular outline. In the case of prostatic cancer ultrasound may prove to be of diagnostic value. It may also help in assessing the results of endocrine treatment.

18. Antibiotics, Postoperative Infection, and Deep-vein Thrombosis: A. N. Nicolaides, V. V. Kakkar, E. S. Field, and J. Spindler, King's College Hospital, London.

It has been suggested that infection may be an important factor in the aetiology of deep-vein thrombosis (D.V.T.), particularly by wall-deficient bacteria ('L' forms) which are often induced by antibiotics (penicillin) with an action against cell-wall formation (Altemeier et al., 1969).

The incidence of postoperative D.V.T. has been studied in 424 surgical patients, using the ^{125}I-fibrinogen test, and related to the administration of antibiotics and postoperative infection. In 310 patients who received no antibiotics and who had no evidence of postoperative infection the incidence of D.V.T. was 20·3 per cent. In 72 patients who were operated on under ampicillin cover the incidence was 32 per cent. This difference was significant ($P < 0{\cdot}02$). In 42 patients who developed postoperative infection and were treated with ampicillin the incidence was 54·7 per cent. This was also significant ($P < 0{\cdot}0001$) when compared with the control group. The higher incidence in this group of patients was due to an increase in the number of thrombi occurring between the third and eighth postoperative days.

The results show that patients who develop postoperative infection and those who receive prophylactic antibiotics have a high incidence of deep-vein thrombosis.

Altemeier, W. A., Hill, E. O., and Fuller, W. D. (1969), *Ann. Surg.*, **170**, 547.

19. The Effect of Treatment on Postural Blood-flow Changes in Limbs with Varicose Veins: G. Patrikios and O. Murphy (W. G. Fegan), Sir Patrick Dun's Hospital, Dublin.

Change of posture from horizontal to erect results in considerable reduction in blood-flow in the lower limbs. Femoral vein oxygen saturation during passive tilting has been used as an index of blood-flow changes in the lower limb. Seven normal volunteers and 7 patients with varicose veins were examined before and after treatment (compression sclerotherapy) (Fegan, 1963).

Measurements were made in the horizontal and 60° head-up position. All changes in blood-flow were expressed as a percentage of the average in the normal controls in the horizontal position (100 per cent; range 74–114 per cent). After tilting the mean flow in normal limbs was 59 per cent (range 49–72 per cent). In limbs with varicose veins before treatment the mean blood-flow in the horizontal position was 130 per cent (range 100–195 per cent) and after tilting 77 per cent (range 56–98 per cent). After treatment the blood-flow in these limbs was 144 per cent (range 120–195 per cent) in the horizontal position and 62 per cent (range 46–83 per cent) in the tilted position.

These findings indicate that blood-flow in limbs with varicose veins is higher than that in normal limbs in both the horizontal and tilted positions, and after treatment the flow in the horizontal position remains high while in the tilted position it is reduced to near-normal levels. It is postulated that one of the effects of treatment is to enhance the reflex reduction in blood-flow in the lower limb on assuming the upright position (Gaskell and Burton, 1963).

Fegan, W. G. (1963), *Lancet*, **2**, 109.
Gaskell, P., and Burton, A. C. (1963), *Circulation Res.*, **1**, 27.

20. A Study of Normal and Abnormal Femoral Venous Flow Velocity using a Directional Doppler: J. D. Lewis, J. T. Hobbs, and S. T. Yao, Surgical Unit, St. Mary's Hospital, and Wayne State University, Detroit.

As an aid to the differential diagnosis of the swollen limb, femoral venous flow velocity was monitored with a directional doppler (Parkes models 805 and 806) in 50 patients. Thirty-eight patients were diagnosed as having iliac vein occlusion; a 94 per cent correlation with radiology. During this investigation it became apparent that in normal subjects in the horizontal position the femoral venous signal shows a phasic change with respiration, rising on expiration and falling to a minimum on inspiration. This phenomenon has been described (Strandness et al., 1967; Sigel et al., 1968) but never presented before as being the reverse of that occurring in the subclavian vein.

Simultaneous recordings from the femoral and subclavian veins, monitoring respiratory movements with a strain gauge, were made with the patient on a tilt table. Regardless of posture the subclavian venous signal tended to remain in the same phase with respiration. The femoral signal, however, became reversed at about 45° (reversed Trendelenburg), falling to a minimum on expiration and increasing on inspiration. In the erect position at rest flow occurred only on deep inspiration. In trained subjects phasic change with respiration could be produced by altering the mode of respiration from thoracic to abdominal regardless of posture.

In incompetence in the upright position excessive back-flow may be demonstrated on quiet respiration alone and enhanced by a Valsalva manœuvre. The Trendelenburg position resulted in a continuous signal over the femoral vein. Following paralysis under anaesthesia a continuous signal also occurred which was interrupted by the inspiratory phase of positive-pressure ventilation.

Patient position is important in interpreting femoral venous signals, and variations of posture may improve diagnostic accuracy.

Sigel, B., Popky, G., Wagner, D., Boland, J., Mapp, J., and Feigle, P. (1968), *Surgery Gynec. Obstet.*, **127**, 339.
Strandness, D. E., Schultz, R. D., Summer, D. S., and Rushmer, R. F. (1967), *Am. J. Surg.*, **114**, 311.

21. A Comparison of Flow Patterns in the Long Saphenous Vein of Normal and Abnormal Subjects using an Atraumatic Technique: A. L. Kline and P. Byrne (W. G. Fegan), Sir Patrick Dun's Hospital, Dublin.

Flow patterns were studied in the long saphenous vein in asymptomatic patients with gross varicosity of the long saphenous vein, in patients with minimal varicose veins but gross signs and symptoms of calf pump dysfunction, and in control subjects.

All 20 patients with varices had valvular incompetence in the long saphenous system indicated by the presence of retrograde flow seen during deep breathing and the Valsalva manœuvre. This was not seen in normal people, indicating valvular competence.

Ambulatory subjects studied on a treadmill produced three reproducible and fundamentally different patterns.

Normal subjects produced an initial peak of forward flow as walking began and then no net flow during rhythmic walking or when walking stopped.

The first group of patients (no symptoms) showed a pattern of rapid turbulent retrograde flow during walking, and when walking stopped this increased in velocity and was prolonged for an average of 10 seconds (range 7–14 seconds). In the second group (with symptoms) there was less retrograde flow down the long saphenous vein while walking and when walking stopped the flow lasted an average of 2·5 seconds (range 1–4 seconds).

In patients with varicose veins retrograde flow down the long saphenous vein depends on the functional ability of the muscle pump to empty the superficial veins. The more efficient the pumps, the greater is the retrograde flow during and immediately after walking.

22. Soleal Veins and Stasis during Operation: A. N. Nicolaides, V. V. Kakkar, E. S. Field, and J. Spindler, King's College Hospital, London.

It has been demonstrated by using a venographic technique that there is considerable stasis in the soleal veins of conscious patients (Nicolaides et al., 1971b). However, this technique cannot be used during surgery.

A new technique has been developed to assess stasis during operation. Thirty ml. of sodium diatrizoate (45 per cent) mixed with 10 μc. of ^{125}I-fibrinogen were injected into a vein on the dorsum of the foot and directed into the tibial and soleal veins using pneumatic cuffs (Nicolaides et al., 1971a). The time taken by the contrast medium and the radioactive fibrinogen to disappear from the tibial and soleal veins of 8 conscious patients was determined simultaneously by intermittent fluoroscopy and scintillation counting. It has been shown that the clearance of the radioactive fibrinogen is an accurate method of assessing stasis without fluoroscopy.

This technique was used in another 8 patients just before and during operation. In these the mean clearance time of ^{125}I-fibrinogen in the tibial veins before and during operation was the same (1 minute). In the soleal veins it was 4·5 minutes before and 8·5 minutes during operation ($P < 0{\cdot}05$). These results indicate that stasis in the soleal veins is increased markedly during operation and may explain the high incidence of thrombi starting there.

Nicolaides, A. N., Kakkar, V. V., Field, E. S., and Renney, J. T. G. (1971a), *Br. J. Radiol.*, **44**, 653.

— — — — and Renney, J. T. G. (1971b), *Br. J. Surg.*, **58**, 307.

23. The Value of Cinephlebography in detecting Incompetent Venous Valves in the Post-phlebitic State: E. S. Field, V. V. Kakkar, G. Stephenson, and A. N. Nicolaides, King's College Hospital, London.

Ligation of incompetent perforators of the calf is not always successful in preventing recurrent varicose ulceration. Popliteal vein ligation (deTakats, 1951) and superficial femoral vein ligation (Linton, 1953) have been employed with similar results. The implication is that in any patient there might be more than one site of valvular incompetence leading to superficial venous hypertension.

Ascending functional cinephlebography and venous pressure measurement have been used in 42 limbs to examine calf perforators and deep-vein valvular function. In 27 normal or mildly post-phlebitic limbs 12 with incompetent perforators were found, and 4 limbs with incompetent popliteal valves and 5 with absent valves were also discovered. In 15 limbs with persistent ulcers or healed ulcers incompetent perforators were demonstrated in all 15 and non-functioning or absent popliteal valves in 14.

All patients with venous hypertension had incompetent perforators. In addition, the more severely afflicted had absent popliteal valves. Preoperative cinephlebography will distinguish these groups

Linton, R. R. (1953), *Ann. Surg.*, **138**, 415.

deTakats, G. (1951), *Surgery, St Louis*, **29**, 342.

24. The Effect of Pregnancy on Normal and Varicose Veins: Mary Fogarty and P. J. Byrne (W. G. Fegan), Sir Patrick Dun's Hospital, Dublin.

Increased venous distensibility in the calf has been reported during pregnancy (Goodrich and Wood, 1964) and also associated with varicose veins (Eiriksson and Dahn, 1968).

Four groups of patients were studied (15 patients in each): (1) non-pregnant without venous disease; (2) pregnant without venous disease; (3) non-pregnant with varicose veins; (4) and pregnant with varicose veins.

Using a water-filled plethysmograph, venous volume was measured at effective transmural pressures of 10, 20, and 40 mm. Hg., and elasticity of the vein was measured by recording the volume change on decreasing the effective transmural pressure from 40 to 20 mm. Hg.

It was found that pregnancy was associated with a 20 per cent increase in venous volume ($P < 0{\cdot}05$) in both the varicose and non-varicose groups. The two groups with varicose veins were similar and showed a wide range of elasticity, many falling in the normal range but most having increased elasticity. The pregnant patients without varicose veins had normal venous elasticity.

It is concluded that the increased venous distensibility during pregnancy is due to the increased blood-volume and that this, associated with varicose veins, is due to a weakness of the vein wall. Pregnancy does not increase the elasticity of the vein wall in normal patients or in those with varicose veins.

Goodrich, S. M., and Wood, J. E. (1964), *Am. J. Obstet. Gynec.*, **90**, 740.

Eiriksson, E., and Dahn, J. (1968), *Acta chir. scand.*, Suppl., **398**, 19.

25. The Detection of Incompetent Perforating Veins: J. Noble and A. A. Gunn (C. V. Ruckley), Edinburgh.

Methods advocated for the detection of incompetent perforating veins include clinical examination, thermography (Patil et al., 1970), and fluorescein injection (Chilvers and Thomas, 1970). This study aimed to determine the most effective method.

In a controlled series 44 legs were examined using standardized techniques. The legs were marked for each method by a different observer who was unaware of previous markings.

Each marked site was explored at operation and the results were recorded on standardized diagrams which were analysed on punch cards. Incompetent perforators were found at 135 of the 198 sites explored (66 per cent), there being 34 per cent false positives. Sixty-two per cent of the 135 perforators were demonstrated by thermography alone or together with another method; similarly 54 per cent were demonstrated by clinical examination, and 47 per cent by fluoroscopy. Although simple and free from adverse reactions fluoroscopy is only useful below the knee.

Diagnostic success rates were lower than in the series of Patil et al. (1970) or Chilvers and Thomas (1970). Conversely, our average yield of 3·1 incompetent perforators per leg at operation was much higher. Thus, claims as to diagnostic accuracy carry little weight since the true number of incompetent perforators remains unknown.

Chilvers, A. S., and Thomas, M. H. (1970), *Br. med. J.*, **2**, 577.

Patil, M. D., Williams, J. R., and Lloyd-Williams, K. (1970), *Ibid.*, **1**, 195.

26. An Insulin Infusion Test of Gastric Secretion: D. C. Carter, J. R. Kirkpatrick, and R. R. Dozois, Royal Infirmary, Edinburgh.

The conventional insulin test is a potentially dangerous procedure (Read and Docherty, 1970), and its interpretation is hindered by variations in the timing and magnitude of the peak acid response (Baron, 1970). A continuous infusion test has been developed to produce a steady-state acid secretion with minimum insulin administration.

Dose–response curves were constructed in 5 healthy subjects relating insulin dosage to acid output and concentration, fall in blood-glucose, and hypoglycaemic symptoms. Doses investigated ranged from 0·025 to 0·10 I.U. per kg. per hour. The highest secretory response compatible with minimal side-effects was achieved with a dose of 0·04 I.U. per kg. per hr.

The typical secretory response to this dose in 11 healthy subjects was a gradual fall in blood-glucose during the first 60 minutes of infusion to a level which remained constant for the remaining 120 minutes of the test (mean level 21·9 ± 9·43 mg. per cent). This hypoglycaemia was accompanied by a plateau of acid output attained within 90 minutes of commencing infusion.

It is concluded that the test is safe at the dose level described, is accompanied by minimal side-effects, and may be less difficult to interpret than conventional insulin tests. Its application to vagotomized subjects is being explored.

Baron, J. H. (1970), *Scand. J. Gastroent.*, **5**, suppl., 6, 9.
Read, R. C., and Docherty, J. E. (1970), *Am. J. Surg.*, **119**, 155.

27. Relationships between Serum Gastrin and Gastric Acid Secretion during Insulin Hypoglycaemia in Normal Subjects and in Patients with Duodenal Ulcer: D. J. Cowley, J. H. Baron, J. Hansky, and M. G. Korman, Royal Postgraduate Medical School, London, and Monash University, Melbourne.

Insulin hypoglycaemia produces an increase in serum gastrin levels, which is greater in patients with duodenal ulcer than in normal subjects (Hansky et al., 1971). The role of this released gastrin in stimulating gastric secretion was examined.

Serum gastrin was measured in normal subjects and n patients with duodenal ulcer at intervals after the njection of insulin, 0·2 U. per kg. i.v., with and without concomitant gastric aspiration, and also during intragastric neutralization with sodium bicarbonate. The radio-immunoassay of gastrin used antibodies to synthetic human gastrin I.

No significant relationship was found between peak serum gastrin and peak acid output after insulin. Serum gastrin was correlated inversely with blood-glucose. The timing of peak serum gastrin and lowest blood-glucose coincided, but peak acid output lagged behind, occurring n the period 15–30 minutes later. The rise of serum gastrin after insulin during gastric aspiration almost discriminated completely between patients with duodenal ulcer and normal subjects: discrimination was absolute when serum gastrin was measured during hypoglycaemia with simultaneous intragastric neutralization.

The results suggest that vagally released gastrin may prime parietal cells for direct cholinergic stimulation, hat there is an increased G-cell mass with or without an increased parietal cell mass in patients with duodenal ulcer, and that measurement of hypoglycaemia-stimulated serum gastrin during intragastric neutralization may prove a discriminating test for the duodenal ulcer diathesis.

Hansky, J., Korman, M. G., Cowley, D. J., and Baron, J. H. (1971), *Br. J. Surg.*, **58**, 863.

28. Gastric Acid Secretion and Changes in Blood-glucose after Insulin in another Healthy Man: D. J. Cowley and J. H. Baron, Royal Postgraduate Medical School, London.

The gastric acid response to insulin is not an 'all-or-none' phenomenon; it is dose-dependent (Baron, 1970). In one healthy man (Baron, 1970) insulin hypoglycaemia provided a quantitative glycopenic stimulus producing a quantitative vagal acid response, but such relationships were not found by others (Isenberg et al., 1969). Another healthy man has therefore been tested with eight doses of insulin, 0·003–0·4 U. per kg. In each test gastric secretion was collected in 15-minute periods for 1 hour before and 2 hours after the intravenous injection of insulin.

There was a correlation between peak acid output after insulin (P.A.O.$_I$) and log dose, with maximal secretion after 0·05 U. per kg. There was a similar, and parallel, linear correlation between the percentage decrease in blood-glucose and log dose of insulin. After doses greater than 0·05 U. per kg. blood-glucose decreased still further, but P.A.O.$_I$ also decreased. The best fit for correlation of P.A.O.$_I$ and lowest blood-glucose was a quadratic curve. In this man insulin-stimulated gastric acid increased as blood-glucose decreased to a blood-glucose level of 20 mg. per 100 ml., below which acid output was inhibited.

The results strongly support the postulated insulin hypoglycaemia/acid-output relationships (Baron, 1970). Although 0·2 U. per kg. may be an optimum dose of insulin no specific dose can be guaranteed to achieve that degree of hypoglycaemia (? 20–25 mg. per 100 ml.) which provides maximum vagally stimulated acid output.

Baron, J. H. (1970), *Gut*, **11**, 826.
Isenberg, J. L., Stening, F., Ward, S., and Grossman, M. I. (1969), *Gastroenterology*, **57**, 395.

29. The Effect of Propranolol on Acid and Pepsin Secretion in Cats: W. L. Bruckner and C. Muller-Rabe, University of Munich, Germany.

The role of the sympathetic nervous system in affecting gastric secretion has not been investigated as thoroughly as that of the parasympathetic nervous system. Literature on the sympathetic system, though controversial, shows antisecretory effects (Code, 1951).

Attempts were made to investigate further the nature of this adrenergic inhibition. A classic β-receptor-blocking agent was tested. Propranolol (Dociton) was injected in subcutaneous doses of 90 mg. per kg. The spontaneous and the histamine-induced gastric secretions were studied in 6 cats with gastric fistulas.

Propranolol reduced significantly the volume (24 per cent) and the pepsin output (60 per cent) of spontaneous gastric secretion, whereas the output of acid was increased markedly (150 per cent).

Propranolol increased the volume (25 per cent) and the output of acid (36 per cent) of histamine-induced secretion and reduced the output of pepsin (20 per cent).

On the basis of these experiments it appears that acid and pepsin secretions are related to different receptors.

Code, C. F. (1951) *Pharm. Rev., Lond.*, **3**, 59.

30. A Study of Pathways for the Co-ordination between Myoelectric Activities of the Antrum and Duodenum: B. S. Bedi and C. F. Code, Western Infirmary Glasgow, and the Mayo Clinic, Rochester, Minnesota.

There is good evidence of co-ordination between the motor activities of the gastric antrum and those of the duodenum (Thomas and Crider, 1935). The pathway of co-ordination between the antral and duodenal electric activities was investigated.

Myoelectric activities from the antrum and duodenum were recorded using chronically implanted silver–silver-chloride electrodes in fully conscious dogs. Recordings were made after the ingestion of a meat meal or the instillation of saline into the stomach. After a controlled study the gastroduodenal junction was transected and the continuity restored by anastomosis of either the mucosa alone (3 dogs) or the gastric and duodenal walls (3 dogs). A method of cross-correlation (Allen et al., 1964) was applied to the electric recordings obtained before and after the division of the gastroduodenal junction. A relationship between the antral pace-setter potentials and the occurrence of duodenal action potential was observed in the control studies. This relationship was lost after transection of the gastroduodenal junction. Gastric emptying time and radiological examination of these dogs showed no obstruction at the site of transection. The correlation between the myoelectric activities of the antrum and duodenum is accomplished by impulses transmitted via the neural elements in the wall of the gastroduodenal junction.

ALLEN, G. L., POOLE, E. W., and CODE, C. I. (1964), *Am. J. Physiol.*, **207**, 906.
THOMAS, J. E., and CRIDER, J. O. (1935), *Ibid.*, **111**, 124.

31. Histological Changes in the Enteric Plexuses following Truncal Vagotomy in Pigs:

A. J. B. MISSEN (G. W. Taylor), St. Bartholomew's Hospital, London.

In contrast to the physiological sequelae of truncal vagotomy the degenerative changes in the distal fibres of the vagus have been studied but little, and then mainly in small laboratory animals. The low mortality from vagotomy performed for duodenal ulceration in man makes it difficult to obtain material for examination. This paper reports the histological changes seen in the enteric plexuses following bilateral truncal vagotomy in pigs in the course of a liver-transplant programme.

The plexuses were examined by a modification of Schofield's silver-impregnation technique in specimens of stomach and small bowel taken from vagotomized pigs at intervals varying from 36 hours to 3 weeks after operation. Corresponding tissues from normal (donor) pigs were used as controls.

This study demonstrated that degenerative changes taking the form of axonal swellings and fragmentation of the terminal branches of efferent vagal fibres occurred throughout the myenteric and submucous plexuses of the stomach and small bowel. These changes were detectable 36 hours after vagotomy and persisted throughout the period of study. The changes were most marked in the small bowel, where the large number of vagal terminations demonstrated by the degenerative process implied a far greater degree of branching in vagal efferents than had been recognized previously.

32. Gall-bladder Size and Emptying after Truncal, Selective, and Highly Selective Vagotomy in Man:

G. PARKIN and D. JOHNSTON, Department of Surgery, University of Leeds.

After vagotomy the gall-bladder may dilate (Rudick and Hutchison, 1965), the bile-flow may decrease, and the bile may become more lithopenic in composition. Although truncal vagotomy (T.V.) is incriminated usually, the work of Tinker and Cox (1969) suggests that bilateral selective vagotomy (S.V.) may also denervate the gall-bladder.

The resting volume of the gall-bladder was measured by oral cholecystography, and its contraction in the 90 minutes after a normal meal was also determined (with barium to the time of entry into the duodenum) in 1 patients with duodenal ulcer before operation (D.U.) an in patients more than 1 year after T.V. + P. (pyloroplasty (13), S.V. + P. (4), and highly selective vagotomy withou a drainage procedure (H.S.V.) (10). The groups wer matched for sex, age, weight, maximal acid output, insuli negativity, and Visick status.

Mean resting volumes of the gall-bladder in ml. ± 1 S.E were: D.U., 27·6 ± 1·6; T.V. + P., 44·5 ± 4·7; S.V. + P. 41·2; H.S.V., 26·1 ± 2·0. After a meal the gall-bladde contracted by: D.U., 54 per cent; T.V., 79 per cent H.S.V., 52 per cent. The results confirm that the gall-bladder is significantly ($P < 0·2$) dilated after T.V. Afte H.S.V. it is normal. After S.V. the gall-bladder wa dilated in 3 out of 4 patients. The rate and degree o contraction after a meal were similar in all four groups

Highly selective vagotomy without drainage maintain normal biliary function.

RUDICK, J., and HUTCHISON, J. S. F. (1965), *Ann. Surg.* **162**, 234.
TINKER, J., and COX, A. G. (1969), *Br. J. Surg.*, **56**, 779

33. The Comparison of Gall-bladder Bile i patients with Gall-stones and in Patients wit Duodenal Ulcer before and after Vagotomy

D. C. SMITH, J. N. CROOK, R. A. MCALLISTER, an C. MACKAY, Western Infirmary, Glasgow.

Gall-stones are reported to occur more commonly i vagotomized patients (Fletcher and Clark, 1968). Gall-bladder bile was obtained from 9 patients with cholestero gall-stones and from 10 patients with duodenal ulcer b duodenal aspiration following cholecystokinin administration. Further specimens were obtained from the ulce patients 1 week after vagotomy and drainage. The completeness of vagotomy was confirmed by an insuli test. The concentrations of bile-salt, cholesterol, an phospholipid were estimated and the relative compositio of each sample was calculated and plotted on triangula co-ordinates (Admirand and Small, 1968).

The relative composition of bile-flow from both gall-stone and ulcer patients lay well within the zone o cholesterol solubility on the phase diagram, although th former lay closer to the limits of solubility. The relativ amount of cholesterol was significantly greater in bil from gall-stone patients compared with that from ulce patients. Vagotomy produced no significant alteration i the relative composition of gall-bladder bile in th immediate postoperative period. If vagotomy has lithogenic action it does not appear to be mediated b altering the relative composition of bile in the immediat postoperative period.

Patients	*Bile-salt* (per cent)	*Cholesterol* (per cent)	*Phospholipid* (per cent)
With gall-stones	69·4 ± 6·7	8·8 ± 3·1	21·8 ± 4·0
With duodenal ulcer			
Before operation	72·6 ± 6·2	4·9 ± 0·9	22·5 ± 5·9
After operation	75·0 ± 4·9	5·3 ± 1·3	19·7 ± 4·0

ADMIRAND, W. E., and SMALL, D. M. (1968), *J. clin. Invest.* **47**, 1043.
FLETCHER, D. M., and CLARK, C. G. (1968), *Br. J. Surg.* **55**, 895.

34. Trickle Perfusion for Organ Preservation

R. Y. CALNE, D. C. DUNN, R. GAJO-REVERO, E. J HADJIYANNAKIS, and A. J. ROBSON, Department o Surgery, University of Cambridge.

The two most successful methods of preserving canin kidneys are those described by Belzer et al. (1967) an Collins et al. (1969). The Collins system has the advantag of extreme simplicity. The main disadvantage is that t obtain the best results it is essential that there should b no warm ischaemic damage to the kidney.

The Belzer system allows a longer period of preservation at 10° C. with better initial function on transplantation after 24 hours and is successful with kidneys that have suffered ischaemic damage. The apparatus, however, is complicated, expensive, and difficult to transport.

A simple perfusion system is described here for hypothermic organ preservation in which the perfusate passes through the organ and is then discarded. This has permitted 24–26-hour preservation of canine kidneys and 11-hour preservation of a porcine liver, with immediate life-sustaining function of the preserved organs after transplantation. Analysis of the perfusate compared with the effluent permits the metabolism of the organ to be studied at low temperatures and appropriate adjustments can be made to improve the preservation.

BELZER, F. O., ASHBY, B. S., and DUNPHY, J. E. (1967), *Lancet*, **2**, 536.
COLLINS, G. M., BRAVO-SHUGARMAN, M., and TERASAKI, P. I. (1969), *Ibid.*, **2**, 1219.

35. Seventy-two-hour Preservation of Canine Kidneys: M. E. SNELL, W. I. HOPKINSON, and R. R. SHEPHERD (J. R. Kenyon), St. Mary's Hospital, London, and Vickers Research Establishment, Sunninghill.

Canine kidneys were stored for 72 hours in a Vickers THS/4 unit. The conditions of storage were hypothermia (5° C.), hyperbaric oxygen (4 A.T.A.), and pulsatile perfusion at a rate of 2 ml. per minute. The perfusate was recirculated and passed through a 25-μ filter. The perfusate was a modified Collins's solution (Collins et al., 1969) with magnesium sulphate omitted and dextran 40 and chlorpromazine added.

Immediately prior to nephrectomy phenoxybenzamine, 2·5 mg., was injected into the renal artery. The excised kidney was flushed with chilled perfusate and then stored under the conditions described. Perfusion was discontinued after 4 hours.

At the end of the period of storage the kidneys were reimplanted as autografts into the iliac fossa following a further injection of phenoxybenzamine, 2·5 mg., into the renal artery. Immediate contralateral nephrectomy was performed.

Six out of 7 dogs survived and in all survivors the blood-urea nitrogen and serum creatinine had returned to normal limits when they were killed.

COLLINS, G. M., BRAVO-SHUGARMAN, M., and TERASAKI, P. I. (1969), *Lancet*, **2**, 1219.

36. Experimental Preservation of Ischaemically Injured Kidneys by Ice Storage and Subsequent Perfusion: R. W. G. JOHNSON, MARILYN ANDERSON, R. M. R. TAYLOR, and JOHN SWINNEY, Department of Surgery, University of Newcastle upon Tyne.

Continuous perfusion is a better method for preserving kidneys damaged by warm ischaemia than is simple ice storage (Johnson et al., 1971). Facilities for continuous perfusion, however, are not always immediately available. It may therefore be necessary to store kidneys in ice for short periods until perfusion can be commenced.

A study was planned to evaluate the practicability of combining the two preservation methods.

Canine kidneys were subjected to 30 minutes' warm ischaemia and then stored in ice for up to 6 hours. After ice storage the kidneys were perfused continuously for 24 hours with oxygenated plasma-protein fraction at 6° C. Preserved kidneys were replaced as autografts and the contralateral kidneys were removed. Results were assessed by postoperative serum creatinine levels. Three kidneys out of 4 functioned immediately after 3 hours' ice storage and 21 hours' perfusion.

Eight kidneys were preserved for 6 hours in ice and then perfused for 18 hours. In 3 dogs immediate contralateral nephrectomy resulted in death. The other 5 kidneys functioned immediately.

Changes in perfusion pressure, kidney weight, and perfusate lactic dehydrogenase of the 4 failures were compared with the 8 successes. It was not possible to predict which kidneys would not function immediately. Histological examination suggested that 3 of the 4 failures would probably have survived if contralateral nephrectomy had been delayed.

Combined methods of storage are therefore possible, but with ischaemically injured kidneys the duration of simple ice storage is critical; when this period exceeds 6 hours return of function will be delayed.

JOHNSON, R. W. G., MORLEY, A., SWINNEY, J., and TAYLOR, R. M. R. (1971), *Br. J. Surg.*, **58**, 299.

37. Liver Storage: 12-hour Preservation of the Pig Liver: H. SPILG, ROSEMARY HICKMAN, C. J. UYS, S. J. SAUNDERS, and J. TERBLANCHE, Cape Town, South Africa.

A prerequisite for a clinical liver-transplantation programme is a successful method of storage. Dog livers cannot be preserved beyond 2–3 hours by simple methods, and complex techniques are infrequently successful beyond 10 hours.

In this study simple hypothermia using various preserving solutions and the role of hyperbaric oxygen to store pig livers were investigated. Success of storage was assessed by orthotopic transplantation. Four basic preserving solutions were tested for varying periods at different temperatures: (1) a balanced salt solution, (2) plasma, (3) plasma with cell-membrane-stabilizing drugs, and (4) a solution similar in cation composition to intracellular fluid.

Consistently successful results following 6–8 hours' storage were obtained in 10 pigs using solution 2 (plasma) at 8–12° C. Reduction of temperature to 2–5° C., or the use of solutions 1, 3, or 4, failed to extend preservation beyond this period.

When hyperbaric oxygen at 3 A.T.A. was combined with simple hypothermic immersion storage in a plasma-preserving solution at 2–5° C, storage was successfully extended to 12 hours in 5 pigs.

The results of liver storage achieved by these simple methods should have wider clinical application than the currently used complex techniques.

38. Pig-liver Perfusion: A Comparison of Function with Porcine or Human Blood, with and without Hypothermia: J. WINCH, J. KOLTHAMMER, R. HAGUE, and R. WILLIAMS (J. G. Murray), King's College Hospital, London.

Before using pig-liver perfusion to treat a patient in hepatic failure the liver is cleared of porcine blood by flushing the portal vein with a cooled, balanced, electrolyte solution. Cooling is said to be essential for protection against ischaemia.

We present the results of 36 4-hour perfusions of isolated pig livers divided into four groups. Groups A and B were cooled to 7° C. during flushing and were subsequently rewarmed to 38° C. before perfusion on circuit (Winch, 1971). This rewarming took 30 minutes. Groups C and D were flushed with the same solution at 38° C. and placed in the circuit already warmed to 38° C. Groups A and C were perfused with fresh porcine blood, and groups B and D with fresh human blood. The efficiency of liver function in the four groups was compared by measuring bile volume and the rate at which a loading dose of bromsulphthalein was excreted into bile. Intravascular coagulation was assessed using the ^{125}I-fibrinogen test (Winch et al., 1971).

There was no difference between the four groups in the extent of intravascular coagulation occurring, but biochemical function was better when the liver was perfused with porcine blood. However, livers perfused with either porcine or human blood were less efficient if they had been cooled and rewarmed than if they had not been cooled at all. Therefore hypothermia is not only unnecessary but is harmful in the preparation of a pig liver for extracorporeal perfusion.

Winch, J. (1971), *Br. med. J.*, **1**, 216.
— — Fleisher, R., Hague, R., Kolthammer, J., Bentley, P., Shilkin, K. B., and Williams R. (1971), *Br. J. Surg.*, **58**, 301.

39. Estimation of Tissue Compartments in the Isolated Perfused Canine Liver: R. J. Nicholls (H. D. Ritchie), The London Hospital.

Inulin space, total tissue water, the erythrocyte mass, and albumin 'space' were measured simultaneously in the perfused canine liver using ^{14}C-inulin, ^{3}H$_2$O, ^{51}Cr-red cells, and ^{131}I-albumin as tracers.

Twenty experiments were performed. Perfusion flow rate (0·6 ml. per g. per minute) and P.C.V. (40) were kept at a standard value in each experiment; perfusate albumin concentration was varied deliberately from 1·2 to 5·0 g. per cent.

'Spaces' from the ratio of tissue to plasma radioactivity were estimated and expressed as ml. per g. wet liver per cent.

A lymph fistula was established. Lymph ^{131}I-albumin activity was 87 ± 6 per cent plasma ^{131}I-albumin activity.

The inulin compartment rose by 16·5 per cent per hour during the second hour of perfusion when lymph ^{14}C and ^{3}H activity had equilibrated with plasma. At 1 hour after the addition of the isotopes the inulin compartment was 25 ± 4·4 per cent. Total tissue water (75·7 ± 8·3 per cent at 1 hour) remained unchanged over the same time whilst intracellular flnid volume showed a steady fall.

A linear regression was obtained when the inulin compartment at 1 hour was plotted against the lymph/plasma-albumin ratio ($r = 0·88$) and the lymph/plasma-albumin difference ($r = 0·85$).

Lymph-flow was related to inulin compartment size. There was no correlation between inulin compartment and plasma-albumin, plasma-globulin, or portal pressure.

The technique provides a method of studying tissue compartments under dynamic conditions in isolated viscera.

40. In vivo Radio-isotope Assessment of Liver Regeneration in the Rat: S. J. Karran, K. G. Leach, and L. H. Blumgart, Department of Surgery, Cardiff.

Extensive liver resection is possible because the remnant will regenerate. This paper reports an investigation of the uptake of technetium sulphur colloid (T.S.C.) and selenomethionine (S.M.) by normal and regenerating liver, and scintiscanning to assess liver weight in the rat.

Scintiscans of the liver were obtained in 32 animals using the gamma-camera with a pin-hole collimator. In 17 of these, S.M. scans were less well defined than T.S.C. scans and were distorted by uptake in other organs. Despite concentration by different cellular systems (Croft, 1969) there was no difference in the areas of post-mortem liver scans ($P = 0·95$) nor in the distribution of these compounds.

Twenty-one sets of T.S.C. scans were obtained from 4 minutes to 44 days after partial hepatectomy. The mean lateral area (A_L) was compared with liver weight (W) ($r = 0·95$). The linear regression equation was $W = 0·026A_L - 0·48$.

In addition 2 animals were scanned sequentially up to 99 days after hepatectomy.

In no animal did liver weight increase after the tenth postoperative day, other than that accounted for by normal growth.

The technique offers an *in vivo* method of assessing liver regeneration in the rat and supports the recent use of T.S.C. scans in assessing liver size after partial hepatectomy in man (Blumgart et al., 1971).

Blumgart, L. H., Leach, K. G., and Karran, S. J. (1971), *Gut*, **12**, 922.
Croft, D. N. (1969), in *Diagnostic Uses of Radioisotopes in Medicine*. London: Hospital Medical Publications.

41. Effect of Truncal (T.V.), Selective (S.V.), and Highly Selective Vagotomy (H.S.V.) in Man on Gastric Emptying of Food and Barium: A. R. Wilkinson and D. Johnston, Department of Surgery, University of Leeds.

The crucial questions after H.S.V. (Johnston and Wilkinson, 1970) concern gastric emptying and recurrent ulceration. To provide objective evidence about the first question the pattern of gastric emptying of a semi-solid meal of food and barium was studied by serial radiographs taken from 15 to 150 minutes after eating. Between radiographs the patients sat or walked about. Three criteria of gastric emptying were used: (1) when it started, (2) when it finished (stomach empty), and (3) when the head of the meal reached the caecum. Eleven pre-operative patients with duodenal ulcer and patients more than 1 year after T.V. + P. (pyloroplasty) (12), S.V. + P. (10), and H.S.V. (14) were studied.

Gastric emptying had started by 15 minutes in 63 per cent of D.U.s, in 100 per cent of T.V. + P.s, in 100 per cent of S.V. + P.s, and in 78 per cent of H.S.V.s. Emptying was complete by 90 minutes in 0 per cent of D.U.s, in 75 per cent of T.V. + P.s, in 60 per cent of S.V. + P.s, and in 14 per cent of H.S.V.s, and by 150 minutes in 54 per cent of D.U.s, in 92 per cent of T.V. + P.s, in 80 per cent of S.V. + P.s, and in 50 per cent of H.S.V.s. The head of the meal had reached the caecum by 45 minutes in 0 per cent of D.U.s, in 58 per cent of T.V. + P.s, in 50 per cent of S.V. + P.s, and in 14 per cent of H.S.V.s.

Gastric emptying after truncal and selective vagotomy, with pyloroplasty, is significantly ($P < 0·02$) faster than before operation. After H.S.V. gastric emptying is almost normal.

Johnston, D., and Wilkinson, A. R. (1970), *Br. J. Surg.*, **57**, 289.

42. Inhibitory Function of Gastric Antral, Hepatic, and Coeliac Fibres in Man: R. B. Smith, C. S. Humphrey, P. J. Lyndon, and D. Johnston, Department of Surgery, University of Leeds.

The gastric antral, hepatic, and coeliac branches of the vagus inhibit gastric secretion in the dog (Hart, 1968; Griffith, 1969). We wished to find out if they also did so in man. They are sacrificed in truncal vagotomy (T.V.) but preserved in highly selective vagotomy (H.S.V.).

Five groups of subjects were studied: 8 normal patients (N.), 6 preoperative patients with duodenal ulcer (D.U.), and patients more than 1 year after T.V. + P. (pyloroplasty) (29), selective, S.V. + P. (9), or H.S.V. (23). Each subject underwent two intramuscular injections of pentagastrin (P.G.T.) on separate days. One test was preceded by the intravenous administration of insulin, 0·2 U per kg., 2 hours earlier to stimulate vagal activity. The tests were done in random order. The insulin tests were positive in 60 per cent of the T.V. + P., S.V. + P., and H.S.V. patients.

Mean peak acid outputs ± 1 S.E. in mEq./hour, the first figure referring to P.G.T. alone, the second to P.G.T. after insulin, were: N., 33·3 ± 2·0 and 41·1 ± 2·9 ($P < 0·001$, potentiation 29·7 per cent); D.U., 41·6 ± 1·8 and 47·5 ± 2·9 ($P < 0·05$, potentiation 12·9 per cent); T.V. + P., 23·9 ± 2·31 and 24·2 ± 2·6 (not significant increase, 9·1 per cent); S.V. + P., 31·8 ± 6·9 and 33·2 ± 7·2 (not significant increase, 6 per cent); H.S.V., 19·8 ± 2·1 and 16·7 ± 1·6 ($P < 0·05$, inhibition 15·9 per cent).

The acid outputs in the three consecutive 5-minute periods (2–4) with P.G.T. after insulin, expressed as a percentage of the same period with P.G.T. alone, were: N., 193·8 ± 34·2 per cent; D.U., 129·3 ± 10·4 per cent; T.V. + P., 155·9 ± 53·2 per cent; S.V. + P., 106·24 ± 8·94 per cent; and H.S.V., 76·5 ± 11·4 per cent (inhibition).

Background vagal activity therefore led to a significant potentiation of the pentagastrin response in normal subjects and in patients with duodenal ulcer. In patients after H.S.V. insulin inhibited the pentagastrin response significantly.

This is the first evidence that the vagal fibres preserved in H.S.V. inhibit gastric secretion in man.

GRIFFITH, C. A. (1969), *Am. J. Surg.*, **118**, 251.
HART, W. (1968), *Arch. Klin. Chir.* **322**, 703.

43. The Effect of Vagotomy on the Inhibition of Gastric Secretion by Intraduodenal Fat: A. S. WARD (G. Slaney), Birmingham.

Fat in the duodenum inhibits gastric secretion in man. Johnston and Duthie (1969) suggested that inhibition by fat is dependent on a vagal reflex despite considerable animal evidence to the contrary. A study was undertaken to reassess the effect of intraduodenal fat on gastric secretion before and after total vagotomy.

Six patients with duodenal ulcer were tested before operation and a further 6 patients were tested 1 year after complete truncal vagotomy (proved by Hollander test). Two additional patients were examined both before and after operation. A suction tube was placed in the stomach and a perfusion tube in the distal duodenum. Gastric secretion was stimulated by an intravenous infusion of pentagastrin (6 μg. per kg. per hour), and after a secretory plateau had been reached 20 ml of Prosparol were instilled into the duodenum over 5 minutes. Gastric collection was then continued for a further hour.

Marked inhibition of gastric secretion occurred in all patients following duodenal infusion. The response was similar both before and after vagotomy. These results suggest that inhibition of gastric secretion by intraduodenal fat is mediated by a non-vagal mechanism in man as well as in animals. From this point of view there is little advantage in preserving the nerve-supply to the duodenum at vagotomy.

JOHNSTON, D., and DUTHIE, H. L. (1969), *Scand. J. Gastroent.*, **4**, 561.

44. The Correlation between the Rate of Gastric Emptying and Dumping and Diarrhoea after Truncal, Selective, and Highly Selective Vagotomy: C. S. HUMPHREY, A. R. WILKINSON, and D. JOHNSTON, Department of Surgery, University of Leeds.

A fluid test meal of hypertonic glucose (300 ml. 25 per cent) was used to investigate the relationship between gastric emptying and the side-effects of dumping and diarrhoea after truncal and selective vagotomy with pyloroplasty (T.V. + P., S.V. + P.) and highly selective vagotomy without drainage (H.S.V.). Phenol red was used as marker.

In the first 20 minutes 46 ± 8 per cent of the meal emptied in preoperative patients with duodenal ulcer, compared with 79 ± 6 per cent after T.V. + P., 62 ± 9 per cent after S.V. + P., and 52 ± 9 per cent after H.S.V. ($n = 12, \times 4$). T.V. + P. accelerated emptying significantly ($P < 0·02$), while H.S.V. and S.V. + P. did not.

After the meal, dumping and diarrhoea occurred significantly less frequently after H.S.V. than after T.V. + P. and S.V. + P.—dumping: 73 per cent of 15 T.V. + P.s, 80 per cent of 15 S.V. + P.s, and 47 per cent of 15 H.S.V.s ($P < 0·05$); diarrhoea: 66 per cent T.V. + P., 60 per cent S.V. + P., and 13 per cent H.S.V. ($P < 0·01$).

A significant correlation ($R = 0·84$, $P < 0·01$) was found between the rate of rise of blood-glucose concentration (mg. per cent per minute) and the proportion of the test meal emptied in 20 minutes. In the first 20 minutes the rate of rise of blood-glucose was 2·2 ± 0·2 in 15 D.U.s, 4·5 ± 0·4 in 15 T.V. + P.s, 3·7 ± 0·3 in 15 S.V. + P.s, and 3·0 ± 0·4 in 15 H.S.V.s.

A clinical study showed that 1 year after operation there was significantly less dumping ($P < 0·05$) and diarrhoea ($P < 0·01$) after H.S.V. than after T.V. + P. and S.V. + P.

The stomach is continent and emptying is still controlled after H.S.V.

45. The Gastro-oesophageal Junction in Duodenal Ulcer after Operation: P. THOMAS and R. EARLAM, The London Hospital.

Thirty-seven patients with duodenal ulcer were studied with oesophageal manometry preoperatively and then between 6 and 12 months later. Twenty-eight had vagotomy and either a pyloroplasty or gastro-enterostomy performed. Nine had a Polya partial gastrectomy with or without a vagotomy. Using non-perfused water-filled open tips (internal diameter 1·12 mm.) the mean maximum pressure above intragastric (barrier) was 9·8 ± 6·4 cm. H_2O, and the zone of elevated pressure (Z.E.P.) was 4·4 ± 1·1 cm. long. These are similar values to those obtained in a previous study on 70 patients with duodenal ulcer (Earlam, 1971). The barrier was unchanged following vagotomy and drainage but was reduced significantly after partial gastrectomy (3·2 ± 2·5 cm. H_2O, $P < 0·05$). Z.E.P. was shortened in both groups (3·5 ± 1·0 cm. and 2·9 ± 0·8 cm., $P < 0·05$). These parameters were also significantly different when measured by balloon. The mean intragastric pressure (open tip only) was increased in both groups postoperatively from 17·9 ± 5·0 to 22·6 ± 4·7 cm. H_2O ($P < 0·05$).

These manometric findings suggest that the gastro-oesophageal sphincter is not impaired following vagotomy and drainage operations. By these techniques there is no increased incidence of hiatal hernia following either type of operation. The low pressures following a partial gastrectomy may be due to removal of the antrum which produces gastrin which is known to increase the sphincteric pressure.

EARLAM, R. J. (1971), *Br. J. Surg.*, **58**, 296.

46. Ischaemia as a Factor in the Aetiology of Stress Ulceration: J. E. L. SALES (G. W. Taylor), University of Colorado Medical Centre, Denver, U.S.A., and St. Bartholomew's Hospital, London.

Stress ulceration of the gastroduodenal mucosa is a recognized complication of trauma and haemorrhage. The reasons for the development of the ulceration are obscure but mucosal ischaemia due to alterations in splanchnic blood-flow has been suggested. This paper defines the relationship of ulceration to the distribution of blood-flow in the stomach wall.

Fifteen 10-kg. piglets were bled to a systolic blood-pressure of 40 mm. Hg by 40 per cent haemorrhage. Five animals were killed immediately, 5 after 2 hours' hypotension, and a further 5 after 2 hours' hypotension and retransfusion.

Blood-flow was measured by two series of 25-μ diameter microspheres labelled with either ^{141}Ce or ^{51}Cr. The excised stomach was divided into 1-cm. squares and assayed for isotope activity. Gastric blood-flow (G.B.F.) and flow per g. were calculated. Cardiac output and sphere measurement in the gastric venous blood were also quantitated.

G.B.F. decreased linearly with 40 per cent haemorrhage. There was no evidence of arteriovenous shunting. After 2 hours of shock G.B.F., previously evenly distributed, became uneven. Acute ulceration occurred at disproportionately ischaemic sites. Retransfusion restored an even distribution of flow. Areas of disproportionate ischaemia of the gastric mucosa follow prolonged post-haemorrhagic hypotension. Acute ulceration occurs principally at these sites.

47. Exocrine Secretory Responses of the Pancreas to Pentagastrin and to a Standard Meal in Dogs:

SAROJ GUPTA and J. B. ELDER (I. E. Gillespie), Department of Surgery, University of Manchester.

It is well established that pentagastrin stimulates the exocrine secretion of the pancreas and that doses maximal for acid are also maximal for pancreatic secretion (Emas et al., 1968). Little is known of the relationship between the response to pentagastrin and food-stimulated pancreatic secretion.

In 4 dogs with chronic pancreatic and gastric fistulae (G.F.) (Preshaw and Grossman, 1965) the following were studied: (1) acid dose–response curves to intravenous pentagastrin with the G.F. open; (2) protein and bicarbonated outputs from the pancreas over a 4-hour period to pentagastrin as a dose maximal for acid secretion in each animal with the G.F. both open and closed; and (3) the exocrine response of the pancreas to a standard 400-g. meat meal.

In response to pentagastrin, with the G.F. closed, the total 4-hour bicarbonate output ($21{\cdot}57 \pm 1{\cdot}87$ mEq.) was significantly greater than that with the G.F. open ($2{\cdot}42 \pm 0{\cdot}77$ mEq.; $P < 0{\cdot}001$), and not significantly different from that observed in response to a standard meat meal ($20{\cdot}6 \pm 3{\cdot}2$ mEq.; $P < 0{\cdot}4$).

Total 4-hour protein output to pentagastrin with the G.F. closed (2305 ± 250 mg.) was significantly greater than that with the G.F. open (1291 ± 258 mg.; $P < 0{\cdot}005$), and not significantly greater than that to a standard meal (1883 ± 222 mg.; $P < 0{\cdot}2$).

These results suggest that the exocrine response of the pancreas to food can be reproduced by pentagastrin infusion alone.

EMAS, S., BILLINGS, A., and GROSSMAN, M. I. (1968), *Scand. J. Gastroent.*, **3**, 234.

PRESHAW, R. M., and GROSSMAN, M. I. (1965), *Gastroenterology*, **48**, 36.

48. Bile-acid Absorption by Jejunum and Colon after Ileal Resection in the Rat:

P. M. PERRY, JUNE WHITE, and R. H. DOWLING (G. W. Taylor), Royal Postgraduate Medical School and St. Bartholomew's Hospital, London.

Although ileal resection causes bile-salt (B.S.) malabsorption, post-ile-ectomy jejunal B.S. concentrations are often normal. This could be due to increased hepatic B.S. synthesis and/or non-ileal B.S. reabsorption. Since the ability of the liver to increase B.S. synthesis is limited (Dowling et al., 1970) B.S. absorption in the ile-ectomized rat was studied in order to quantify jejunal and colonic contributions to the B.S. enterohepatic circulation and to look for any compensatory increase in B.S. absorption following resection.

B.S. absorption was measured using an *in vivo* recirculation perfusion system in bile-fistula ile-ectomized and sham-operated control rats. ^{14}C-cholate (5 mg., 0·1 μc. per rate) and taurocholate absorption were measured both by the fall in luminal B.S. concentration and by cumulative isotope excretion in the bile. Absorption of water and glucose, and net Na^+, K^+, and Cl^- movement were measured simultaneously.

Our results show that, per unit length, jejunal B.S. absorption was twice as efficient as that of the colon which did not compensate for the loss of the ileum in B.S., glucose, water, or electrolyte absorption. Jejunal cholate absorption increased significantly after resection (68 ± 15 μg. per cm. intestine per 3 hours) compared with the controls (50 ± 17 μg.; $t = 2{\cdot}85$, $P < 0{\cdot}02$). Significant increases were also found for glucose, water, and electrolyte absorption in the jejunal remnant after ile-ectomy.

It is concluded that the jejunum is more important than the colon both in normal B.S. absorption and in adaptive ability to increase absorption after ileal resection.

DOWLING, R. H., MACK, E., and SMALL, D. M. (1970), *J. clin. Invest.*, **49**, 232.

49. Hepatitis in a Renal Transplant Unit:

D. R. THOMAS, W. BOGIE, J. D. BLAINEY, B. H. B. ROBINSON, P. DAWSON-EDWARDS, and A. D. BARNES, Queen Elizabeth Hospital, Birmingham.

Hepatitis is a serious disease in dialysis and transplantation units and has resulted in morbidity and mortality of patients and staff. Since the discovery of hepatitis-associated antigen (H.A.A. or Australia antigen) it has been possible to study the disease more fully. This paper describes the incidence of clinical liver disease among the patients and staff of a renal unit. H.A.A. screening was introduced 4 years after 1 dialysis patient developed clinical hepatitis. This uncovered a high incidence of 'subclinical carriers' of H.A.A. who appeared to be infecting other patients, their relatives, and the staff of the unit. Retrospective analysis at that time showed that the H.A.A.-positive patients had never been jaundiced but had usually shown a raised transaminase between 3 and 6 months after starting dialysis. Prospectively, about 60 per cent of the new patients were becoming H.A.A.-positive between 3 and 6 months after starting dialysis.

Although none of the staff and relatives had died from hepatitis it was decided to try to rid the unit of infection. The majority of patients dialysed in the unit were selected as unsuitable for home dialysis for social or other reasons.

Therefore, the patients were submitted to cadaveric renal transplantation at the earliest opportunity. Six patients who were H.A.A.-positive and 6 patients who were also dialysed within the unit and who may have been infected were transplanted with 13 kidneys between June, 1970, and January, 1971, with the best-matched kidneys available. None of the patients is now on dialysis or attending the hospital; 5 have renal transplants that are functioning satisfactorily at 16–20 months, 2 patients died from uncontrollable rejection, 4 patients died from infection, and 1 died from a subarachnoid haemorrhage.

As a result of this policy there have been no new cases of hepatitis or H.A.A.-positive patients in the unit for the past 10 months and no cases among the staff or relatives of the patients.

50. Donor Kidney Selection for Transplantation—Relationships between Glomerular Structure, Vascular Supply, and Age:

M. SWORN and M. FOX, University of Sheffield.

Kidneys from 50 consecutive post-mortems were examined macroscopically and histologically to assess and to compare glomerular appearance, vascular changes, and renal artery circumference. Correlation was also made with previous history of hypertension. The aim of the investigation was to determine the age beyond which persons without obvious parenchymal disease should best not be considered as kidney donors. Out of the 100 kidneys examined, 82 were used for the study; 18 were excluded because of renal parenchymal disease. Glomeruli were graded as normal, obsolescent, and intermediate.

Significant correlations between age, renal artery circumference, and the percentage of completely normal glomeruli were found. The percentage agreements and selection proportions were determined by comparing the percentage of normal glomeruli cut-off points with 10-year period age steps. If greater than 60 per cent completely normal glomeruli and less than 80 years were taken as cut-off points, the percentage agreement was 90 per cent. If, however, 90 per cent or more completely normal glomeruli were required the percentage of such kidneys varied from 67 per cent at less than 50 years of age to 8 per cent for kidneys from subjects older than 70 years. There was no significant difference between the percentage of normal glomeruli in patients with previous diastolic blood-pressure above or below 100 mm. Hg in the range examined.

51. **Survival of Canine Renal Allografts after Antilymphocytic Serum and Bone-marrow Treatment:** D. T. CARIDIS, A. LIEOGEOIS, I. BARRETT, B. W. LYTLE, and A. P. MONACO, Harvard and Aberdeen.

The principle of augmenting antilymphocytic serum-induced suppression of allograft immunity by infusion of specific donor bone-marrow cells was studied.

Adult dogs received rabbit anti-dog lymphocytic serum (R.A.D.L.S.) in doses of 1 ml. per kg. or 2 ml. per kg. from days -7 to $+7$ relative to bilateral nephrectomy and renal allotransplantation from unmatched non-litter-mate mongrel donors. Half of each group of R.A.D.L.S.-treated animals received intravenous donor bone-marrow ($2–4 \times 10^8$ nucleated cells per kg.) on day $+10$.

The mean survival time for the untreated controls was 10 days. In the 1 ml. per kg.-R.A.D.L.S. group bone-marrow-infused dogs survived for 14–33 days and the non-infused dogs survived for 14–24 days. In the 2 ml. per kg.-R.A.D.L.S. group non-infused dogs survived for 14–31 days while the bone-marrow-treated dogs showed a significant prolongation of survival (20–78 days). No overt graft-versus-host reaction was observed clinically.

It is possible that the results are caused by increased antigenic challenge (bone-marrow infusion) producing transient host-versus-graft activity which may in turn lead to the establishment of an enhancement phenomenon resulting in augmented survival.

52. **The Use of Radioactive Fibrinogen for detecting Rejection of Human Renal Transplant:** E. D. YEBOAH, R. SHACKMAN, and G. D. CHISHOLM, Royal Postgraduate Medical School, London.

The use of ^{125}I-labelled human fibrinogen in the detection of kidney transplant rejection has been reported (Salaman, 1970). The present study concerns 33 patients after kidney transplantation.

Radioactive ^{125}I-labelled human fibrinogen was given and the radioactivity of the transplant measured with an external scintillation counter. In 7 patients with no clinical or biochemical evidence of rejection there was no increase in radioactivity. In 14 patients with clinical and biochemical evidence of acute rejection there was an increased transplant radioactivity; in 3 of these the increased radioactivity preceded clinical evidence of rejection.

False positives were observed in cases with extravasation of urine, perirenal haematoma, and malacoplakia, and during arvin therapy.

The method is a useful aid for the early diagnosis of acute rejection but false positives may be found. It is not useful in cases of chronic rejection.

SALAMAN, J. R. (1970), *Br. med. J.*, **2**, 517.

53. **A Study of Renal Allograft Rejection in the Rat using ^{125}I-fibrinogen:** J. R. SALAMAN, Cardiff.

^{125}I-fibrinogen localizes in human renal transplants during periods of rejection (Salaman, 1970). Experiments were carried out in rats and the phenomenon was studied more closely and possible sources of error were defined.

Kidneys were transplanted from AGUS- to PVG/C-strain rats as rejection occurs rapidly with this combination (8·7 days). The recipient's left kidney was retained as a control, and after 3 days ^{125}I-labelled rat fibrinogen was injected intravenously. The kidneys were excised on the seventh day and their radioactivities were compared. Isografted rats and rats with renal ischaemia, ureteric obstruction, and renal vein thrombosis were also studied.

Renal Allografts (10 rats): The renal allografts took up radioactivity and by 7 days were up to three times more radioactive than the control kidneys.

Renal Isografts (10 rats): No differences were observed between the normal and the grafted kidneys.

Renal Ischaemia (10 rats): The kidneys were rendered ischaemic for 40 minutes and were no more radioactive than the controls.

Ureteric Obstruction (11 rats): The radioactivity of the hydronephrotic kidney was not significantly increased.

Renal Vein Thrombosis (8 rats): The thrombosed kidneys became highly radioactive after ligation of the renal vein.

^{125}I-fibrinogen is deposited in rejecting kidney transplants. Renal vein thrombosis may give similar results and this should be recognized when using ^{125}I-fibrinogen as a test for rejection.

SALAMAN, J. R. (1970), *Br. med. J.*, **2**, 201.

54. **An in vivo Antilymphocytic Serum (ALS) Efficacy Test:** A. A. VAN DEN BROEK and CH. R. H. WILDEVUUR, Groningen, Holland.

Although ALS is widely used to prevent or suppress graft rejection there is no general agreement as to its efficacy. This efficacy is tested mainly by its ability to modify graft rejection, which can be influenced by various other factors such as different degrees of histocompatibility (Keuning and van den Broek, 1968).

As ALS primarily interferes with thymus-derived lymphocytes, ALS treatment in thymectomized dogs should give complete depletion of lymphocytes in the thymus-dependent areas of lymph-nodes.

Experiments were performed to test the efficacy of samples of ALS in thymectomized dogs treated with a prescribed effective ALS dosage. Immunosuppression was tested by means of skin-grafting. The histology of the lymph-nodes was studied after the last ALS injection.

Samples of ALS giving complete depletion in the thymus-dependent areas of lymph-nodes correlated with prolongation of skin-graft survival up to 30 days. Samples of ALS giving incomplete depletion of the thymus-dependent areas correlated with unmodified graft rejection in 10–20 days.

It was concluded that the histology of lymph-nodes in thymectomized dogs after ALS treatment is a reliable *in vivo* test for the immunosuppressive potency of the ALS used.

KEUNING, F. J., and VAN DEN BROEK, A. A. (1968), *Exp. Hem.*, **17**, 4.

55. Human Tumour Xenografts: J. E. Castro and D. N. H. Hamilton, Clinical Research Centre, Harrow.

As a model for the investigation of human tumours, *in vivo* maintenance in xenogeneic hosts allows study of tumour growth in a near-normal environment and it allows the toxicity of therapeutic agents to be assessed without the disadvantages of excessive stromal overgrowth or infection as may occur *in vitro*.

Samples of different types of human tumours obtained at operation were implanted into CBA mice which had undergone adult thymectomy, lethal irradiation (900–1000 r), and reconstitution with syngeneic bone-marrow (Davies et al., 1969). Tumour fragments were implanted beneath the kidney capsule or subcutaneously and they were examined histologically.

Two weeks after implantation 60 per cent of the tumours were viable and results showed certain tumours, particularly colonic ones, to be easier to grow. Some tumours were maintained for 2 months or more but none metastasized.

Histological examination of viable grafts showed good correlation with the original cytology and there were typical appearances in dead specimens of a sparse cellular infiltrate and fibrosis.

Davies, A. J. S., Carter, R. L., Leuchars, E, and Wallis, V. (1969), *Immunology*, **17**, 111.

56. A Histological Technique for assaying the Efficacy of Methods designed to reduce Allograft Rejection: P. A. Hamilton Stewart and J. Swinney, Postgraduate School of Studies, Bradford, and Department of Surgery, University of Newcastle upon Tyne.

Rejection of allografts is associated with a marked lymphocytic infiltration. The effect of immunosuppression on lymphocytic infiltrate was studied in rats.

A disk, 3 × 1 mm., was taken from the decapsulated donor kidney with a skin-biopsy punch.

Incision and elevation of the recipient renal capsule allowed the slice to be placed with its decapsulated surface in contact with the anterior surface of the renal cortex of the recipient.

Microscopy of 10-day autografts and isografts showed the tubules of the graft touching those of the recipient kidney but with negligible evidence of cellular infiltration.

In contrast, allografts transplanted under controlled immunogenic conditions across a strong histocompatibility barrier displayed a marked band of lymphocytes and a few plasma cells with some fibroblasts in the junctional zone of the graft.

Using an eye-piece graticule 'blind' lymphocyte counting was performed in the same five junctional areas in each of 100 grafts.

No difference was detected between autografts and isografts ($P = 0{\cdot}3$).

A highly significant difference was observed between autografts and allografts ($P < 0{\cdot}001$) and between azathioprine- and prednisolone-treated allografts compared with controls ($P < 0{\cdot}001$).

If lymphocytic infiltration is a measure of host immunological reaction, then this is a sensitive method for the evaluation of immunosuppressive drugs and differences in genotype.

57. A New Atraumatic Isotope-labelling Technique for the Assessment of Digital Cutaneous Blood-flow: M. J. Fox and J. C. Milliken (W. G. Fegan), Department of Vascular Surgery, Sir Patrick Dun's Hospital, Dublin.

A technique has been devised in which digits of the hands or feet may be selectively, uniformly, and atraumatically labelled in a specially designed inexpensive irradiation chamber with ^{133}Xe gas. A direct estimate of the local cutaneous blood-flow can be made from the observed clearance curves (Sejrsen, 1968).

In order to demonstrate the flow-dependence of the clearance curves 10 normal volunteers were subjected to tourniquet tests during the initial clearance period. Clearance virtually ceased when the circulation was arrested and release of the tourniquet was followed by enhanced clearance due to resultant reactive hyperaemia.

Fingers of 5 normal volunteers were investigated at weekly intervals for 4 weeks. There was a close correlation between clearance half-times in individual subjects. The toes of 5 normal volunteers were examined similarly with consistent results.

Four patients with primary Raynaud's disease and 10 patients with peripheral atherosclerosis were examined. In each case there was an increased clearance half-time value compared with that in normal subjects. One patient with erythrocyanosis frigida was assessed before and after lumbar sympathectomy. A 50 per cent reduction in half-time was observed postoperatively.

This technique has the advantage of being simple, non-intrusive, safe for both the patient and the examiner, and readily reproducible.

Sejrsen, P. J. (1968), *Appl. Physiol.*, **24**, 570.

58. Raynaud's Disease and Cooling of the Fingers: I. A. Miller and D. N. Walder, Department of Surgery, University of Newcastle upon Tyne.

It is generally believed that following cooling of the fingers arteriovenous anastomoses in the terminal pulp and nail-bed dilate and the subsequent increase in blood-flow results in a rise of pulp temperature (Lewis, 1930); simultaneously the capillary flow at the base of the finger nail is reduced (Grant and Bland, 1931).

It seemed possible that the symptoms of Raynaud's disease might be due to a disturbance of this mechanism. In order to test this hypothesis estimations of (1) total finger blood-flow by venous occlusion plethysmography, (2) capillary blood-flow by a radio-isotope clearance technique, and (3) finger-tip temperature by a thermocouple were made before and after cooling of a digit in 8 normal subjects and in 10 patients with Raynaud's disease.

In the normal subjects there was no significant difference between the total finger blood-flow (15·91 ± 7·039 ml. per 100 g. per minute) and the capillary blood-flow (17·6 ± 11·09 ml. per 100 g. per minute) ($P > 0{\cdot}2$) before cooling, thus suggesting that the arteriovenous anastomoses were closed. After cooling the finger there was a highly significant difference between the total finger blood-flow (26·28 ± 9·467 ml. per 100 g. per minute) and the capillary flow (8·77 ± 8·105 ml. per 100 g. per minute) ($P < 0{\cdot}001$), indicating that the arteriovenous anastomoses were open.

In the patients with Raynaud's disease the findings were similar, that is, there was no significant difference between the total finger blood-flow (12·62 ± 7·136 ml. per minute) and the capillary blood-flow (13·8 ± 8·378 ml. per 100 g. per minute) ($P > 0{\cdot}2$) before cooling, but after cooling there was a highly significant difference between the total finger blood-flow (20·08 ± 11·137 ml. per 100 g. per minute) and the capillary blood-flow (4·91 ± 4·299 ml. per 100 g. per minute) ($P < 0{\cdot}001$). Thus in Raynaud's disease there is no alteration in the normal interrelationship of blood-flow through the arteriovenous anastomoses and capillaries so that the fault must lie in the vasculature proximal to the arteriovenous anastomoses.

Grant, R. T., and Bland, E. F. (1931), *Heart*, **15**, 385.
Lewis, T. (1930), *Ibid.*, **15**, 177.

59. Animal Experiments on the Effect of Various Haemostyptic Drugs: H. E. Koehnlein and U. Mergard, Freiburg, Germany.

An attempt was made to find a reproducible test to compare the effect of six systemically and four locally administered haemostyptic drugs.

A standardized liver section was performed in 300 rats. Bleeding time and blood-loss were measured exactly. The same test was performed on healthy animals and on animals who had received 0·2 ml. CCl_4 and 0·2 ml. of olive oil per 100 g. 24 hours before the operation. The following drugs were tested: (1) epsilon-amino-caproic acid (17·14 mg. per 100 g.) i.v. 15 minutes before liver section; (2) Anvitoff (0·0073 ml. per 100 g.) i.v. 60 minutes before operation; (3) vitamin K (0·06 ml. per 100 g.) i.v. 3 hours before operation; (4) Tachostyptan (0·04 ml. per 100 g.) i.v. directly before operation; (5) Epsilon-Tachostyptan (0·04 ml. per 100g.) i.v. 10 minutes before operation; (6) reptilase (0·003 ml. per 100 g.) i.v. 10 minutes before operations; locally: Clauden powder, collagen powder, Tabotamp gauze, and Topostasin.

Locally applied collagen was superior to all other haemostyptic drugs in both experiments. The bleeding stopped immediately in every animal. Blood-loss and bleeding time were not measurable. From the intravenously administered drugs reptilase showed the best effect: blood-loss was 24 mg. as compared with 65 mg. in the controls; bleeding time was 2·6 minutes versus 4·4 minutes. Consequently collagen powder has been used in 25 patients with very good effect.

60. Preliminary Studies on the Effect of Adrenergic Blockade on Haemorrhage-induced Changes in Blood Coagulability and Fibrinolysis: M. H. Irving and Christine Hawkey, St. Bartholomew's Hospital and Nuffield Institute of Comparative Medicine, London.

Haemorrhage and both accidental and operative trauma cause an increase in the coagulability and fibrinolytic activity of the blood. Venous thrombosis and disseminated intravascular coagulation are manifestations of the increased coagulability.

The exact mechanisms which stimulate hypercoagulability and fibrinolysis in such circumstances are not known, but intravenous adrenaline infusion has been shown to activate both systems. This observation is of significance, for adrenaline and noradrenaline levels in the blood attain high values in haemorrhagic shock.

Four groups of 3 sheep each were subjected to 3 hours' haemorrhagic shock by the elevated reservoir technique. One group acted as a control, while the other groups were premedicated with phenoxybenzamine (B), propranolol (C), and phenoxybenzamine and propranolol in combination (D). Measurements of platelet count, cephalin clotting time, fibrinogen, factor V, and fibrinolytic activity were made at regular intervals throughout the period of haemorrhagic shock.

Marked changes in the activity of all the measured indices were found in the control and alpha-blocked (phenoxybenzamine) animals but did not occur in the beta-blocked (propranolol) group. The results in the animals with the combined blockade were equivocal.

The results suggest that haemorrhage-induced hypercoagulability and fibrinolysis are mediated through the beta-activity of endogenously released catecholamines.

61. The Effect of Pyridinol Carbamate Treatment on the Platelet Response to ADP in Patients with Peripheral Atherosclerosis: R. C. Cotton, K. Bloor, and G. Archibald, Royal Infirmary, Manchester, and I.C.I. Research Laboratories, Macclesfield.

It is claimed that treatment with pyridinol carbamate results in an improvement of blood-flow in the affected limbs in patients with peripheral atherosclerosis (Shimamoto et al., 1970). It is suggested that this effect is produced by inhibiting processes involved in the continuing development of the atheromatous/thrombotic lesions.

The platelet response to ADP was investigated in patients with peripheral atherosclerosis using the platelet-aggregation filtration pressure (P.A.F.P.) method (Dhall and Matheson, 1969). The mean P.A.F.P. in 21 patients (mean age 56·9 ± 1·7 years) was 95·3 ± 6·6 mm. Hg. In 14 healthy male subjects of similar age the P.A.F.P. was 55·5 ± 5·2 mm. Hg and in 11 younger normal males (mean age 24·2 ± 0·9 years) the P.A.F.P. was 50·2 ± 1·0 mm. Hg. The difference between the means in each of these groups was significant (*P* < 0·001).

In an open trial 13 of the patients were treated with pyridinol carbamate for 4 months. The mean P.A.F.P. in these patients was reduced from 91·5 ± 9·5 to 69·5 ± 4·8 mm. Hg by the sixth week of treatment and this effect on the platelets persisted for the rest of the period of treatment.

It is concluded that pyridinol carbamate reduces the sensitivity of the platelets to ADP to normal levels in these patients. This effect is probably an indirect one.

Dhall, D. P., and Matheson, N. A. (1969), *Cardiovasc. Res.*, **3**, 155.

Shimamoto, T., Atsumi, T., Yamashita, S., Motomiya, T., and Isokane, N. (1970), *Am. Heart J.*, **79**, 5.

62. Use of the Scanning Electron Microscope in studying the Effect of Implanted Emboli on Canine Arteries: John D. Hamer, Department of Surgery, Queen Elizabeth Hospital, Birmingham.

Limb salvage following arterial embolectomy is most satisfactory when operation is performed soon after embolism (Thompson et al., 1970). There appears to be a critical period after embolism during which embolectomy is frequently followed by rethrombosis.

This investigation was carried out to search for morphological changes in the surface ultrastructure of canine arteries exposed to implanted emboli, and to investigate the association of such changes with rethrombosis after embolectomy. The significance of post-embolectomy blood-flow rate was also examined.

Nine dogs in three equal groups were investigated. Electrostatically induced venous thrombus was implanted into the carotid and femoral arteries on one side, each contralateral artery acting as a control, and embolectomy was performed 7 days later. Blood-flow restriction was imposed in groups II and III by 30 per cent and 50 per cent respectively, whereas in group I flow was unrestricted.

Seven days later all vessels were inspected and it was found that three out of six vessels in group I had rethrombosed against one control. In group II four out of six vessels had rethrombosed, and in group III all six arteries had rethrombosed.

Scanning electron microscopy has revealed characteristic surface changes in vessels exposed to emboli for 7 days. These changes are reversible in the presence of sustained arterial patency. Although platelet adhesion to endothelial cells has been described after physical trauma (Sheppard and French, 1970) this phenomenon was not observed in this investigation.

Sheppard, B. L., and French, J. E. (1970), *Nature, Lond.*, **225**, 1054.

Thompson, J. E., Sigler, L., Rant, P. S., Austin, D. J., and Patman, R. D. (1970), *Surgery, St Louis*, **67**, 212.

63. A Further Trial comparing Dextran 70 with Warfarin in the Prophylaxis of Postoperative Venous Thrombosis: A. I. Davidson, M. E. A. Brunt, and N. A. Matheson, Aberdeen.

Dextran 70 (Macrodex) has been reported to afford significantly better protection against postoperative venous thrombosis in gynaecological patients than Warfarin begun 36 hours after operation. In the Warfarin group, however, half of the patients developing venous thrombosis did so before the commencement of the anticoagulant. The efficacy of dextran 70 (500 ml. during operation; 250 ml. daily on the first 3 days after operation) was therefore compared with that of Warfarin begun at least 36 hours before operation (30 mg. followed by additional doses to maintain the Quick one-stage prothrombin time at 2 to 2·5 times the control level) in 60 patients undergoing pelvic floor repair and randomly allocated to either treatment. Venous thrombosis was diagnosed by ^{125}I-fibrinogen uptake which was positive in 4 of the 30 patients on Warfarin and in 3 of the 30 patients on Macrodex. The efficacy of Warfarin was improved by its earlier administration, but in these patients Macrodex appeared to be at least equally effective.

There was no significant difference in the volume of operative blood-loss measured by haemoglobin extraction in the two groups of patients.

64. Fibrinolysis after Operation and its Relationship to Deep-vein Thrombosis: I. C. Gordon-Smith, J. A. Hickman, and L. P. Le Quesne, The Middlesex Hospital, London.

Studies of postoperative fibrinolytic activity using conventional lysis-time methods are influenced by the rise in fibrinogen concentration following operation. Fibrinolytic activity in patients undergoing major surgery was re-examined by a technique employing ^{125}I-fibrinogen; this gives a quantitative measurement of systemic fibrinolytic activity independent of the plasma-fibrinogen concentration (Hickman, 1971).

So far 45 patients have been studied before operation, immediately afterwards, and daily for a further 7 days. In 85 per cent of the patients fibrinolytic activity was increased immediately following operation ($P < 0{\cdot}001$). There was no evidence of sustained inhibition, or fibrinolytic 'shutdown', in the postoperative period. Indeed, compared with mean preoperative levels fibrinolytic activity tended to increase from the second postoperative day and this was significant by the sixth day ($P < 0{\cdot}01$).

These results do not confirm the pattern of postoperative fibrinolytic activity previously described (Brown et al., 1971), probably because the lysis-time methods employed in those studies were influenced by the postoperative rise in plasma-fibrinogen concentration.

Patients with deep-vein thrombosis, diagnosed by the ^{125}I-fibrinogen technique, exhibited lower fibrinolytic activity during the first postoperative day than patients with no thrombosis ($P < 0{\cdot}05$).

Brown, I. K., Haggart, B., Murray, G. H., Downie, R. J., Littler, J., Rob, M., and Anter, G. J. (1971), *Lancet*, **1**, 774.

Hickman, J. A. (1971), *Br. J. Haemat.*, **20**, 611.

65. Congenital Stenosis of the Gut: An Experimental Study in the Chick Embryo: R. J. Earlam, The London Hospital.

Ischaemia associated with a volvulus or obstruction in an umbilical hernia has been postulated as a cause of congenital intestinal atresia and stenosis (Louw, 1959), but there is only one supportive experiment, in which puppies were operated upon *in utero* (Barnard, 1956), and that is for atresia alone.

In the present study the blood-supply to a segment of the chick-embryo gut early in its development was divided when a normal large umbilical hernia containing gut was still present. Fertile incubated eggs were opened between the ninth and seventeenth days (normal incubation period 21 days). After dividing the covering layers a loop of bowel was carefully lifted out and the mesenteric vessels supplying it were cut. The gut was replaced and the layers so arranged as to prevent leakage of amniotic fluid.

One hundred and six technically successful attempts were made to open the eggs and lift up a loop of bowel without causing a haemorrhage or immediate death, but only 20 survived longer than 24 hours; 5 had their mesenteric vessels divided and 15 acted as controls without interruption of the blood-supply. An area of stenosis was found in 3 of these 5 which were killed within 6 days after the operation. This supports the idea that ischaemia can cause stenosis of the gut before birth.

Barnard, C. (1956), *Surg. Forum*, **7**, 393.

Louw, J. H. (1959), *Ann. R. Coll.*, **25**, 209.

66. Water and Electrolyte Transfer by Colonic Mucosa studied in vitro: E. Q. Archampong, J. Harris, and C. G. Clark, Department of Surgery, University College Hospital, London.

A technique is described for studying the ability of isolated colonic mucosa to transport water and electrolytes. The mucosa was placed between two Perspex chambers and bathed with modified oxygenated Tyrode solution. Polyethylene glycol was used as a marker and isotopes of sodium, potassium, and chloride were added to the chamber bathing the luminal aspect of the mucosa. The potential difference of the membrane was continuously recorded and a short-circuit device was added to measure the current required to bring the mucosa to electrical neutrality, thereby providing another measure of sodium transport.

In seven experiments with mucosa from colon obtained from cancer patients (controls) it was found that water was absorbed at a rate of 0·001 ml. per minute per cm.^{2} and sodium at 0·170 μEq. per minute per cm.^{2} Potassium was secreted at a rate of 0·020 μEq. per minute per cm.^{2} A negative potential difference was maintained and the short-circuit current was 0·116 μEq. per minute per cm.^{2} In parallel experiments with identical mucosa Salazopyrin significantly increased the absorption of water to 0·002 ml. per minute per cm.^{2} and that of sodium to 0·314 μEq. per minute per cm.^{2} with no change in potassium excretion. Azathioprine had no apparent effect in this system.

In inflammatory bowel disease eight studies show gross alteration in mucosal function which can be restored to more normal patterns by Salazopyrin or Azathioprine depending on the nature of the disease.

67. The Response of the Dog Colon to Ischaemia: J. W. L. Robinson, C. Rausis, and V. Mirkovitch, Lausanne, Switzerland.

The blood-supply to loops of dog colon was interrupted for 1, 2, or 3 hours by clamping the mesenteric and marginal arteries as well as the intestine. The mucosal active transport of sodium was abolished after 1 hour's ischaemia with a reduction in Na$^+$-K$^+$-ATPase in mucosal homogenates. After 2 and 3 hours' ischaemia there was a large increase in the passive permeability of the colonic wall with no active transport and only very low values of Na$^+$-K$^+$-ATPase. One hour's ischaemia provoked only minor changes in histology and microcirculation, but after 2 hours considerable desquamation of the surface cells was observed with venous thrombosis. After 3 hours, heavy oedema and haemorrhagic infiltration without microperfusion of the crypts were seen.

The recovery of the colon from 3 hours' ischaemia was uncertain, both functionally and morphologically, but there was a close correlation between the histological picture, the sodium transport capacity, and the Na^+-K^+-ATPase levels of the experimental loops. One of 4 animals recovered after 1 week, and the majority had recovered after 3 or 4 weeks even though 1 out of 4 dogs had a completely non-functional loop 4 weeks after the ischaemia. Recovery followed a pattern that may be more or less protracted in time. The mucosal regeneration was rapid since no loop with discrete zones of regeneration surrounded by cryptless tissue was observed. The submucosal tissues were greatly thickened and the loop was shortened in length.

68. The Relationship of Colonic Symptoms to the Muscular Abnormality of Diverticular Disease: L. E. Hughes, Department of Surgery, Cardiff.

An increased interest in abnormal muscular activity in diverticular disease has led to the proposal of sigmoid myotomy as a rational therapeutic measure, particularly when 'functional' symptoms predominate. This approach presupposes that such symptoms (abdominal pain, severe constipation, or diarrhoea) are associated closely with diverticular muscle patterns. This paper describes a study of the relationship of diverticulosis and diverticular muscle patterns with colonic symptoms.

Fifty patients undergoing colonic investigation were studied in a prospective fashion. Patients in whom a clear pathological cause for their symptoms could be demonstrated were excluded. The series was otherwise consecutive. Muscular patterns were determined by the silicone-foam-enema technique (Hughes, 1970). Accessory radiological, surgical, pathological, and autopsy studies were carried out to confirm the validity of this technique. The presence of diverticula was determined by combined studies of barium and silicone enema. Symptoms were recorded prior to silicone-enema examination.

Results showed that there is no significant correlation between the presence of diverticula or diverticular muscle patterns and any individual functional symptom. When all three functional symptoms were grouped together there was a negative correlation which just reached the 5 per cent significance level.

It is concluded that caution should be exercised in the use of therapeutic measures that presume a causal relationship between 'functional' symptoms and diverticular disease.

Hughes, L. E. (1970), *Gut*, **11**, 111.

69. An Animal Model to study Diverticular Disease: I. Hodgson (B. N. Brooke), St. George's Hospital, London.

Painter (1962) and Arfwidsson (1964) have demonstrated colonic pressure changes in diverticular disorders. In order to pursue this further an animal model was devised using rabbits.

Adult New Zealand White rabbits were given gas induction and chloralose anaesthetics and were then maintained on oxygen after placing fluid-filled open-tipped narrow-bore polythene tubes in the colon through a caecostomy. After a resting period of 30 minutes colonic activity was induced using a dose of 0·05 mg. per kg. prostigmine and the resulting intracolonic pressure changes were measured for 30 minutes.

The rabbits were placed on a free diet of white bread, butter, milk, and sugar supplemented by vitamins. After 4 months on this diet the rabbits had put on weight, had become constipated, their general condition had deteriorated, and their colon had contracted. Repeat pressure measurements using the same dose of prostigmine showed the mean colonic motility index (C.M.I.) to be five times greater than the pre-dietary mean C.M.I.

Furthermore, after prostigmine scattered intertaenial temporary diverticula, similar to those demonstrated by Painter (1962) in humans, appeared. They were wide-necked, hemispherical, 0·5 cm. in diameter, blue-black in colour, and regularly appeared to be superimposed on the haustra at the same spot during contraction.

Arfwidsson, S. (1964), *Acta chir. scand.*, suppl., **342**, 1.
Painter, N. S. (1962), M.S. thesis, London University.

70. Colomyotomy and Intraluminal Pressures studied in the Rabbit: T. Balfour, V. Giannakos, and A. N. Smith, Edinburgh.

Twenty rabbits were submitted to colomyotomy of the Reilly type under anaesthesia (Reilly, 1966). The intracolonic pressures were studied manometrically. There was an initial fall to minimal pressures on stimulation by cholinergic agents, with a return to 50 per cent of normal in 2 months and completely in 3 months. Closure of the myotomy site by resuturing the outer muscle-coat was followed by the return of the pressure responses in 3–4 weeks.

The response of the myotomy site to distension was examined by inflating a standard excised segment; comparisons were made with normal loops and after an anastomosis. The pressures required to rupture an anastomosis were low initially. For the myotomy, pressures at or even above those required to rupture normal intestine were required.

It is concluded that the effects of myotomy in the rabbit as in man (Smith et al., 1971) are temporary. Protection of the intact myotomy site by resuture is unnecessary since the resistance to rupture is high. The fact that resuture of bowel is followed by very early return of pressure suggests that myotomy may lower pressure by widening the lumen more than by division of muscle.

Reilly, M. (1966), *Br. J. Surg.*, **54**, 859.
Smith, A. N., Giannakos, V., and Clarke, S. (1971), *J. R. Coll. Surg., Edinb.*, **16**, 276.

71. DL-A and Isolated Pancreas Allograft: J. de Gruyl, L. Verschoor, H. M. Vriesendorp, P. Horchner, D. L. Westbroek, and H. A. M. Hulsmans, Rotterdam, The Netherlands.

The technical and functional possibilities of an isolated pancreas transplantation without adjacent duodenum was studied in the dog (Lillehei et al., 1970), and the influence of DL-A histocompatibility on isolated pancreas allograft survival was examined (Vriesendorp et al., 1971). Three groups of dogs were studied: total exocrine duct ligation was carried out on 12 dogs; autotransplantation of the isolated pancreas was performed in 17; and allotransplantation of the isolated pancreas without immunosuppressive therapy was carried out in 10 non-identical litter-mate beagles and in 10 identical litter-mate beagles.

After duct ligation only in 3 dogs some exocrine pancreas function was found, as measured by faecal α-chymotrypsine and trypsin. At a second laparotomy in these dogs some normal pancreatic tissue was found. Endocrine function of the pancreas with ligated ducts showed a decrease, as measured by the glucose-tolerance test and serum insulin, but prediabetic or diabetic levels were not reached. During the follow-up period of 2 years a restoration of function was observed. Autotransplantation in the dog had a high technical failure rate because of the triple pancreas vascularization. Some surviving dogs showed up to 3 years' normal endocrine function. The mean survival time of the non-treated non-identical group was 12 days. The mean survival time of the identical group was 40 days. The intravenous glucose-tolerance test was an impractical parameter of rejection, because it is only when the pancreas is totally necrotic that this test is abnormal.

DL-A identity showed a strong influence on non-treated isolated pancreas allograft survival.

LILLEHEI, R. C., SIMMONS, R. L., NAJARIAN, J. S., WEIL, R., UCHIDA, H., RUIZ, J. O., KJELLSTRAND, C. M., and GOETZ, F. C. (1970), *Ann. Surg.*, **172**, 405.

VRIESENDORP, H. M., ROTHENGATTER, C., BOS, E., WESTBROEK, D. L., and VAN ROOD, J. (1971), *Transplantation*, **11**, 440.

72. Transplantation of the Endocrine Pancreas in Guinea-pigs: J. FERGUSON and R. J. SCOTHORNE (I. D. A. Johnston), Department of Anatomy, University of Newcastle upon Tyne.

A number of reports have described transplantation of the whole pancreas by vascular anastomosis (Reemtsma et al., 1964). More recently Lillehei et al. (1971) have reviewed the current status of clinical allotransplantation of the pancreas, as a combined pancreaticoduodenal graft.

The fate of pancreatic islets isolated from all exocrine pancreas by the method of Hellerström (1964) and implanted into the testis or omentum was studied. Grafts were recovered at intervals and studied microscopically in sections stained with Gomori's aldehyde fuchsin.

Intratesticular isografts between Duncan Hartley guinea-pigs from a closed colony survived for periods of up to 90 days without any evidence of lymphocytic infiltration.

Intratesticular allografts (outbred to Duncan Hartley guinea pigs) were recovered at intervals of up to 11 weeks and showed varying degrees of lymphocytic infiltration. A minority of rejected grafts was found, the earliest at 20 days after transplantation.

Intra-omental allografts were all alive when recovered at intervals from 10 days to 11 weeks.

Intratesticular islet-cell allografts in hosts sensitized by a previous skin-graft from the same donor were rejected in an accelerated fashion, all being dead by 8 days.

This study shows the feasibility of transplanting isolated endocrine pancreatic islets in guinea-pigs. Evidence is presented which suggests that the extended survival of islets in the testis may be related to a block in the afferent side of the 'immunological reflex arc'.

HELLERSTRÖM, C. (1964), *Acta endocr., Kbl.*, **45**, 122.

LILLEHEI, R. C., SIMMONS, R. L., NAJARIAN, JOHN S., KJELLSTRAND, CARL M., and GOETZ, F. C. (1971), *Transplantn Proc.*, **3**, 318.

REEMTSMA, K., HEWITT, R. L., and SMITH, P. E. (1964), *Ann. N.Y. Acad. Sci.*, **120**, 656.

73. Quantitative Studies of Bone Transplantation—The Role of the Allograft Barrier: V. M. GOLDBERG and E. M. LANCE (A. Cox), New York.

The healing of full-thickness iliac bone-grafts over a 3-month interval was studied in young adult New Zealand White rabbits, focusing on the rates of revascularization and new bone formation. The former was measured by determining the distribution of ^{51}Cr-labelled erythrocytes (Albert et al., 1958), while the latter was estimated from the uptake of ^{85}Sr (Bauer and Ray, 1958).

Revascularization of autografts proceeded rapidly for 4 weeks, peaked at 6 weeks, and was followed by a slow decline. New bone formation was maximal at 3 weeks and remained at a high plateau thereafter. The revascularization of allografts in untreated animals did not show an initial rise and remained significantly lower than autografts after the second week of observation ($P<0\cdot01$). New bone formation in allografts was comparatively slow for the first 6 weeks ($P<0\cdot001$) and rose slowly thereafter. By contrast the curves for both revascularization and new bone formation in allografts of animals treated with azathioprine were virtually superimposable on those for autografts.

These studies document and quantify the barrier imposed on bone-implant acceptance by antigenic differences and demonstrate the removal of this barrier with immunosuppressive treatment.

ALBERT, C. A., THERGAONKAR, R. D., HENLEY, E. E., BAIN, M., RAFEI, A., and ALBERT, S. N. (1958), *Surgery Gynec. Obstet.*, **107**, 685.

BAUER, G. C. H., and RAY, R. D. (1958), *J. Bone Jt Surg.*, **40**, 171.

74. Transplantation of the Porcine Pancreas—Observations on the Metabolism of Glucose and Insulin: R. A. SELLS, M. BRAMLEY, P. MILLARD, and R. Y. CALNE, Cambridge and Liverpool.

Pancreatic transplantation in the pig has not hitherto been reported in detail. This paper describes the technique and the biochemical effects of orthotopic and heterotopic pancreaticoduodenal allografts following recipient pancreatectomy.

Nineteen pancreatic allografts were transplanted. The 12 pigs studied survived for a mean of 25 days (range 11–50 days). No immunosuppression was used.

Pancreatectomy without grafting was performed in 4 animals.

Control intravenous glucose-tolerance tests were carried out on 16 fasting, anaesthetized, normal pigs.

With orthotopic transplants (6 pigs) glucose tolerance was found to be similar to the normal control group and rejection of the pancreas was noted at post-mortem examination.

In the heterotopic transplants (6 pigs) a rapid fall in blood-sugar in response to a glucose load was noted, with greatly increased (ten times normal) rise in insulin level ($P<0\cdot005$).

Six animals with combined liver, kidney, and pancreatic transplants survived for more than 1 day, and 3 were studied at 5, 15, and 20 days. Glucose tolerance was normal. Little evidence of pancreatic rejection was found at post-mortem examination.

Orthotopic transplants secreting insulin into the portal vein result in normal peripheral blood-glucose and insulin levels.

Heterotopic grafts draining into a systemic vein produce hypoglycaemia and hyperinsulinaemia.

Pancreatic rejection occurs in the pig and may be modified by simultaneous transplantation of the liver and the kidney.

75. Hand Function—A Practical Method of Assessment: R. A. DICKSON and J. S. CALNAN, Royal Postgraduate Medical School, London.

Quantitative assessment of hand function is based largely on the measurement of grip strength using the pneumatic dynamometer (Wright, 1959). There is no method of measuring the contribution of individual digits to hand function which is so important to both patient and hand surgeon when only one digit is affected by disease. An instrument, the cybernometer, was developed for this purpose (Dickson et al., 1972).

Forty normal hands and 20 rheumatoid hands were studied using the cybernometer and the pneumatic dynamometer. The grip strength, individual digital flexion force, and pinch force (three recordings of each) were measured in random order. Fatigue was not observed.

In the normal hands the index and middle fingers were significantly stronger than the ring and little fingers ($P<0\cdot05$). The fingers of the dominant hand were significantly stronger than their non-dominant counterparts ($P<0\cdot05$). The force of pinch was approximately twice that of flexion. The grip strengths of both normal and rheumatoid hands bore no relation to the forces of their individual digits, weaknesses in rheumatoid fingers not being reflected in a diminution in grip strength.

We therefore question the value of grip strength measurements in the assessment of hand function and present the cybernometer as a more specific and accurate instrument.

DICKSON, R. A., PETRIE, A., NICOLLE, F. V., and CALNAN, J. S. (1972), *Biomed. Engng.* (in the press).
WRIGHT, V. (1959), *Clin. Sci.*, **18**, 17.

76. Force and Cortical Thickness—A Relationship in the Individual Digits of the Hand: R. A. DICKSON, J. S. M. BEALES, A PETRIE, and J. S. CALNAN, Royal Postgraduate Medical School, London.

The relationship between total hand function and the cortical thickness of the hand bones has been described (Virtama et al., 1968). However, the relationship between the forces of individual digits and the dimensions of their small bones has never been reported. Such an investigation has been carried out in the hands of 15 normal adult males.

The flexion forces and pinch forces of the digits of both hands were measured using the cybernometer. Radiographs of the hands were obtained under standard conditions and the dimensions of the metacarpals and proximal phalanges were measured. From these parameters the area index was calculated (Exton-Smith et al., 1969). Correlation coefficients of flexion force and pinch force with area index were determined.

There was a significant trend at the 1 per cent level for the correlation coefficients to be positive for the metacarpal area index with pinch force. A similar trend at the 5 per cent level was observed for the proximal phalanx area index with pinch force. Flexion force and area index did not appear to be related.

EXTON-SMITH, A. N., MILLARD, P. H., PAYNE, P. R., and WHEELER, E. (1969), *Lancet*, **2**, 1153.
VIRTAMA, P., HELELA, T., and KALLIOMAKI, J. L. (1968), *Acta rheum. scand.*, **14**, 276.

SHORT NOTES OF RARE OR OBSCURE CASES

GASTRIC NECROSIS: A RARE COMPLICATION OF CHLORAL HYDRATE INTOXICATION

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SUMMARY

A rare complication of chloral hydrate intoxication is described. Added to the initial acute cardiorespiratory and central nervous system depression, subsequent gastric necrosis and perforation provided a difficult problem in management. A satisfactory outcome was finally achieved using the Roux-en-Y technique to by-pass the stricture at the oesophagogastric anastomosis.

THE popularity of chloral hydrate as a hypnotic agent has waxed and waned over the years. First synthesized by Liebig in 1832 it proved to be an excellent hypnotic drug. It became less widely used as a result of numerous deaths from overdosage. The introduction of the barbiturates to clinical medicine by Fischer and Von Mering in 1903 (Goodman and Gilman, 1965) hastened the decline in popularity of the drug. Although chloral hydrate is a well-known irritant of the skin and mucous membranes and the effects of acute intoxication have been well documented, there have been no reports of actual necrosis of the stomach wall following its ingestion. We present this case to highlight the management of this very rare complication of chloral hydrate poisoning.

CASE REPORT

F. A., a 25-year old female, was admitted to St. Vincent's Hospital, Melbourne, on 29 Nov., 1969. The patient had suffered from depression in the past and on the day before admission she had ingested 200 ml. of syrup of chloral. This contained 20 g. of chloral hydrate. She was found unconscious and was admitted to the local hospital. Examination then showed a deeply unconscious areflexic woman with a blood-pressure of 70 mm. Hg systolic. She required intubation and assisted ventilation and was then transferred to St. Vincent's Hospital.

On admission, some 24 hours after the ingestion of the chloral hydrate, the patient was hypothermic (rectal temperature 35° C.), deeply unconscious, and areflexic, with a blood-pressure of 80 mm. Hg and a pulse-rate of 90 per minute. Widespread crepitations were heard over both lungs and it was assumed that the patient had vomited and had inhaled the vomit. A radiograph of the chest confirmed the diagnosis of widespread pulmonary oedema. Blood-gas analysis on admission showed a Po_2 of 110 mm. Hg, Pco_2 of 100 mm. Hg, and *p*H of 6·95.

The patient was treated with mannitol, frusemide, steroids, and antibiotics. The assisted ventilation was continued, and 24 hours after admission the Pco_2 had fallen to 35 mm. Hg, the rectal temperature had risen to 37·5° C., and the conscious state had improved. Three days after admission a tracheotomy was performed. The patient had become intolerant of the endotracheal tube but still required assisted ventilation to control the pulmonary oedema. The next day abdominal distension was noted. A plain radiograph revealed a large amount of gas beneath the diaphragm and a laparotomy was performed. A severe generalized peritonitis was found. The peritoneal cavity contained 2 litres of bile-stained fluid. Mobilization of the stomach then revealed that the entire fundus had necrosed. Bile was welling out through the ragged opening in the upper stomach. Owing to the difficulty encountered in the abdominal dissection and the possibility of oesophageal involvement the left chest was entered after excision of the eighth rib. The diaphragm was incised and the necrotic perforation was visualized. The perforation extended right up to the oesophagogastric junction and its edges consisted of bile-stained slough. The adjacent stomach was thick-walled and oedematous. The necrotic stomach was excised by performing an upper gastrectomy (*Fig.* 1). The cut end of the oesophagus bled freely and the mucosa appeared normal. The cut end of the stomach was oversewn and invaginated and the oesophagus was anastomosed to the posterior wall of the gastric remnant. A pyloroplasty was also performed.

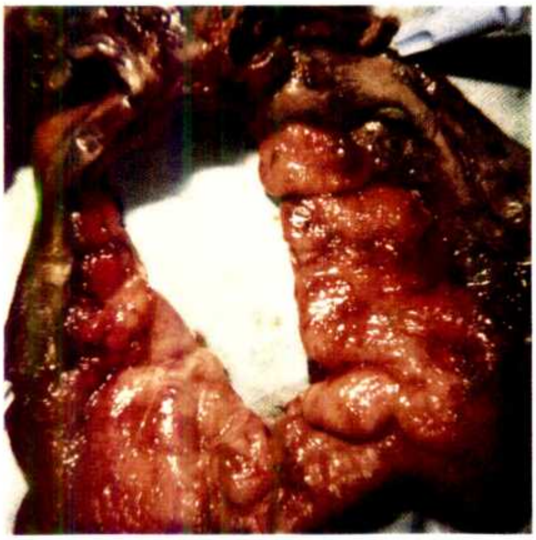

FIG. 1.—Resected stomach showing necrotic edge.

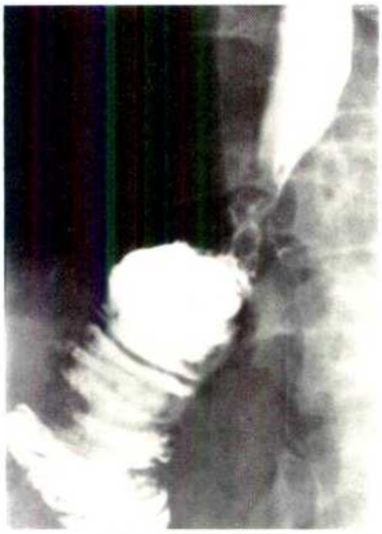

FIG. 3.—Patent oesophagojejunal anastomosis.

The patient's immediate recovery from this procedure was satisfactory and by the second postoperative day she was fully conscious. She became very confused on the third postoperative day and removed the nasogastric tube and the abdominal and thoracic drain tubes. On the fifth postoperative day dehiscence of the abdominal incision required resuturing. No leaks were apparent at this time. However, on the eighth postoperative day bile-stained fluid commenced to discharge from the thoracic wound. A Gastrografin swallow confirmed the presence of a leak from the oesophagogastric anastomosis. A further laparotomy was performed and this showed leakage from the anterior aspect of the oesophagogastric anastomosis and also leakage from the pyloroplasty. The pyloroplasty was oversewn, a large drain was replaced down to the oesophagogastric anastomosis (which was extremely friable and would not hold sutures), and finally a tube jejunostomy was fashioned using a Foley catheter.

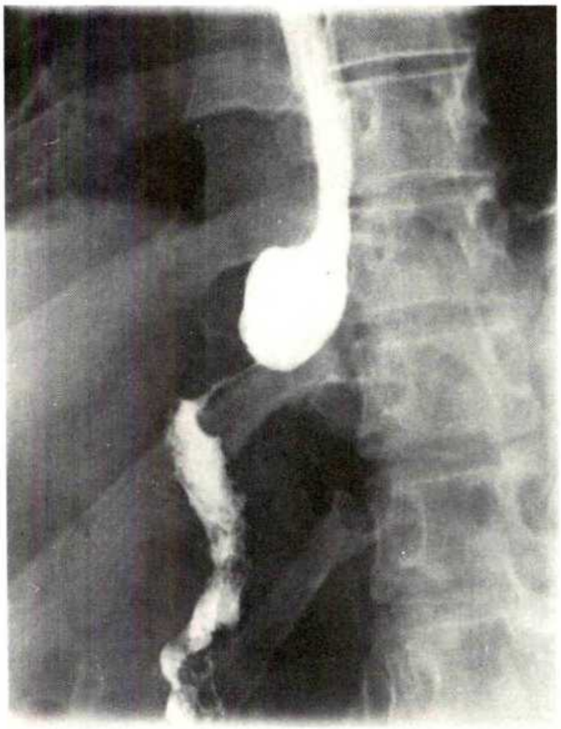

FIG. 2.—Stricture at the oesophagogastric anastomosis.

A stormy postoperative course followed. Over the next 3 weeks the patient showed a continuing pyrexia of 39°–40° C. Three massive haemorrhages from the upper gastro-intestinal tract required a total of 10 litres of blood to be infused. The thoracotomy wound became infected and partially broke down. Eventually the infection at the left lung base resolved and the drainage of gastro-intestinal fluid from the abdominal drain lessened and then stopped. A further Gastrografin swallow now showed no leak from the oesophagogastric anastomosis and the patient gradually recommenced oral feedings. The tube jejunostomy was functioning satisfactorily and the patient commenced to put on weight. However, 2 weeks later she complained of dysphagia. A tight stricture at the level of the oesophagogastric anastomosis was demonstrated (*Fig.* 2). This was confirmed by oesophagoscopy. It proved impossible to dilate the stricture. At this stage the patient was stabilized on jejunostomy feedings and was discharged home 3 months after her original admission.

One month later the patient was readmitted for definitive surgery to the stricture. She was depressed and was unable to swallow her saliva but her nutritional state was good. A barium swallow showed complete obstruction at the level of the oesophagogastric anastomosis. The thoracotomy wound had almost healed except for a number of superficial sinuses. It was proposed to by-pass the stricture using a Roux loop. As the left pleural cavity had previously been infected it was necessary to approach the lower oesophagus from the right side.

An exploratory laparotomy was performed. There were surprisingly few adhesions in the peritoneal cavity except beneath the left side of the diaphragm. The stomach remnant was shrunken and indurated. It was an easy matter to fashion a Roux loop, and then the patient was turned on her left side and a right thoracotomy was performed through the eighth interspace. The lower oesophagus was mobilized and transected just above the diaphragm. The distal end of the oesophagus was oversewn. The jejunum was led in front of the colon and the left lobe of the liver and then through a hole in the diaphragm and finally was anastomosed end to end to the oesophagus. The Roux-en-Y loop was completed by an end-to-side anastomosis of proximal to distal jejunum within the abdomen.

The postoperative course on this occasion was satisfactory and a Gastrografin swallow 7 days later revealed an intact anastomosis (*Fig.* 3). Three weeks later an oesophagoscopy was performed and this confirmed a widely patent anastomosis between the oesophagus and the jejunum. The patient was discharged swallowing well 1 month after the operation.

DISCUSSION

Acute intoxication by chloral hydrate is manifested by cardiovascular, respiratory, and central nervous system depression. Clinically, hypotension and various cardiac arrhythmias may occur (Gleich, Mongan, and Vaules, 1967). Chloral hydrate apparently accelerates the breakdown of coumarin derivatives. This action may lead to inadvertent overdosage of the anticoagulant when the administration of chloral hydrate is discontinued (Cucinell, Odessky, Weiss, and Dayton, 1966). The local irritant effect of chloral hydrate is well known. The nausea and vomiting which may follow its ingestion are undoubtedly due to its irritant effect on the gastric mucosa. There have only been 2 reports incriminating chloral hydrate intoxication with damage to the gastro-intestinal tract. One case (Gleich and others, 1967) presented as an oesophageal stenosis after the ingestion of 18 g. of chloral hydrate. This responded satisfactorily to dilatation. The second case (Feller, 1929) died after ingesting 150 g. of chloral hydrate. At autopsy the gastric mucosa showed widespread necrosis. Full-thickness necrosis of the stomach wall following the ingestion of a potentially lethal amount of chloral hydrate has not previously been reported.

The case presented here provided continuing difficulty in management. The initial respiratory failure, hypotension, hypothermia, and pulmonary oedema in a deeply unconscious patient merged into the management of massive gastric necrosis with generalized peritonitis. The catastrophe resulting from the suture-line leaks may have been precipitated in part by the presence of even more extensive gastric damage than was realized at the time of operation. It is possible that this may have impaired healing at the anastomosis, thus contributing to the leaks from the pyloroplasty and oesophagogastric suture lines (Gray and Holmes, 1948). The formation of a feeding jejunostomy proved to be of vital importance in maintaining nutrition as the patient eventually developed complete obstruction at the oesophagogastric junction. Fortuitously, the line of jejunal transection in fashioning the Roux loop coincided exactly with the site of the jejunostomy. Though the approach through the right chest added somewhat to the technical difficulties, a satisfactory by-pass of the stricture was achieved using the Roux technique. This was confirmed radiologically, at oesophagoscopy, and by the ability of the patient to swallow solids without difficulty.

Acknowledgement.—We wish to thank Professor Bennett for permission to report this case.

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A CASE OF XANTHOGRANULOMATOUS PYELONEPHRITIS

By CLIVE BARTRAM and DAVID JAGELMAN

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SUMMARY

A patient with a non-functioning kidney was investigated. Although the arteriographic findings suggested an inflammatory process, a malignant lesion could not be excluded. The appearance of the kidney at operation suggested malignancy but histological examination following nephro-ureterectomy showed xanthogranulomatous pyelonephritis. This is an uncommon reaction to severe renal infection and is often associated with upper renal tract obstruction. The clinical and radiological findings of this condition are reviewed.

The case which is presented here illustrates the difficulty of diagnosing an unusual condition in a non-functioning kidney. Radiologically the presence of a neoplasm could not be excluded, and at operation the appearances of the renal mass suggested an invasive malignant process. The infective nature of the lesion was only revealed histologically on paraffin section, a frozen section at the time of operation being inconclusive.

CASE REPORT

A 47-year-old woman presented with a 2-year history of left loin pain and recurrent urinary infection. On clinical examination she was mildly anaemic and had a palpable left-sided renal mass.

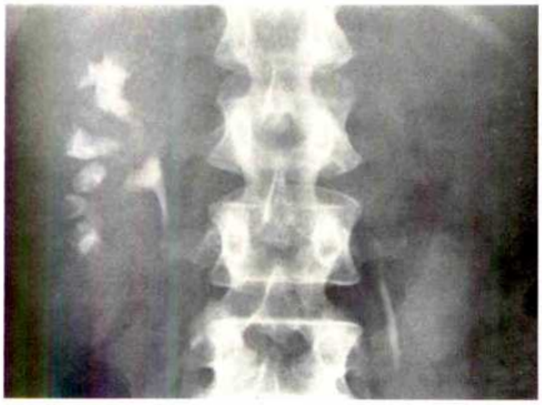

FIG. 1.—Post-micturation intravenous pyelogram, showing a non-functioning left kidney but with contrast present in the left upper ureter.

Investigations showed the following: haemoglobin, 11·1 g. per 100 ml.; W.B.C., 10,300 per c.mm.; E.S.R., 54 mm. per hour (Wintrobe); and a midstream specimen of urine contained a lactose-fermenting coliform. Culture for *Mycobacterium tuberculosis* was negative. An intravenous pyelogram showed a normal right kidney and a non-functioning left kidney. However, on the full-length post-micturition film (*Fig.* 1) some contrast was seen in the upper part of the left ureter. A micturating cystogram confirmed left vesico-ureteric reflux, and the left renal pelvis was dilated. However, both the micturating cystogram and a left retrograde pyelogram examination failed to define the calices adequately. A selective left renal arteriogram was performed via a right femoral catheterization. The capillary phase (*Fig.* 2 A) showed a large capsular artery, a thinned cortex with areas of increased capillary density, and stretching of the vessels in the region of the dilated pelvis. The nephrographic phase (*Fig.* 2 B) confirmed the presence of only a small amount of functioning tissue of irregular density and some opacification of the pelvis. It was thought that the left kidney was extensively damaged and hydronephrotic as a result of reflux and repeated infections. Although there was no definite neoplastic circulation, the presence of an abnormal capillary circulation raised the possibility of malignant change.

The left kidney was explored via a left paramedian incision. The renal substance was irregular and was whitish yellow in appearance. It was firmly adherent to the surrounding structures, invading the transverse mesocolon, and there was an associated perinephric abscess. The features suggested a neoplasm but a frozen section was inconclusive. A left nephro-ureterectomy was performed (*Fig.* 3) and the patient made an uneventful recovery.

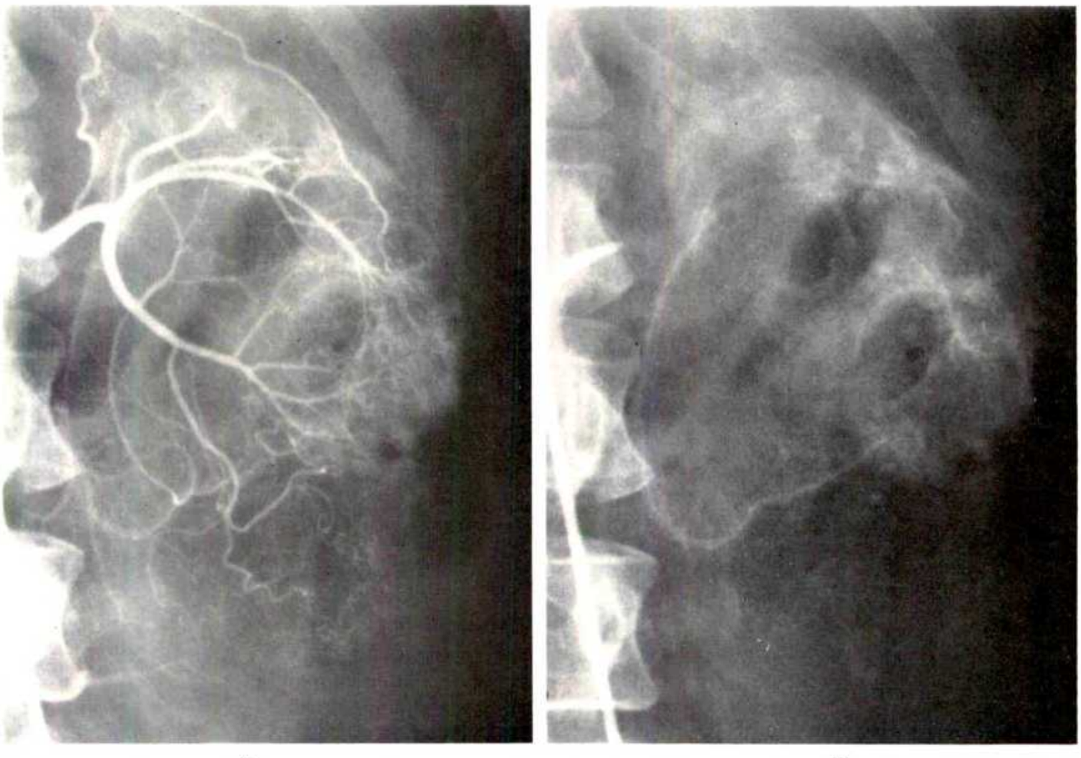

FIG. 2.—Selective left renal arteriogram. A, The capillary phase showing reduced renal tissue, irregular capillary density, and stretching of the vessels around the pelvis. B, The nephrographic phase confirms the irregular density of the cortex and shows opacification of the pelvis.

Pathological examination of the specimen revealed a grossly distorted kidney with severe hydronephrosis and pyelonephrosis. On the cut surface there were numerous yellow nodules, some of which extended into the perinephric fat. Histologically, there was severe pyelonephritis with focal areas of granulomatous reaction with giant cells and macrophages containing foamy cytoplasm. No acid-fast bacilli were seen. These features were regarded as compatible with a diagnosis of xanthogranulomatous pyelonephritis.

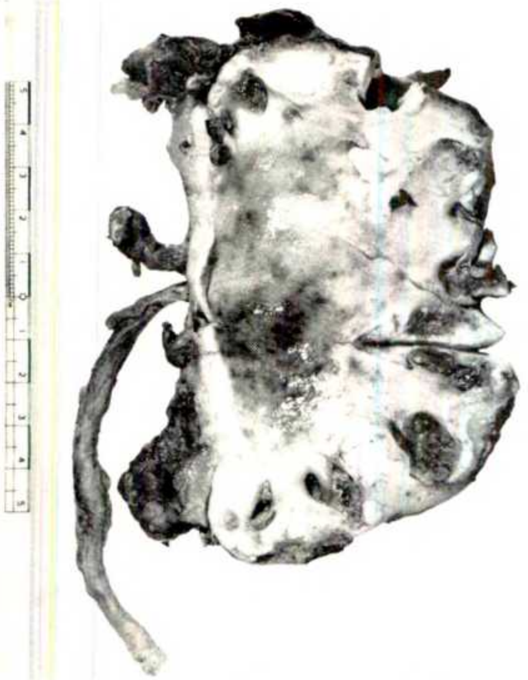

FIG. 3.—The left nephrectomy specimen. Note the presence of nodules and extensive renal damage.

DISCUSSION

Xanthogranulomatous pyelonephritis was first described by Schlagenhaufer in 1916. It is an uncommon reaction to severe renal infection, probably occurring in about 3 per cent of such cases (Elliott, Johnson, and Balfour, 1968), involvement being on one side only. Clinically, the following features are often present: recurrent urinary-tract infection, loin pain, a tender palpable renal mass, low-grade fever, mild anaemia, and bacteriuria (Hooper, Kempson, and Schlegel, 1962; Friedenberg and Spjut, 1963; Rios-Dalenz and Peacock, 1966).

The usual finding on intravenous pyelography is that the kidney is non-functioning owing to calculus or pelvi-ureteric obstruction, and when the kidney is visualized it is often enlarged. Xanthogranulomatous pyelonephritis does not appear to occur in the small shrunken kidney. The cortex is irregular and filling defects are present; these may also be seen in the pelvis. The pelvi-ureteric junction is often irregular. The loss of perinephric fat may suggest a perinephric abscess. The defects seen on pyelography raise the possibility of renal carcinoma, and quiescent renal tuberculosis should be considered in the differential diagnosis.

Few case reports have included arteriographic findings. Salmon and Koehler (1967), however, demonstrated that xanthogranulomatous pyelonephritis is vascular, and the arteriographic differences between an inflammatory and a malignant process are summarized in *Table I*.

Unfortunately the use of epinephrine will not help to distinguish the lesion, for, as was demonstrated by Kahn and Wise (1967), the renal arteries in the affected area fail to show the normal vasconstriction. The arteriographic findings, therefore, may be able to suggest that the lesion is inflammatory but verification must await histological examination. The microscopic features, as described by Heptinstal (1966), are of giant cells and macrophages containing a foamy cytoplasm.

Table I.—SUMMARY OF THE ARTERIOGRAPHIC FEATURES THAT DIFFERENTIATE AN INFLAMMATORY PROCESS FROM A MALIGNANT PROCESS

Inflammatory Process	*Malignant Process*
Stretching of vessels over lesion	Arteries of irregular calibre
Minimal irregularity of arteries	Early filling of abnormal circulation
Dense capillary blush in affected areas during normal capillary phase	Rapid filling of large irregular veins
Veins fill at normal rate	Pooling of contrast
No contrast pooling	Feeding arteries may be present
Large capsular artery if perirenal involvement	

Acknowledgements.—We wish to thank Mr. M. Naunton Morgan and Dr. F. Starer of the Westminster Hospital, London, for permission to publish this case report.

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A CASE OF CARCINOMA OF THE COLON IN ASSOCIATION WITH NEUROFIBROMATOSIS

By D. H. R. JENKINS* and W. GILL
DEPARTMENT OF CLINICAL SURGERY, UNIVERSITY OF EDINBURGH

SUMMARY

A case is presented of neurofibromatosis of the large bowel associated with a primary adenocarcinoma of the colon. This is believed to be the first report of such an association.

NEUROFIBROMATOSIS occurs once in every 2500–3000 live births (Lukash and Johnson, 1969). The disease was first described in 1882 by von Recklinghausen and may involve the skin, bladder, blood-vessels, bones, stomach, ileum, colon, and tongue (Russel, 1965). The severity of the cutaneous lesions bears no relationship to the presence of disease in other tissues (Leader Article, *Br. med. J.*, 1966), and the condition may be associated with mental deficiency, endocrinal somatic retardation, and phaeochromocytoma. Visceral neurofibromatosis is infrequent, and a study of 1399 examples of benign neoplasms of the small intestine revealed only 14 cases of neurofibromatosis (River, Silverstein, and Tope, 1956). These authors commented on the restricted involvement of the intestine when the disease was present.

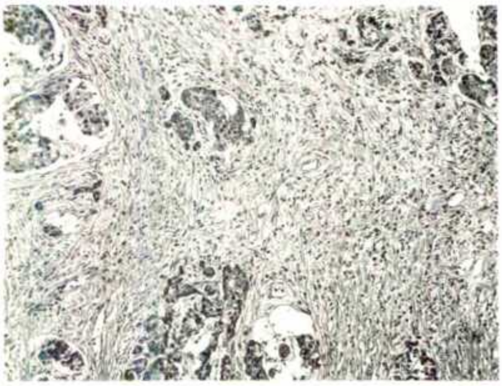

FIG. 1.—Clumps of adenocarcinoma intimately mixed with neurofibromatous tissue. H. and E. (× 66.)

Involvement of the large bowel by neurofibromatous tissue is rare (Weston, 1963) and usually becomes apparent only with malignant change of the abnormal tissue, which may occur in 10–15 per cent of cases (Hosoi, 1931; Crowe, Schull, and Keel, 1956) and results in sarcoma.

The case described here is that of an adenocarcinoma growing within neurofibromatous tissue in the colon. We have been unable to find any record of this association in the literature.

CASE REPORT

A 49-year-old unemployed labourer suffering from cardiac asthma presented as a surgical emergency to the Royal Infirmary of Edinburgh. The patient complained of constant, severe, generalized abdominal pain and appeared markedly dehydrated. One month prior to admission he had experienced intermittent, central abdominal pain of a colicky nature which had been relieved by the passage of flatus and diarrhoea. The diarrhoea had persisted and the faeces had occasionally been black in colour.

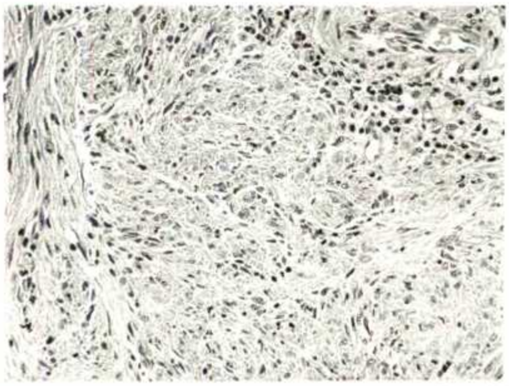

FIG. 2.—Photomicrograph of a representative polyp. H. and E. (× 100.)

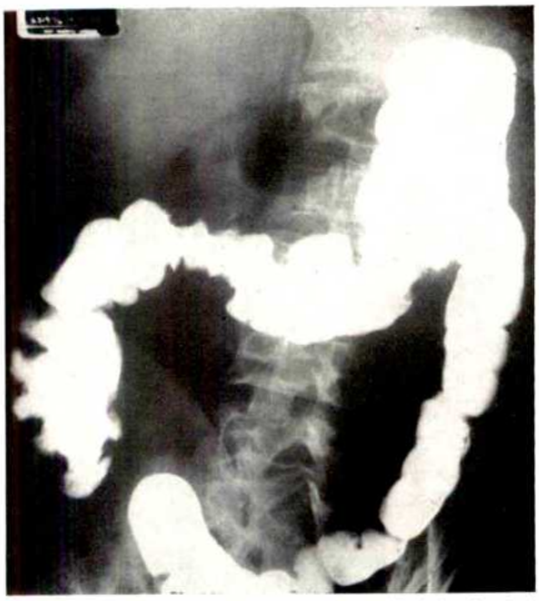

FIG. 3.—Barium-enema film demonstrating multiple intraluminal nodules in the ascending colon.

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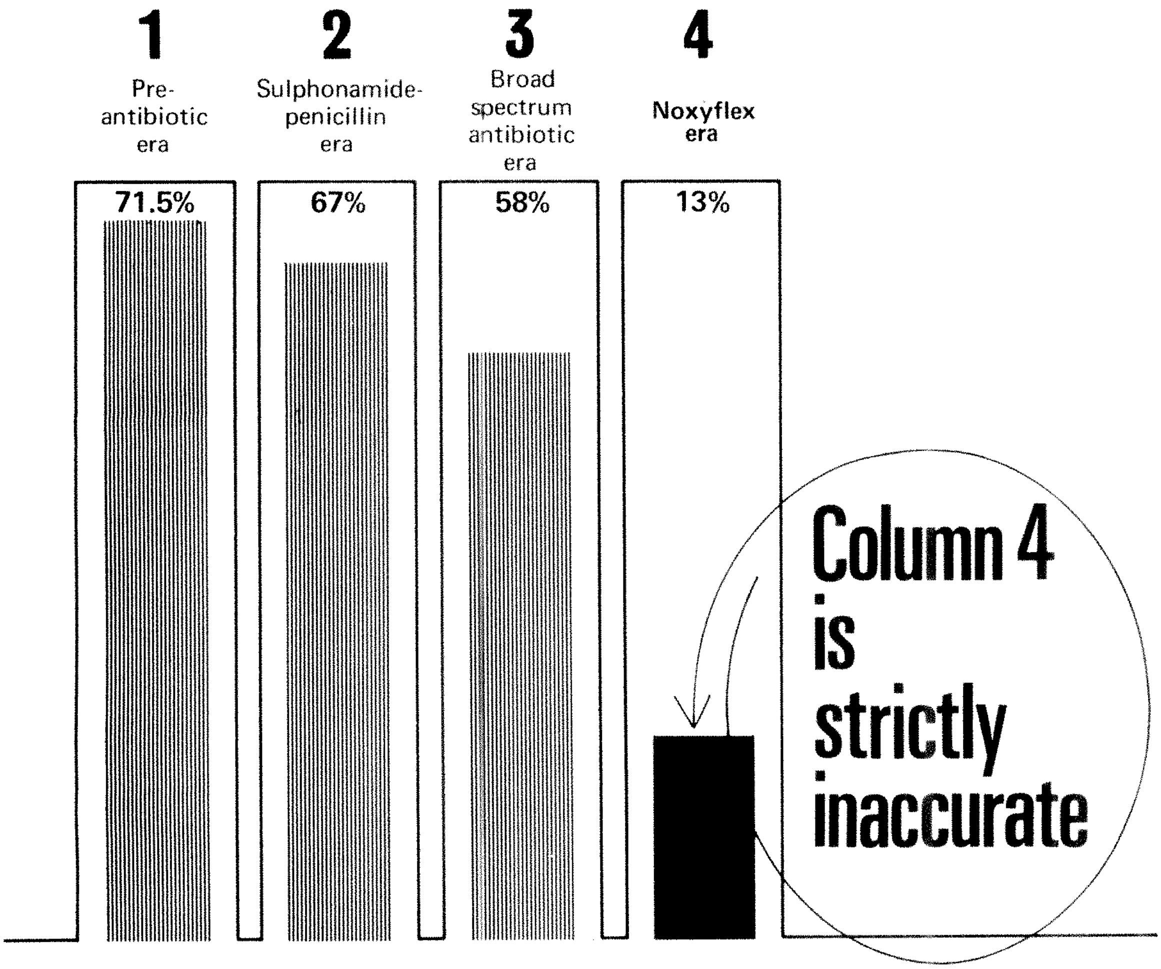

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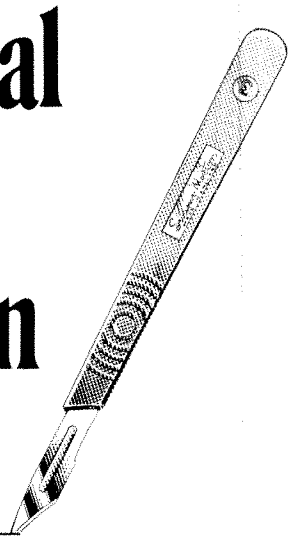

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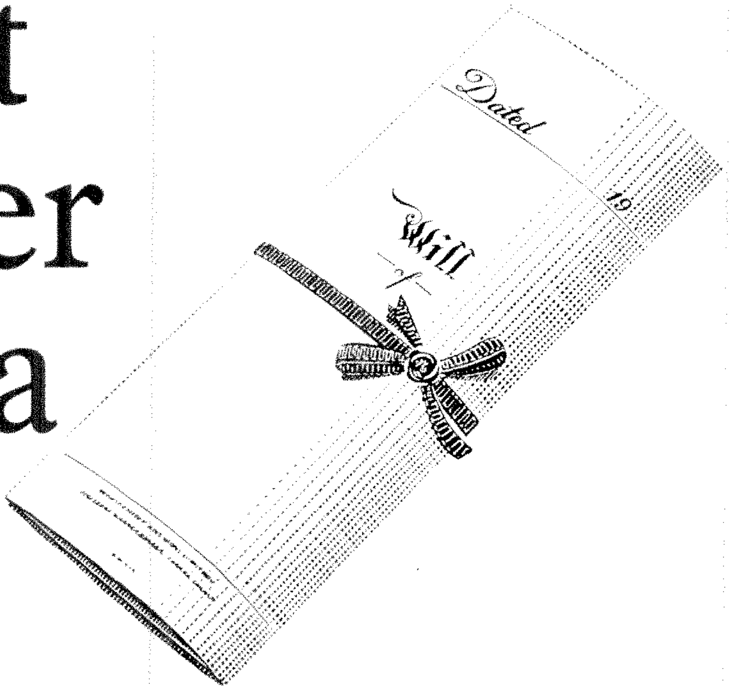

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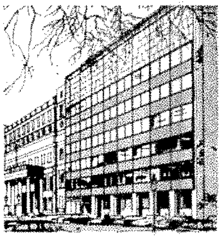
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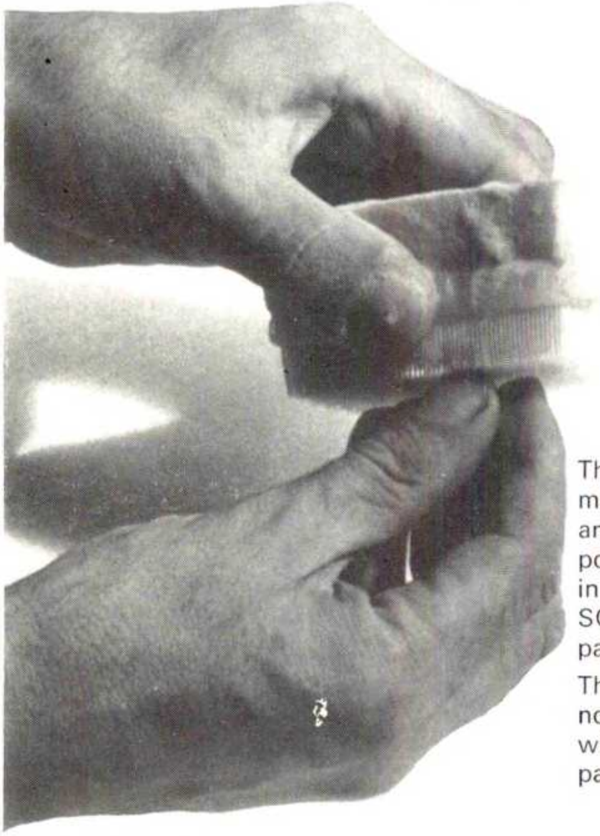

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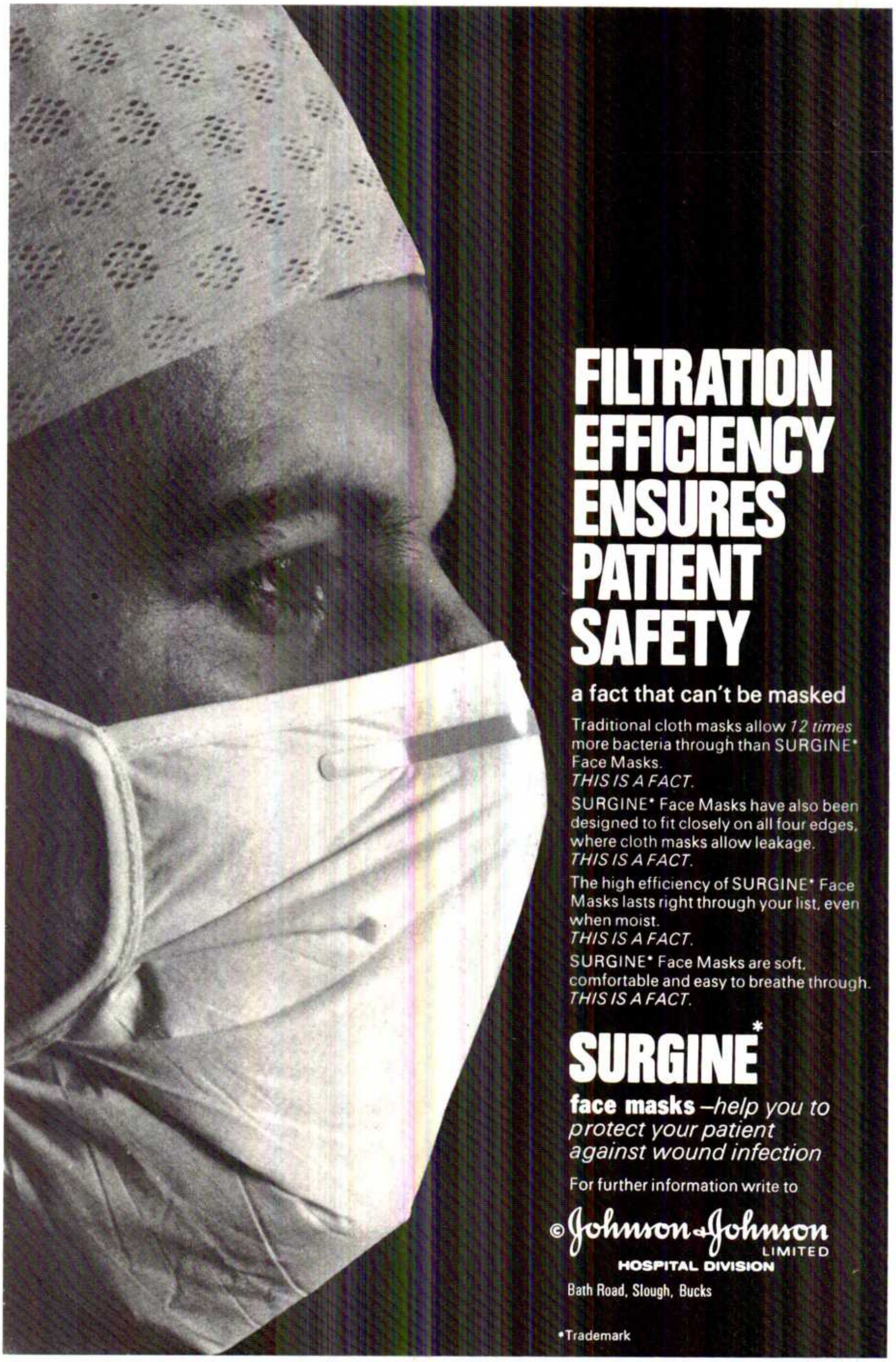

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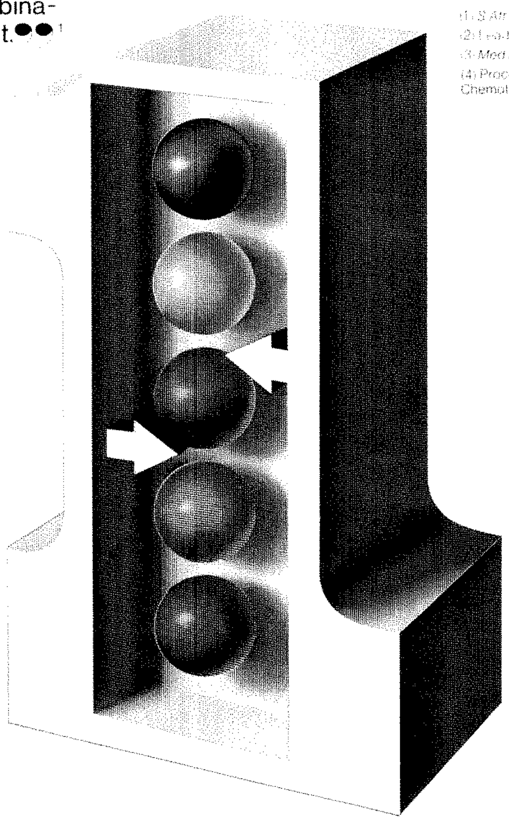

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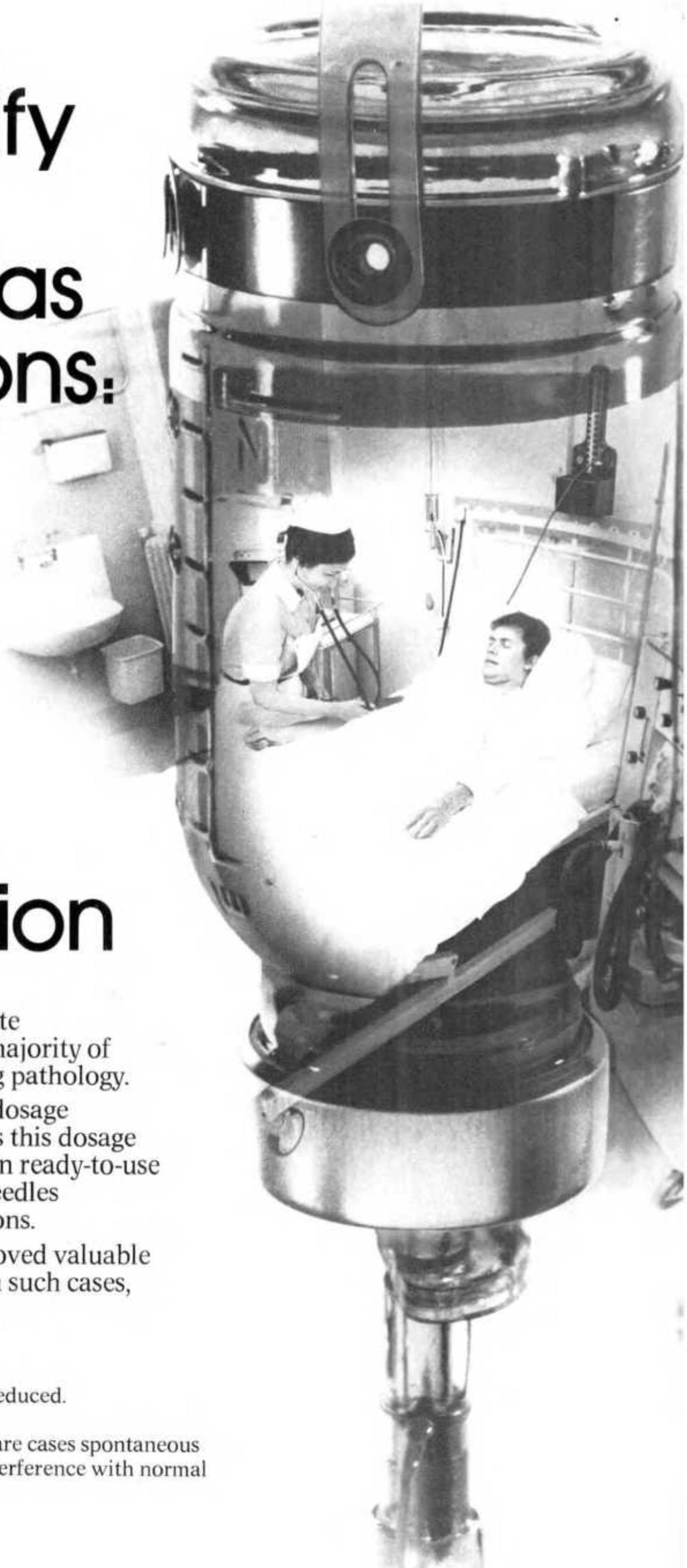

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The patient claimed a loss in weight of 12 kg. over this period.

On examination the patient had generalized cutaneous neurofibromatosis and café-au-lait spots. His abdomen was acutely tender in all areas, with apparent rebound tenderness. No palpable intra-abdominal masses were present and a rectal examination was unhelpful, although the test for faecal occult blood was positive. The white blood-count was 10,100; haemoglobin, 9·8 g. per cent; blood-urea, 39 mg. per cent, and the serum amylase and electrolytes were normal. Plain radiographs of the abdomen indicated obstruction of the small bowel and the ascending colon, although clinically the abdomen was not distended.

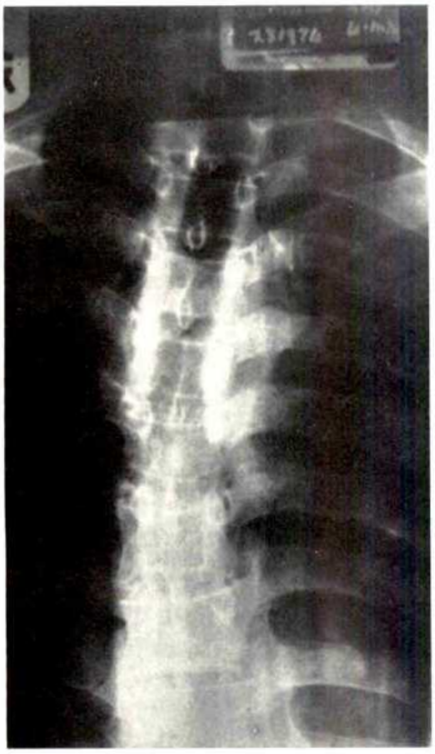
FIG. 4.—Collapsed 5th thoracic vertebra.

At laparotomy a stenosing annular neoplasm of the transverse colon was present, with regional lymph-node involvement. The transverse colon was unusually long and pendulous, and the entire colon contained numerous yellowish-white intramural nodules of a rubbery consistency which were situated so that no line of resection free from involvement could be found. A limited transverse colectomy was performed, transecting colon which was involved by the neurofibromatosis. The end-to-end anastomosis was carried out with difficulty owing to the irregular thickness of the bowel wall containing the intramural nodules.

A small anastomotic leak developed on the sixth postoperative day but had closed spontaneously 5 days later. Thereafter the patient made an uneventful recovery.

Macroscopic examination of the surgical specimen showed that the ulcerating annular neoplasm had fully penetrated the colonic wall and was surrounded by polypoidal masses in the adjacent bowel. Histological examination demonstrated an adenocarcinoma with massive involvement of the lymph-nodes. The carcinomatous tissue was intimately mixed with neurofibromatous tissue (*Fig.* 1) and the adjacent polyps showed the microscopic features of neurofibromata (*Fig.* 2).

A barium-enema examination 2 weeks after the resection displayed multiple intraluminal nodules, varying in size and distributed predominantly in the ascending and residual transverse colon (*Fig.* 3). A skeletal survey at this time revealed thoracic scoliosis in association with a collapsed fifth thoracic vertebra (*Fig.* 4).

DISCUSSION

Neurofibromatosis is a hereditary condition dependent on a dominant gene. Fifty per cent of cases have affected relations (Lukash and Johnson, 1969). The identity of our patient's parents and siblings is unknown, but his children appear to be unaffected. Kyphoscoliosis is the most common osseous abnormality reported, and it occurs in approximately 10 per cent of all patients with neurofibromatosis (Meszaros, Guzzo, and Schorsch, 1966). The scoliosis and vertebral collapse which were present in our patient may indicate replacement of the vertebral body by neurofibromatous tissue or it may be due to secondary spread from the carcinoma.

Levy and Khatib (1960) in their report of a case of von Recklinghausen's disease with asymptomatic involvement of the small and large intestines suggest that visceral involvement is more common than is normally supposed. They suggest that thorough radiological examination of the chest and the gastro-intestinal tract in all cases of von Recklinghausen's disease and prompt surgical excision of the affected bowel should be carried out. Lukash, Morgan, Sennett, and Neilson (1966) support the suggestion of Levy and Khatib (1960) on the incidence of gastro-intestinal involvement and favour local excision as the treatment of choice. Zbinden (1951), in contrast, recommends a conservative policy of observation.

This prognosis of the patient presented here is especially poor in view of the double pathology, the extensive lymphatic metastases, and the vertebral erosion of unknown aetiology. In the presence of sarcomatous degeneration most authors favour resection and continuing supervision of the residual involved bowel. The controversial aspect of this case is in the management of the remaining neurofibromatous bowel.

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A CASE OF INTRALUMINAL DIVERTICULUM OF THE DUODENUM

BY HUGH P. GUERRIER AND MAURICE J. TURNER
NEWTON ABBOT HOSPITAL, DEVON

SUMMARY

The rare anomaly of intraluminal duodenal diverticulum is illustrated by a case history. Twenty-three earlier cases are quoted. In the discussion attention is drawn to the varied clinical presentation which may occur, including the possibilities of intestinal haemorrhage and subacute obstruction. The importance of radiology in making a pre-operative diagnosis is stressed. Theories of possible causation are briefly reviewed.

DIVERTICULA of the duodenum are common enough to be seen almost daily by the practising radiologist. Taking the form of protrusions of the duodenal wall and often lying within the curve of the second part, they occur frequently in the periampullary region. These diverticula are regarded as being usually of little clinical significance. Very rare, by contrast, is the intraluminal diverticulum, only 23 reports of which have been found in the literature. Seventeen cases including the 1 reported here have been confirmed at operation. The remaining cases showed such characteristic radiographic appearances that a confident diagnosis was made (although in 1 patient in this group who later came to operation no diverticulum was found; Heilbrun and Boyden, 1964).

An intraluminal diverticulum is a pouch lying inside the lumen of the duodenum and attached by its neck to the duodenal wall. The opening of the pouch communicates with the duodenal lumen. In the published cases the sex incidence was equal, and the average age at the time of diagnosis was 35 years, the youngest patient being 11 and the oldest 59. Only 1 case has been reported in a child.

The lesion, although rare, is worthy of notice because it can cause serious abdominal symptoms, in particular, intestinal haemorrhage and subacute obstruction. Haematemesis or melaena occurred in 5 of the 24 cases and in 3 patients was associated with severe anaemia (Hb 5·6 g. per cent or less). Another patient suffered from haemorrhagic diarrhoea. Symptoms suggesting repeated attacks of subacute obstruction were reported in 5 of the cases, including our patient. In the majority of instances there were symptoms of mild, chronic, or intermittent dyspepsia, often dating from childhood.

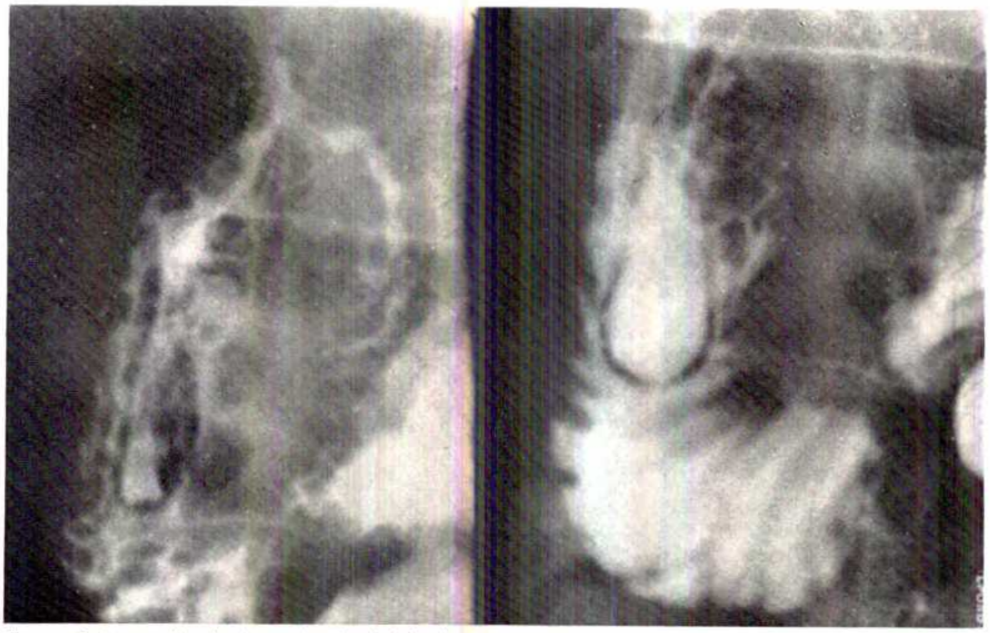

FIG. 1.—Barium studies showing an intraluminal duodenal diverticulum (A) almost empty and (B) distended with barium.

CASE REPORT

A carpenter, aged 41 years, complained of 3-weekly bouts of epigastric pain and vomiting over the previous 12 months, usually occurring about half an hour after a heavy meal. The pain was relieved by vomiting, after which he felt quite well again. He reported a loss of weight of 6·3 kg. Bowel function was regular and there had been no haematemesis or melaena. The patient had

had an appendicectomy 12 years previously but denied any digestive troubles in childhood.

Physical examination was entirely negative.

RADIOLOGICAL FINDINGS.—Barium meal showed a normal oesophagus and stomach, but in the second part of the duodenum barium was held up intermittently in the form of a pouch inside the lumen (*Fig.* 1 B). This pouch varied in shape and size with peristaltic movements. At times it was so small as to be scarcely visible (*Fig.* 1 A). At other times it measured 4 cm. in length and 1·5 cm. in width.

The appearances were interpreted as being caused by an intraluminal diverticulum attached fairly high up on the internal wall of the second part of the duodenum. From this point the diverticulum reached distally as far as the third part of the duodenum when distended. On the radiographic films the shadow of the barium was bounded by a thin radiolucent line which was taken to represent the membranous wall of the diverticulum.

There was some degree of dilatation of the first part of the duodenum, suggesting that intermittent obstruction of the second or third parts had taken place.

OPERATION.—Laparotomy was performed through a midline incision. Considerable peristalsis was seen in the region of the pylorus and the first and second parts of the duodenum, but no other abnormality was visible at this stage. The first and second parts of the duodenum were fully mobilized. A small portion of aberrant pancreatic tissue was found in close association with the second part of the duodenum, but this did not amount to a true annular pancreas nor was the abnormality sufficient to be considered a likely cause of obstruction. The second part of the duodenum was then opened and an intramural diverticulum or pouch was found on the posterior wall. The point of attachment was comfortably clear of the ampulla of Vater. The diverticulum was mobilized, everted, and excised, and a running suture was placed through the excised mucosal edges into the duodenum, which was closed in two layers. The abdomen was closed with a Redivac drain.

The patient made an uninterrupted recovery and 2 years later he is symptom-free and eating very well.

DISCUSSION

Table I shows the details of the 24 reported cases of intraluminal duodenal diverticulum. There seems no reason to doubt that the majority are of congenital origin, and one theory is that the diverticulum is produced by peristaltic pressure on the upper surface of a perforate congenital diaphragm of the duodenum. Several descriptions accord well with this theory (Silcock, 1885; Nelson, 1947; Meyer and Edgren, 1956; Coors and Mitchum, 1962; Curtis, Simpson, and Lowdon, 1965). In other cases, however, the pouch is attached only to a small part of the circumference of the gut and other theories have been proposed, such as partial reduplication of the duodenum or a pulsion effect upon a prominent mucosal fold. The fact that different structural forms of diverticula are found at operation suggests that more than one mode of formation is responsible. The case of Wenz (1963) is of particular interest in that two separate intraluminal diverticula were found in the same patient.

There are other associations which may be relevant. One case of intraluminal duodenal diverticulum occurred in a Mongol and there is known to be a relatively high incidence of duodenal stenosis and atresia in Mongols (Curtis and others, 1965). The association of a congenital duodenal septum with an annular pancreas is well known (Harper, 1967), and in 3 of the 24 cases of intraluminal diverticulum, including the case reported here, the presence of a partial degree of annular pancreas or other pancreatic anomaly has been observed (Coors and Mitchum, 1962; Petty and Mousley, 1966). In the case of Buisseret and Van Den Eynde (1962) an associated malrotation of the gut with the common mesentery was recorded.

Table I.—SUMMARY OF THE DETAILS OF 24 RECORDED CASES (12 MALES AND 12 FEMALES)* OF INTRALUMINAL DUODENAL DIVERTICULUM

SIGNS AND SYMPTOMS		RADIOLOGICAL FINDINGS		OPERATION (17 Cases)	
Details	No. of Cases	Details	No. of Cases	Details	No. of Cases
Pain; usually epigastric and intermittent	17	Intraluminal pouch	21	Site of pouch near ampulla of Vater	12
Vomiting	6	Changing size of pouch during examination	13	Histology: pouch formed of mucous and submucous tissues with muscularis mucosae	12
Bleeding; usually melaena	6			Inflamed pouch	1
Symptoms since childhood	5			Ulcerated pouch	2
Diarrhoea	3			Foreign body in pouch	
Physical signs: tender epigastrium only	5				

* Age—average: 35 years; youngest 11 years; oldest 59 years.

In several patients foreign bodies have been found in the diverticula, such as a penny (Meyer and Edgren, 1956) and food debris (Wiot and Spiro, 1963). Ulceration of the diverticulum was found in 2 cases who had presented with melaena (Zatzkin, Macy, and Kveton, 1959; Kessler and Witmer, 1964).

It is noteworthy that in the great majority of cases who had operations the site of attachment of the diverticulum was found to be near the ampulla of Vater, showing the need for special operative care to avoid damage to the biliary or pancreatic ducts, a complication which has been reported in 1 instance (Wiot and Spiro, 1963). The 5 other recorded cases had no special features (Kinzer, 1949; Köhler, 1960; Hirsch and Mal, 1962; Laudan and Norton, 1963; Newman and Nathan, 1968).

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AN UNUSUAL DISLOCATION OF THE HIP

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ROWLEY BRISTOW ORTHOPAEDIC HOSPITAL, PYRFORD, WOKING, SURREY

ANTERIOR dislocations of the hip-joint are classified into pubic, perineal, and obturator types, and of these the last is the most common. We wish to report a case of an obturator dislocation which differs from the usual type, where the head of the femur rests in the obturator foramen, in that the head passed almost completely through the foramen and became locked in this position.

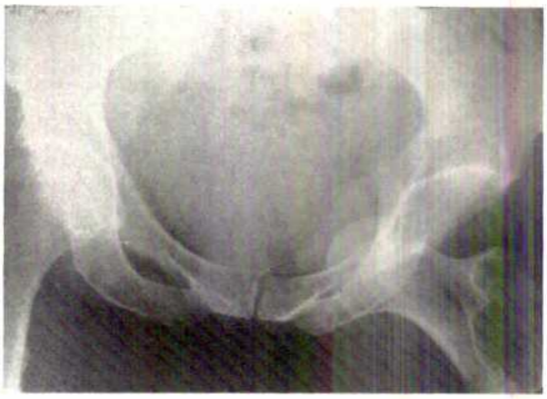
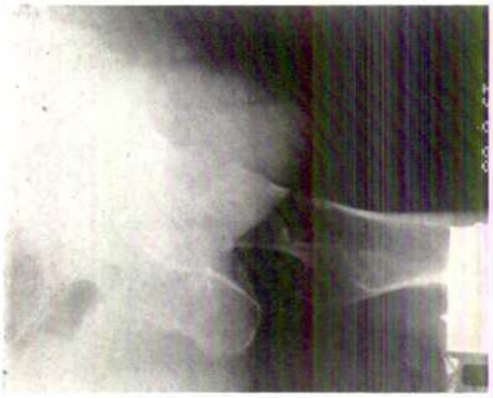
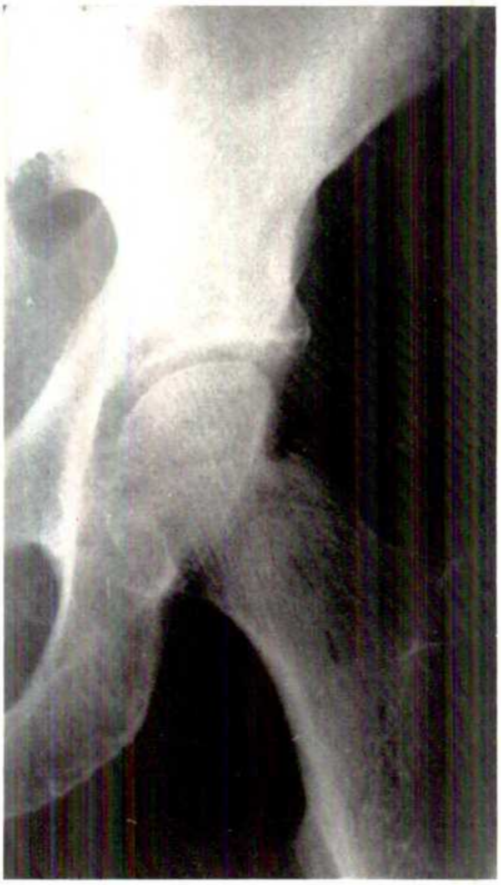


FIG. 1.—Radiograph showing an obturator dislocation of the hip with the head of the femur protruding almost completely through the obturator foramen.



A



B

FIG. 2.—Radiographs showing the dislocation to be reduced. A notch is present on the anterosuperior aspect of the head of the femur. A, Lateral view. B, Anteroposterior view.

CASE REPORT

Mrs. K., aged 57 years, had been a front-seat passenger in a car which had overturned while travelling at about 30 m.p.h. On admission to hospital she was unable to remember the accident clearly owing to a minor head injury, but she did complain of pain in the region of the left hip. There was no previous history of hip trouble. On examination the patient was obese and there was no obvious swelling in the region of the left hip. The left thigh was held fixed in a position of 30 degrees of abduction, slight flexion, and in mid-rotation. The region was moderately tender but careful palpation failed to reveal the head of the femur in the perineum, in the groin, or in the buttock. All pulses in the leg were present and there was no nerve damage. There was neither active nor passive movement at the hip-joint.

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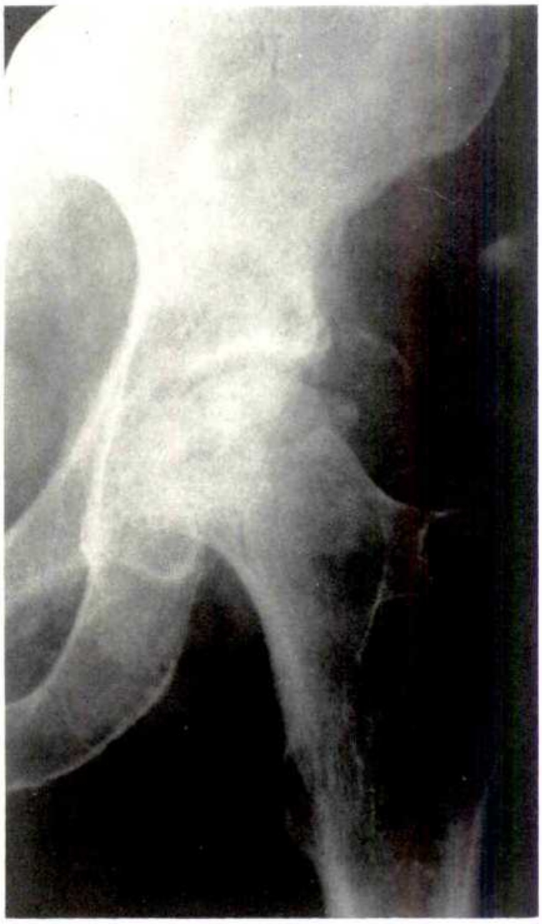

FIG. 3.—Radiograph showing avascular necrosis of the head of the femur.

Radiographs (*Fig.* 1) showed an obturator dislocation of the hip with the head of the femur protruding almost completely through the obturator foramen. The lateral radiograph confirmed that the dislocation was not of the pubic type, but the quality was too poor to reproduce.

Under a general anaesthetic the head of the femur was found to be firmly locked in the dislocated position. Longitudinal traction was applied and an attempt was made to lever the head back into the acetabulum using the operator's knee in the adductor region as a fulcrum. This appeared to fail but it must have disengaged the head, because, while breath was being regained, a simple rotation of the leg was performed and the hip reduced.

Radiographs at this stage (*Fig.* 2) showed the dislocation to be reduced and revealed a notch on the anterosuperior aspect of the head of the femur, which, in retrospect, had also been present in the previous radiographs (*Fig.* 1). Skeletal traction was applied and maintained for 3 weeks, and after a further week's bed-rest with the leg free the patient was allowed to walk, taking partial weight on the leg. She was discharged 7 weeks after injury walking with the aid of elbow crutches.

Subsequently the head of the femur developed avascular necrosis and disintegrated (*Fig.* 3). Eighteen months following injury a McKee–Farrar prosthesis was inserted (*Fig.* 4). The notch shown on the early radiographs could not be identified with certainty at operation owing to the deterioration of the femoral head. Two months after the operation the patient was pain-free and walking with aid of the one stick.

DISCUSSION

A search of the literature has not revealed a case in which the greater part of the head of the femur has passed through the obturator foramen or one in which the head has become immediately impacted in the foramen. There are, however, reports by Cooper (1823) and Watkins (1923) of unreduced dislocations being held by new bone formation, but in none of these did the head pass through the foramen.

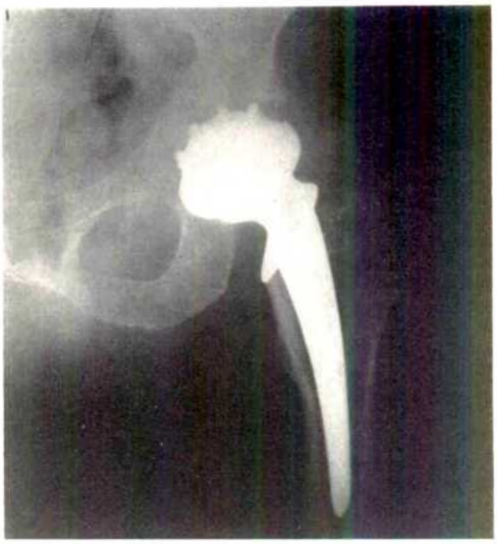

FIG. 4.—Radiograph showing a McKee-Farrar prosthesis in position and the relatively circular obturator foramen.

In the male pelvis the obturator foramen is too small for the head of the femur to pass through, but in 1 out of 25 female pelves examined by one of us (R. F. B.) the foramen was almost able to accommodate the head.

The likely mechanism in the present case is that the hip dislocated into the obturator position by forced abduction of the thigh. As the head passed into the relatively circular obturator foramen the sharp anterolateral margin of the foramen indented the anterosuperior aspect of the head, effectively locking it in the dislocated position. Unfortunately, the exact method of reduction is not known as it occurred semi-accidentally, but it is almost certain that the head was disimpacted and partially reduced by traction and a lateral force on the upper thigh.

The avascular necrosis which occurred in the present case was not surprising as 8·8 per cent of the anterior dislocations reported by Brav (1962) developed this complication.

The report by Thompson and Epstein (1951) indicates that one-quarter of hip dislocations occurs in females and about 5 per cent are of the obturator type. The fact that the event described here appears to be possible only in obturator dislocations in females, and then only once in 25 instances, explains its rarity.

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REVIEWS AND NOTICES OF BOOKS

Current Concepts in the Management of Leukemia and Lymphoma. Edited by J. E. ULTMANN, M. L. GRIEM, W. H. KUSTEN, and R. W. WISSLER. 9½ × 6½ in. Pp. 198 + xiv. Illustrated. 1971. London: William Heinemann. £6·70.

THERE can be little doubt that lymphoma and leukaemia are subjects in which we require far more information as regards treatment.

This volume presents the proceedings of the Fourth Biennial Cancer Teaching Symposium held at the University of Chicago in March, 1970. At this symposium over 450 physicians and scientists took part in the discussions.

Every aspect of the lymphoma and leukaemia problem is considered in the various papers. The value of cytoxan, oncovin, and prednisone are considered at length as to their use in the treatment of acute leukaemia.

At the present time it seems that Hodgkin's disease and Burkitt's lymphoma are to a great extent curable, but there seems little improvement after treatment in the chronic leukaemias.

This is a useful monograph and it will make a strong appeal to all cancer research workers who are working in this all too difficult field.

This book is No. 36 in the series of 'Recent Results in Cancer Research'.

Clinical Anatomy. By HAROLD ELLIS, M.A., M.Ch., D.M., F.R.C.S., London. Fifth edition. 8½ × 5¼ in. Pp. 389 + xiv. Illustrated. 1971. Oxford: Blackwell Scientific Publications. £2·50.

THIS is a book which is most important for the medical student of today, for it highlights those features of anatomy which are of clinical importance. It is right and proper that a practical surgeon should write such a book because he can stress those areas or parts of anatomy which are of real importance to a doctor. Professor Ellis approaches anatomy as an anatomist, as an examiner in anatomy for the Primary Fellowship of the Royal College of Surgeons, and lastly as a lecturer. The popularity of this book can be seen by the fact that five editions have appeared in just over ten years, and one edition was reprinted. These facts speak for themselves.

One of the important features of this book is the excellence of the illustrations. Most of the line illustrations are original and quite simple, but very informative.

In our opinion this new edition will continue to enjoy the popularity it deserves.

The price of the book is moderate and well within the budget of the student.

Mechanical Devices for Cardiopulmonary Assistance. Edited by R. H. BARTLETT, M.D., California, P. A. DRINKER, Ph.D., Boston, and P. M. GALLETTI, M.D., Ph.D., Providence. 9⅖ × 6⅗ in. Pp. 195 + xv. Illustrated. 1971. Basel: S. Kargar. £7·20.

THIS volume is No. 6 in the series of 'Advances in Cardiology'. It contains the proceedings of a symposium on this subject held in Boston, Mass., in March, 1970, under the auspices of the Association for the Advancement of Medical Instrumentation.

The great advances which have been made during the past twenty years in extracorporeal circulation has to be seen to be believed. These advances have been due to the co-operation between surgeons, physiologists, and bio-engineering research workers. In this volume the numerous contributors have set forth in a fascinating way the various uses of silicone-membrane technology. The cardiac surgeon and the cardiac transplant surgeon can now take their time during operations, for there is now no time limit to extracorporeal circulation.

This book contains a vast amount of valuable information concerning gas and particulate embolism, and thrombosis in extracorporeal circuits, all of which are central to further development.

A first-class production on a very important subject.

Oral Pathology. By DONALD A. KERR, B.S., D.D.S., M.S., and MAJOR M. ASH, jun., B.S., D.D.S., M.S., Ann Arbor. Third edition. 9 × 6 in. Pp. 310 + xv, with 165 illustrations. 1971. London: Henry Kimpton. £1·40.

THIS book is an introduction to general and oral pathology for the dental hygienist. It covers this important subject in a lucid and practical way. The illustrations are of a high standard, especially the photomicrographs.

The chapters on developmental disturbances, neoplasia, nutritional disturbances, dental caries, and endocrine diseases are particularly good.

This is the third edition in ten years and this fact speaks for the popularity of the book.

Diseases of the Urinary Tract. Specially Commissioned articles from the *British Medical Journal.* 8½ × 5½ in. Pp. 122. Illustrated. 1971. London: British Medical Association. £1.

THIS paperback contains articles on the diseases of the urinary tract which appeared in the *British Medical Journal* in the year 1970. These articles, all written by experts in their own particular field, are concise and practical and the illustrations are excellent.

Articles on chronic renal failure, the nephrotic syndrome, and cancer of the prostate are the best in the book.

Students and practitioners who wish to bring themselves up to date on modern practice in this field will find this a readable account of the important aspects of the speciality.

The price of the book is cheap and within the purse of any student.

Diseases of the Ear, Nose and Throat. Vols. 1–4. Edited by JOHN BALLANTYNE, F.R.C.S., D.L.O., London, and JOHN GROVES, M.B., B.S., F.R.C.S., London. Third edition. 9½ × 6¼ in. Pp. 2109. Illustrated. 1971. London: The Butterworth Group. £32.

THIS comprehensive four-volume work constitutes the third edition of Scott-Brown's original textbook, which was originally published in 1952.

Volume 1 of some 450 pages is devoted to basic sciences and contains some excellent chapters on the anatomy of the ear, nose, and throat, with a considerable number of original illustrations. Professor David Slome contributes an outstanding account of the physiology of the nose and paranasal sinuses, the mouth and oesophagus, as well as the physiology of the larynx and tracheobronchial tree. The mechanism of normal speech is described in a very practical way by D. B. Fry.

The illustrations throughout the volume are of a very high order and there are ten coloured plates which enhance the value of the book considerably.

A very up-to-date bibliography is given at the end of the book.

Volume 2 contains 670 pages and deals extensively with the ear. The numerous contributors from many centres in England have covered the subject of diseases of the ear in a most comprehensive manner.

Congenital conditions of the ear, infections of the middle ear, facial paralysis, otosclerosis, and acoustic neuroma are some of the best chapters in this volume.

Volume 3 deals with every aspect of diseases of the nose. The outstanding contribution to this volume is by G. H. Bateman, who writes on trans-sphenoidal hypophysectomy. This is an excellent account of the operation.

Volume 4 is devoted to diseases of the throat; it is divided into two parts: Part 1 deals with the diseases of the mouth, pharynx, and oesophagus, while Part 2 is concerned with diseases of the larynx and tracheobronchial tree.

Perhaps the most interesting part of this volume is that dealing with the diseases of the larynx, which is most comprehensive and very well illustrated.

This large work is a credit to British medicine and as a reference work it could not be bettered. Surgeons specializing in diseases of the ear, nose, and throat will certainly want to possess this important work. Postgraduates preparing for the Fellowship of the Royal Colleges in E.N.T. will find everything they need in these volumes.

Outline of Orthopaedics. By J. CRAWFORD ADAMS, M.D., M.S., F.R.C.S., London. Seventh edition. 8½ × 5½ in. Pp. 475 + vii. Illustrated. 1971. Edinburgh: Churchill Livingstone. £2·25.

THE seventh edition of this well-known book has been carefully revised, and in parts rewritten.

Seven editions of a book in fifteen years is good going by any standards, especially when most of the editions were reprinted. This well-written, concise book with clear-cut illustrations is ideal for students and the price is most moderate.

A First Notebook of Head Injury. By KENNETH G. JAMIESON, M.D., M.S. (Melb.), F.R.A.C.S., F.A.C.S., Brisbane. Second edition. 8½ × 5½ in. Pp. 148 + xii. Illustrated. 1971. London: The Butterworth Group. £1·60.

THIS useful paperback contains a wealth of information regarding head injuries. Trauma to the skull and its contents is still on the increase and most of it comes from road accidents.

This book is ideal for the student as it is arranged in notebook form for easy reference.

The numerous line drawings are clear and help the reader to understand the text.

This new second edition gives an account of injury and tumours of the temporal lobes.

The author, with his matured clinical acumen, gives a systematic account of the mechanisms, pathology, clinical picture, and differential diagnosis of the commonly encountered complications of head injury.

An excellent notebook for the student and cheap as well.

Intensive Care of the Surgical Patient. Edited by MARSHALL D. GOLDIN, M.D., M.S., Chicago. 8¾ × 5¾ in. Pp. 500 + xii. Illustrated. 1971. Chicago: Year Book Medical Publishers. $17.95.

WITH the ever-increasing field of modern surgery, particularly in cardiovascular and thoracic surgery, it is inevitable that hospitals should have an intensive care unit. Also the increase in road-traffic accidents, resulting very often in extensive multiple injuries, all require intensive care, especially burn cases. This book covers the whole field of intensive care, and it is made up of articles by 42 contributors from various surgical centres in America. The field is a wide one, from postanaesthetic management to transplantation of organs.

The various methods of electronic monitoring are well described. Tracheostomy is described in some detail; it seems to be a common operation in the treatment of extensive road-traffic accidents. The chapter on postoperative haemorrhage is very practical and informative. Parenteral intubation, drugs useful in the treatment of shock, pediatric cardiac surgery, and peripheral vascular surgery are some of the best chapters in this book.

This is a book which should be available in every intensive care unit in our hospitals.

Today's Drugs. Vol. 2. Specially commissioned articles from the *British Medical Journal.* 8½ × 5½ in. Pp. 204. 1971. London: British Medical Association. £1.

THIS is a useful second volume dealing with today's drugs. It is concerned with hormones and oral contraceptives, cardiovascular agents, and drugs acting on the gastro-intestinal tract.

All clinicians will find this a useful desk book for quick reference.

Scoliosis and Growth. Edited by P. A. ZORAB, M.D., M.R.C.P. 9½ × 7½ in. Pp. 154 + xi. Illustrated. 1971. Edinburgh: Churchill Livingstone. £4.

THIS book contains the proceedings of a Third Symposium held at the Institute of Diseases of the Chest, Brompton Hospital, London, on 13 November, 1970.

Scoliosis is an interesting condition of the spine and it is surely gratifying that the Institute of Diseases of the Chest has arranged three symposia dealing with scoliosis; the first was in July, 1965, the second in December, 1967, and the third in November, 1970.

This third symposium deals with some very interesting aspects of scoliosis, and the various contributors come from near and far. Such problems as growth and scoliosis, causation of idiopathic scoliosis, skeletal growth in Morquio's disease, growth of the spinal articular processes, and the effects of early fusion on spine growth are discussed in great detail.

There is an excellent account by Lynne Reid of lung growth. The bronchial tree is developed by the sixteenth week of intra-uterine life. The alveoli, as is commonly understood, develop after birth, increasing in number until the age of 8 years and in size until growth of the chest wall is finished.

This is an interesting and stimulating book, full of useful information not obtainable from any other source. Anyone interested in spinal curvature, such as orthopaedic surgeons, pathologists, and physiotherapists, will find a mine of information within its pages.

Special Topics in Stereotaxis, Epilepsy, Disorders of Behaviour, and Autonomic Balance. Edited by W. UMBACH, Berlin. 9 × 6 in. Pp. 182. Illustrated. 1971. Stuttgart. Hippokrates Verlag. DM.36.

THIS paperback contains the papers which were presented at a Berlin Symposium in 1970 by notable physicians and scientists from four countries.

The very latest results concerning stereotaxic stimulation and coagulation in cases of special central disturbances are discussed in detail and illustrated with clinical photographs and line drawings showing the exact spot in the brain which undergoes coagulation.

The types of cases which have been investigated are drug-resistant epilepsy, behavioural disturbances, aggressiveness, and those suffering from unbearable extreme pain.

The various methods and techniques for the electrocoagulations are described in a very practical way.

Although this excellent book is published in Germany, the publishers should be congratulated for bringing out this English edition, for it will be found of real value to all neurologists, physiologists, and psychiatrists.

Methods of Ossiculoplasty. By JAMES R. TABOR, M.D., F.A.C.S. 8¾ × 5¾ in. Pp. 88 + ix. Illustrated. 1971. Springfield, Ill.: Charles C. Thomas. $6.75.

THIS monograph is devoted to the indications for, the operation of, and the results following ossiculoplasty. The author records the clinical results regarding 271 consecutive ossiculoplasties.

This book covers the whole subject of ossiculoplasty in a very complete manner and numerous drawings illustrate the technique of the operation.

Specific ossicular reconstructions are described and the results are tabulated in detail. A discussion of statistical comparisons is presented. Advantages and disadvantages of different statistical approaches are discussed as they are related to the results in the different patient populations of the surgical groups.

Regeneration of Liver and Kidney. By NANCY L. R. BUCHER, M.D., and RONALD A. MALT, M.D., Boston. 8⅛ × 5⅝ in. Pp. 277 + xiv. Illustrated. 1971. Edinburgh: Churchill Livingstone. £6.

IN this age of organ transplantation this is an important and useful book, and is indispensable to cancer research workers studying the regulation of cell growth and disorders in whole organs.

The authors have published much of the material in this volume in articles appearing in the *New England Journal of Medicine*, but it is obvious that clinicians and research workers prefer all these facts segregated in one book. Intensified probing into the process of tissue restoration and repair assumes new priority as modern techniques and surgical skills succeed in arresting impairment and in prolonged survival. The regeneration process of the liver and kidney offers an ideal opportunity for examining the transition of tissue from an essentially static condition to active growth. These two organs have 'expanding' cell populations; partial ablation of tissue mass readily induces a regulated growth which ceases when the deficit has been restored.

This book will be a 'must' for cancer research workers, physiologists, and pathologists.

The Craft of Surgery. Vols. 1–3. Edited by PHILIP COOPER, M.D., New York. Second edition. 10 × 7 in. Pp. 1997. Illustrated. 1971. Edinburgh: Churchill Livingstone. £31·50.

THIS comprehensive three-volume work covers the whole field of modern surgery. Although the vast majority of the numerous contributors come from various surgical centres in the United States of America, a few come from Australia and three from England, namely Norman Tanner, John Goligher, and the late Alan Hunt.

The first of these large volumes deals with a wide field, including the head and neck, the skin, the breast, and the thorax including the oesophagus.

George Crile, jun., contributes an excellent account of benign tumours of the thyroid. Articles on achalasia and oesophageal hiatal hernia are excellent.

As one would expect, the various chapters on the surgery of the thorax are comprehensive and include articles on transplantation of the heart and myocardial revascularization. Cardiovascular injuries are covered in a very practical manner; and the many illustrations depicting the various operative techniques are good.

Volume 2 is concerned with the vascular system, the abdomen, and the female genitalia.

Every type of aneurysm is considered in some detail, and various forms of arterial grafting are well described and illustrated. The many forms of shunts are described. The large section dealing with the abdomen is probably the best in the book.

Norman Tanner contributes a very interesting and practical chapter on the use of drains in the peritoneal cavity and the abdominal wall. John Goligher is at his best in his chapter on synchronous combined abdominoperineal excision of the rectum. Milton Porten presents the surgery of hypoglycaemia in a modern setting.

Volume 3 deals with the extremities and urological and pediatric surgery. Neurological surgery and general orthopaedics complete the volume.

William Littler presents the surgery of the hand in a most interesting and practical way. Amputations receive the attention they deserve in this traumatic age.

Renal transplantation is well described and illustrated.

Head injury, which is on the increase in most parts of the world, is dealt with in a very practical manner.

The modern treatment of rheumatoid arthritis by surgery is a great advance in surgical technique.

One of the features of this large work is the excellence of the illustrations; they certainly enhance the value of the written word.

As a work of reference this production could not be bettered, and young surgeons everywhere should obtain a copy for their benefit.

The Illness of Trauma. By GARBETT PIPKIN, M.D., and VICTOR BUHLER, M.D., Kansas. 9 × 6 in. Pp. 167 + ix. Illustrated. 1971. Springfield, Ill.: Charles C. Thomas. $12.75.

THIS book is concerned with the treatment of trauma as seen in America today. Every facet of the diagnosis and treatment of severe injury has been covered. Intensive care can be overdone, as can be seen in *Fig.* 41 on p. 91 :

the multimonitoring system is really too much, the patient appears to have a needle in every vein and a tube in every orifice.

There is a series of care studies which makes interesting reading. Fat embolism in the lungs, kidneys, and brain is a cause of death which we do not see so frequently over here.

It seems that the authors' wish is to alert the clinicians to the cause of the injured patient's morbidity by a study of the clinical indices.

Atlas for Surgical Repair of Cleft Lip, Cleft Palate, and Noncleft Velopharyngeal Incompetence. By Richard B. Yules, M.D., Boston. 11 × 8½ in. Pp. 200 + vii. Illustrated. 1971. Springfield, Ill.: Charles C. Thomas. $24.

This profusely illustrated atlas presents all the common surgical procedures which are in use today for the correction of cleft lip and cleft palate, both primary and secondary deformities. The illustrations are line drawings and they have been ably executed. We agree with the author when he states that there is no 'correct surgical procedure' for any given defect. This book deals with general patient management, the time of operation, a selection of operative techniques, and a description of the surgical technique itself.

All those postgraduate surgeons who want to specialize in plastic repair of the lip and palate will find this book useful.

Chest Injuries. Physiologic Principles and Emergency Management. By Emil A. Naclerio, M.D., F.A.C.S., F.C.C.P., F.A.C.C., New York. 10 × 6¾ in. Pp. 383 + xiv. Illustrated. 1971. New York: Grune & Stratton Inc. $28.50.

In this age of trauma the chest is often injured in road accidents, by gunshot wounds, or by stabbings. In the United States of America accidents are the leading cause of death up to the age of 37 years. This in itself is ample justification for the publication of this book.

The author gives a very practical account of first aid for thoracic injuries and this is illustrated by some sixteen coloured plates by Frank H. Netter. These plates are quite a feature of the book and enhance the value of the volume.

Every aspect of chest injury is amply covered, from tracheostomy to hernia of the lung. The numerous line drawings, the majority of which are original, are a feature of this book.

Thoracic cage injuries and wounds of the pleura and heart all receive good coverage.

There is an excellent bibliography at the end of the book.

This is a book which can be recommended to students, nurses, and resident medical officers. Physiotherapists will find much to interest them in this very practical volume.

Occult Traumatic Lesions of the Cervical Vertebrae. By Martin S. Abel, M.D., Palo Alto. Pp. 148 + viii. Illustrated. 1971. St. Louis: Warren H. Green Inc. $12.50.

This is an interesting monograph written by a radiologist who has spent many years in improving X-ray technique concerning the cervical spine.

The author has made use of many cadaver experiments and microscopical studies of old injuries. These studies over many years have demonstrated in a convincing way that the lateral processes of C.1 and C.2 are commonly fractured in relatively minor extension and flexing injuries.

The X-ray pictures of these fractures are of a very high standard and are very convincing.

The author considers that occult injuries are a significant, and probably the leading, cause of hypertrophic changes limited to the smaller joints of the cervical region of the vertebral column. Similar changes have been found in young adult spastics which point to injury during delivery.

This monograph will serve as a useful reference volume on a particular condition which is not well understood.

Gynaecology. Essentials of Clinical Practice. By Thomas H. Green, jun., M.D., Massachusetts. Second edition. 9⅛ × 6 in. Pp. 511 + xii. Illustrated. 1971. Edinburgh: Churchill Livingstone. £4·50.

The first edition of this paperback was published just over five years ago and the second edition has just been published, and it shows evidence of a thorough revision.

The line drawings throughout the book are clear and instructive.

The chapters on endometriosis and conception control are particularly good.

This is a book for students and its price is moderate and well within the purse of the average student.

Cleft Lip and Palate. Surgical, Dental and Speech Aspects. Edited by William C. Grabb, M.D., Ann Arbor; Sheldon W. Rosenstein, D.D.S., Chicago; and Kenneth R. Bzoch, Ph.D., Gainesville. 10 × 7 in. Pp. 916 + xxxiii. Illustrated. 1971. Edinburgh: Churchill Livingstone. £21.

This is the most comprehensive work on cleft lip and palate that has so far been published.

The exhaustive text, the work of 71 authorities in the fields of surgery, dentistry, and speech, is divided into five parts: Part 1 is concerned with general aspects which include anatomy, embryology, and classification of cleft lip and palate.

Part 2 deals with the surgical aspects of cleft lip and palate; Part 3 is devoted to maxillary orthopaedics and bone-grafting in cleft palate; Part 4 is concerned with the dental aspects of cleft lip and palate; while Part 5 deals with speech and hearing, including communicative disorders related to cleft lip and palate.

As one would expect in a work edited by American surgeons and dentists, the vast majority of the contributors come from American centres, but there are some from England, Canada, Sweden, and Switzerland.

In a comprehensive work such as this, with a multiplicity of operative techniques, good illustrations are essential. The reader is not disappointed, for throughout the volume excellent drawings illustrate the text. The pre- and postoperative clinical pictures are quite a feature of this volume.

At the end of each chapter there is a list of references dealing with the subject-matter. There is also a very complete subject index at the end of the work.

This large and important work will be read by general and oral surgeons, plastic surgeons, dental surgeons, and speech therapists. It will also be the reference volume for students and residents in hospital.

An excellent production.

Klinische Sudeckprophylaxe und Therapie. By Jost L. Bircher, Basel. 9 × 6 in. Pp. 60 + viii. Illustrated. 1971. Berlin: Springer-Verlag. DM.24.

This monograph concerns the experimental production and treatment of Sudeck's atrophy. The author has managed consistently to produce lesions resembling Sudeck's atrophy in rabbits by injecting the area around one of the sciatic nerves with a phenol solution.

The author then continues to show that the exhibition of Tanderil, Hydergin, and Phenergan together are successful in reducing the pathological changes which he initially induced in the experimental rabbits. The clinical relationship of his findings are discussed. The book contains a very extensive bibliography of this very specialized subject.

Atlas of Transbronchial Biopsy. Early Diagnosis of Peripheral Pulmonary Carcinomas. By EITAKA TSUBOI, M.D., Tokyo. 11¾ × 8¼ in. Pp. 151 + viii. Illustrated. 1971. Stuttgart: Georg Thieme Verlag. DM.125.

THIS is one of the best, if not the best, medical book which has been produced in Japan since the Second World War.

Cancer of the lung is one of the commonest causes of death in most places in the world, but especially so in Japan.

Cytology is one of the modern adjuncts to diagnostic methods and is today a fully accepted diagnostic procedure.

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In this large atlas there are some 215 illustrations, 35 of which are in colour. The illustrations of radiographs, operative techniques, pathological specimens, and photomicrographs are of a high order.

This book provides an exhaustive discussion of the method of transbronchial biopsy and describes its importance in the detection of lung cancer in Japan.

This atlas will have a wide appeal not only to chest physicians and surgeons but also to pathologists and research workers. It should find a place in every medical library.

Frontiers of Nuclear Medicine. Edited by WOLFGANG HORST, Zürich. 9¾ × 6½ in. Pp. 306 + xvi. Illustrated. 1971. Berlin: Springer-Verlag. DM.98.

THIS book is a collection of twenty-four separate papers dealing with various aspects of nuclear medicine and has been dedicated to the memory of George von Hevesy, who died in 1966. The subject-matter of the papers ranges from computer analysis of radioactive techniques to the use of various radio-isotopes in medical diagnosis. The majority of the papers are in English and all of them are extremely well illustrated. This volume undoubtedly gives a quick up-to-date review of the most recent advances in radio-isotope techniques, and should be welcomed by all those interested in this field of medicine. The printing and publication are of this publisher's usual high standard.

Encyclopedia of Urology. Edited by C. E. ALKEN, Hamburg; V. W. DIX, London; W. E. GOODWIN, Los Angeles; and E. WILDBOLZ, Bern. 9⅜ × 6½ in. Pp. 256 + x, with 132 illustrations. 1970. Berlin: Springer-Verlag. DM. 142.

FOUR subjects are covered in this volume. Renovascular surgery occupies 33 pages in a tidy account by Kaufman and Lupu. In renal hypertension the most useful tests are described and there is adequate detail of surgical treatment; shorter sections follow on aneurysms, embolism, and thrombosis.

Renal transplantation has the longest section of 74 pages and is the work of Donald Martin of California. This is an excellent account of the current position, which admittedly is not yet stabilized despite the advances made by the contributions of daring surgeons. The technique of transplantation is well described and illustrated and the practice of learning it in 100 canine operations must surely be worth while. The difficult problems of antigen identification and matching are made comprehensible.

The third section of 38 pages dealing with open surgery of the prostate is by Professor Gittes, also of California. Despite his assertion that transurethral prostatectomy has rightly become the method of choice in America, he is prepared to use open surgery for a prostate weighing more than 40 g. He does not favour the repair of the posterior wall of the urethra, yet it was the introduction of retrigonization by Harris which made prostatectomy with closure possible and paved the way to the success of the modern open operation; plain, not chromic, catgut should be used.

The last section on the neurogenic bladder in spinal cord injury comes from Burghele and Ichim of Bucharest and occupies 64 pages. It is the most thought-provoking section in the book. The authors recognize the lack of agreement between the anatomical and functional aspects of the problem and realize that the mechanism of reciprocal relaxation of the bladder-neck with contraction of the detrusor is not known. There are full accounts of the use of electrical stimulation in treatment.

The production of the book lives up to the high standard we have come to expect in this series, and we consider that it will become one of the most popular.

Traumatismes Ostéo-articulaires de la Main. Edited by R. VILAIN, Paris. 10½ × 8 in. Pp. 184 + viii, with 175 illustrations. 1971. Paris: Expansion Scientifique Française. 105F.

THIS latest publication by the study group of hand surgery deals with fractures and joint injuries. It is written in both English and French, one text above the other. This is an advantage for those who cannot read French, but the arrangement is a little confusing. When leafing through this extremely well-produced book, one is primarily struck by the far-reaching consequences that may follow on apparently trivial injuries. It is evident that the initial treatment is frequently decisive—as so often in traumatology—which has important implications for the organization of first-aid departments. The book opens with a minute account of the surgical anatomy of the hand, which admirably summarizes modern knowledge and stays conveniently close to the parts which follow. After this introduction the remainder of the book is about equally divided between primary treatment and treatment of the sequelae. Should the primary treatment not produce the desired results, one can then be guided by the later chapters, which deal with mal-union, non-union, and post-traumatic stiffness, from various point of view. The carpal bones are not included, with one notable exception for the scaphoid bone, non-union of which is covered at length. Perhaps somewhat out of place but nevertheless very interesting is an article on silicone-rubber implants for damaged joints of the hand, mainly tried so far in cases of arthritis. A most interesting publication at postgraduate level, which could serve as a supplement to any textbook on fractures and joint injuries, but rather to study than for reference. The anatomical introduction can be recommended to every surgeon and student of anatomy.

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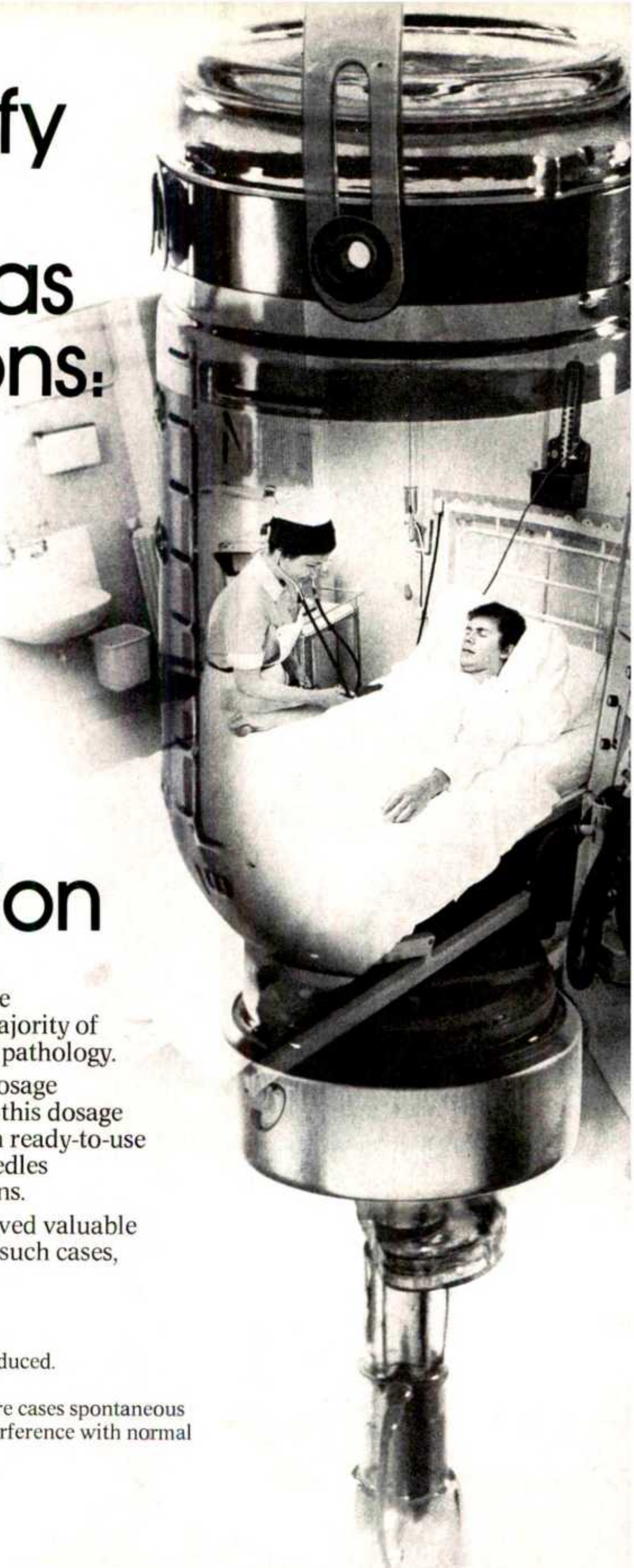

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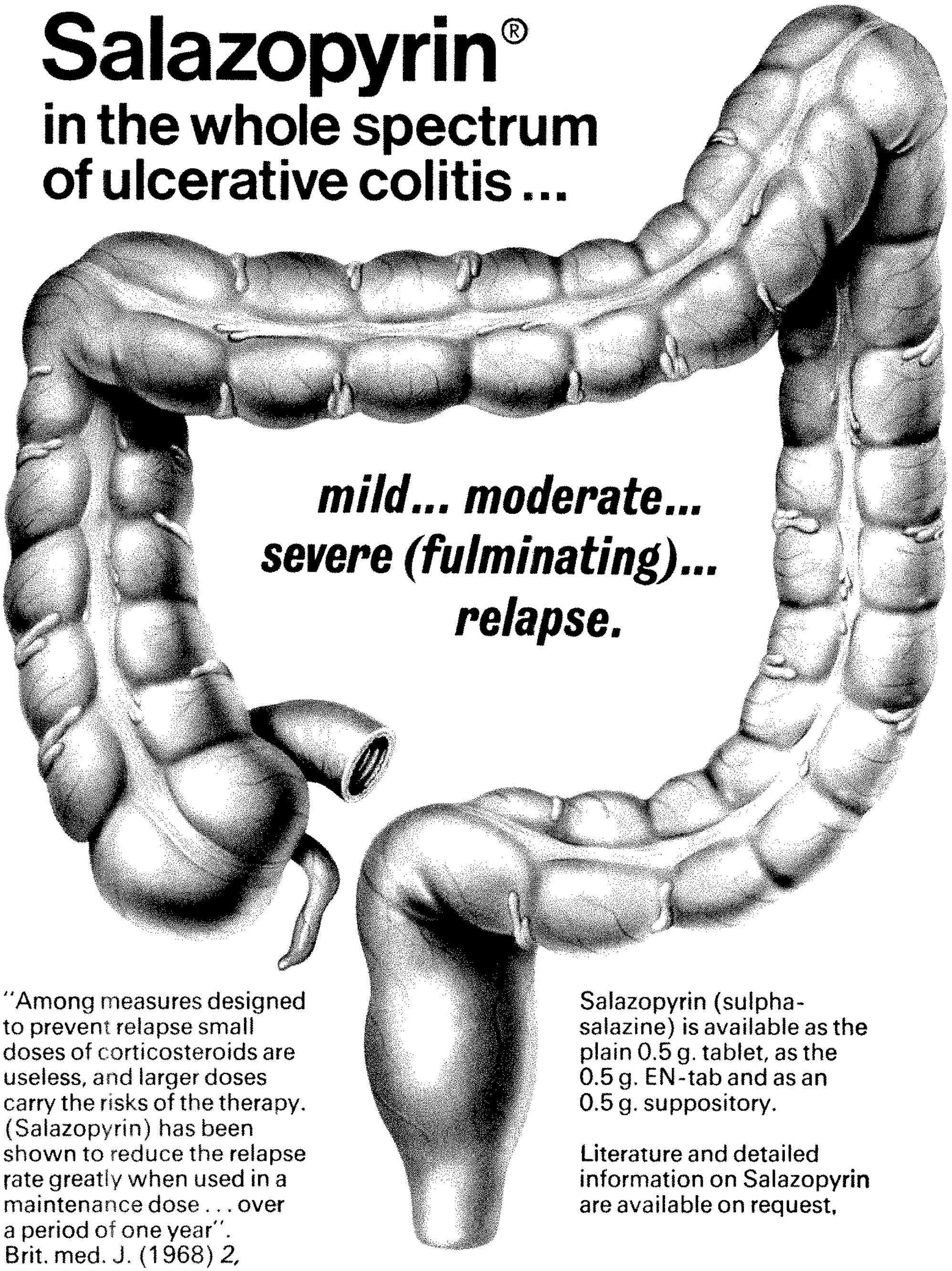

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CONTENTS

PAGE

ORIGINAL PAPERS

THE SCOPE AND SAFETY OF SHORT-STAY SURGERY IN THE TREATMENT OF GROIN HERNIAE AND VARICOSE VEINS *F. S. A. Doran, Mary White, and M. Drury* 333

A CLINICAL TRIAL TO DETERMINE WHETHER A LYTLE'S REPAIR OF A PRIMARY INDIRECT INGUINAL HERNIA NEEDS THE ADDITION OF A RECTUS FLAP - - - - - - - - *F. S. A. Doran* 339

ULCERATIVE COLITIS TREATED BY ILEOSTOMY AND EXCISIONAL SURGERY - - - *Jean K. Ritchie* 345

DEVELOPMENT OF RIGHT INGUINAL HERNIA FOLLOWING APPENDICECTOMY - - - *S. Gue* 352

TUBERCULOUS PERIPHERAL LYMPHADENITIS - - - - - - - *A. A. Hooper* 353

PNEUMOPERITONEUM AS AN AID IN THE SURGICAL TREATMENT OF GIANT HERNIAE - *Henry H. Barst* 360

THE LITHOGENIC EFFECT OF VAGOTOMY - - - - *A. G. A. Cowie and C. G. Clark* 365

SPONTANEOUS AORTODUODENAL FISTULA - - - - *D. M. Evans and J. H. H. Webster* 368

PNEUMOPERITONEUM IN THE MANAGEMENT OF ABDOMINAL INCISIONAL HERNIA *D. B. Hamer and H. L. Duthie* 372

SUBCUTANEOUS NODULAR LYMPHOHISTIOCYTIC HYPERPLASIA - - *J. E. Hale and D. H. Mackenzie* 375

DEEP-VEIN THROMBOSIS IN PATIENTS WITH FRACTURES OF THE FEMORAL NECK *E. S. Field, A. N. Nicolaides, V. V. Kakkar, and R. Q. Crellin* 377

NON-RECURRENT LARYNGEAL NERVE - - *George R. Stewart, John C. Mountain, and Bentley P. Colcock* 379

SQUAMOUS CARCINOMA OF THE STOMACH FOLLOWING CORROSIVE ACID BURNS *Henry Eaton and G. E. Tennekoon* 382

CALCIFYING EPITHELIOMA OF MALHERBE - - - - *S. M. Jones and K. H. Crumplin* 387

DAMAGE FROM THE FOGARTY BALLOON CATHETER *G. E. Mavor, M. G. Walker, D. P. Dahl, and C. A. S. Pegg* 389

ORBITAL HYDATID DISEASE IN IRAQ - - - - - - - - - *H. Talib* 391

PROXIMAL JEJUNAL AND DISTAL ILEAL EXTRINSIC INNERVATION IN THE RABBIT AND DOG *D. H. R. Jenkins and I. B. Macleod* 394

SHORT NOTES OF RARE OR OBSCURE CASES

POST-IRRADIATION FEMORAL ANEURYSM TREATED BY ILIOPOPLITEAL BY-PASS VIA THE OBTURATOR FORAMEN *Harvey B. Ross and John E. L. Sales* 400

RECTAL STONES - - - - - - - - - - *D. G. Jagelman* 405

HAEMANGIOSARCOMA OF THE SPLEEN - - - - *P. J. Toghill, C. C. Rigby, and G. F. M. Hall* 406

LEIOMYOSARCOMA OF THE SPERMATIC CORD - - - - *D. G. Jenkins and S. G. Subbuswamy* 408

DOES SQUAMOUS CARCINOMA OF THE COLON EXIST? - - - - - - *Tom W. Balfour* 410

REVIEWS AND NOTICES OF BOOKS

Hirschsprung's Disease—*Theodor Ehrenpries.* A Short Textbook. Ear, Nose and Throat—*R. Pracy, J. Siegler, and P. M. Stell.* Die gynäkologischen Operationen—*Heinrich Martius and Hugo Husslein.* Trauma to the Liver—*Gordon F. Madding and Paul A. Kennedy.* Die einfachen Kreislaufgrössen beim chirurgischen Patienten—*C. Burri.* Bailey and Love's Short Practice of Surgery—*A. J. Harding Rains and W. Melville Capper.* Total Hip Replacement—ed. *Malcolm Joyson.* Kurzer Leitfaden der praktischen Infusionstherapie—*W. Seifart.* Manuel de l'Aide en Chirurgie—*P. Orsoni.* Idiopathic Ischemic Necrosis of the Femoral Head in Adults—ed. *W. M. Zinn.* Gynaecological Cancer—ed. *T. J. Deeley.* Nouvelle Pratique Chirurgicale illustrée—ed. *Jean Quénu.* Carcinoma of the Bronchus—ed. *T. J. Deeley.* Intestinal Absorption and its Derangements—ed. *A. M. Dawson.* Tumors of Bone and Cartilage—*Harlan J. Spjut, Howard D. Doffman, Robert E. Fechner, and Lauren V. Ackerman.* Les Entretiens de Bichat 1971—ed. *P. L. Chigot and A. Bellin.* An Aid to Clinical Surgery—*Peter R. Scott.* Clinical Organ Transplantation—ed. *R. Y. Calne.* The Polycythemic Disorders—*Baruch Modan.* Diagnosis and Treatment of Abdominal Abscesses—*Irving M. Ariel and Kirk K. Kazarian.* Angiography: Techniques and Procedures—*Joseph E. Whitley and Nancy O'Neil Whitley.* A Textbook of Nursing: A Compendium of Nursing Knowledge—*Evelyn Pearce.* Mediastinoscopy—ed. *Otto Jepsen and H. Rahbeh Sørensen.* 413

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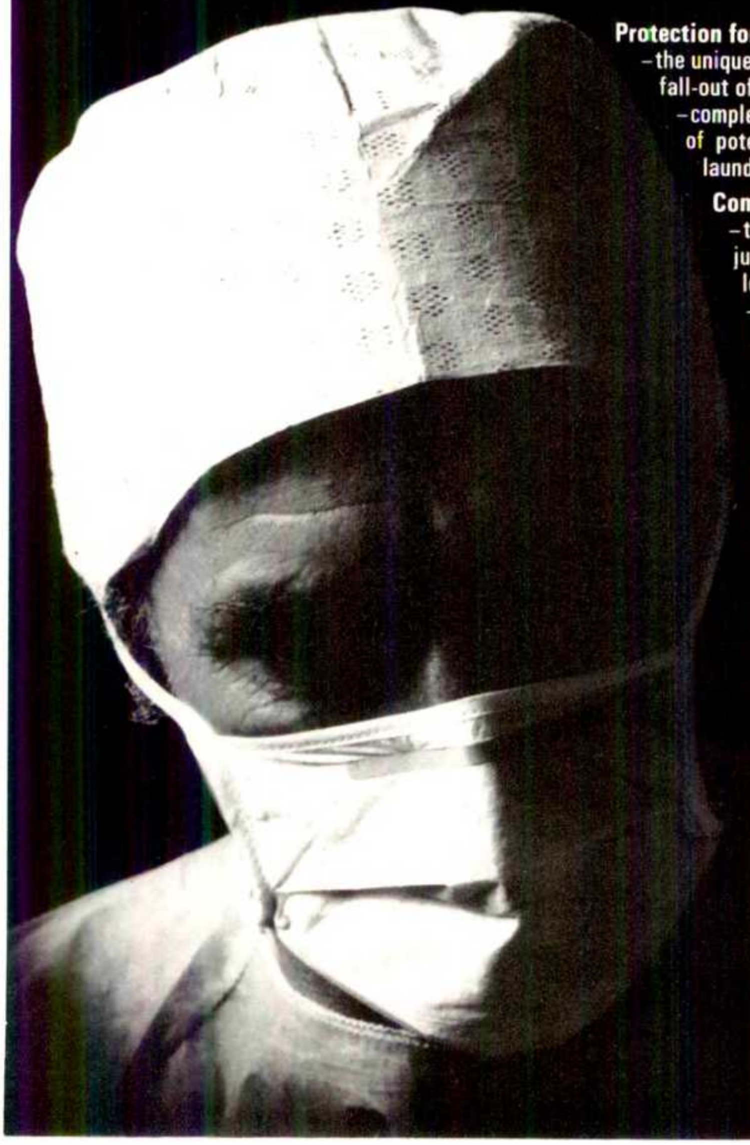

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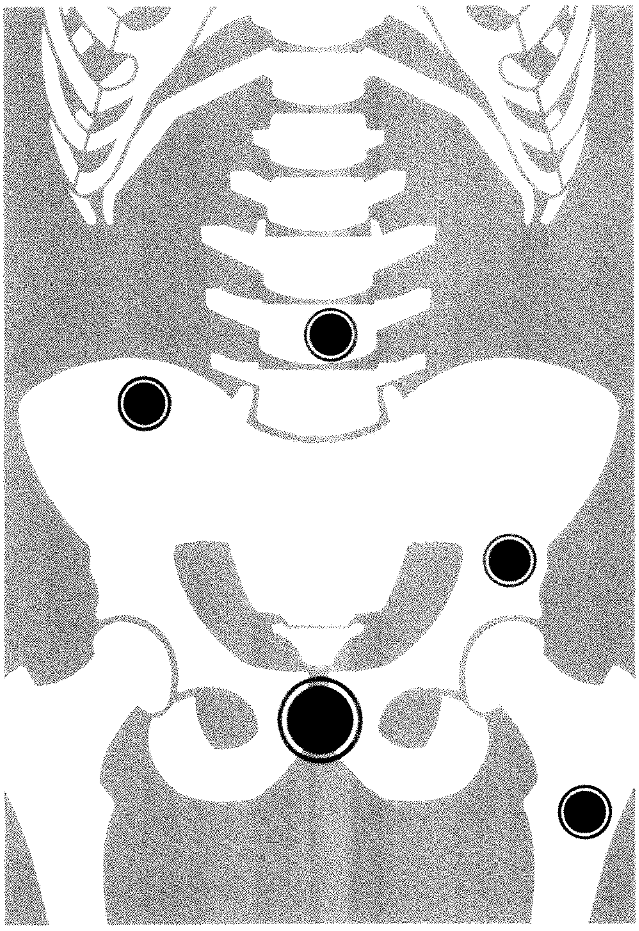

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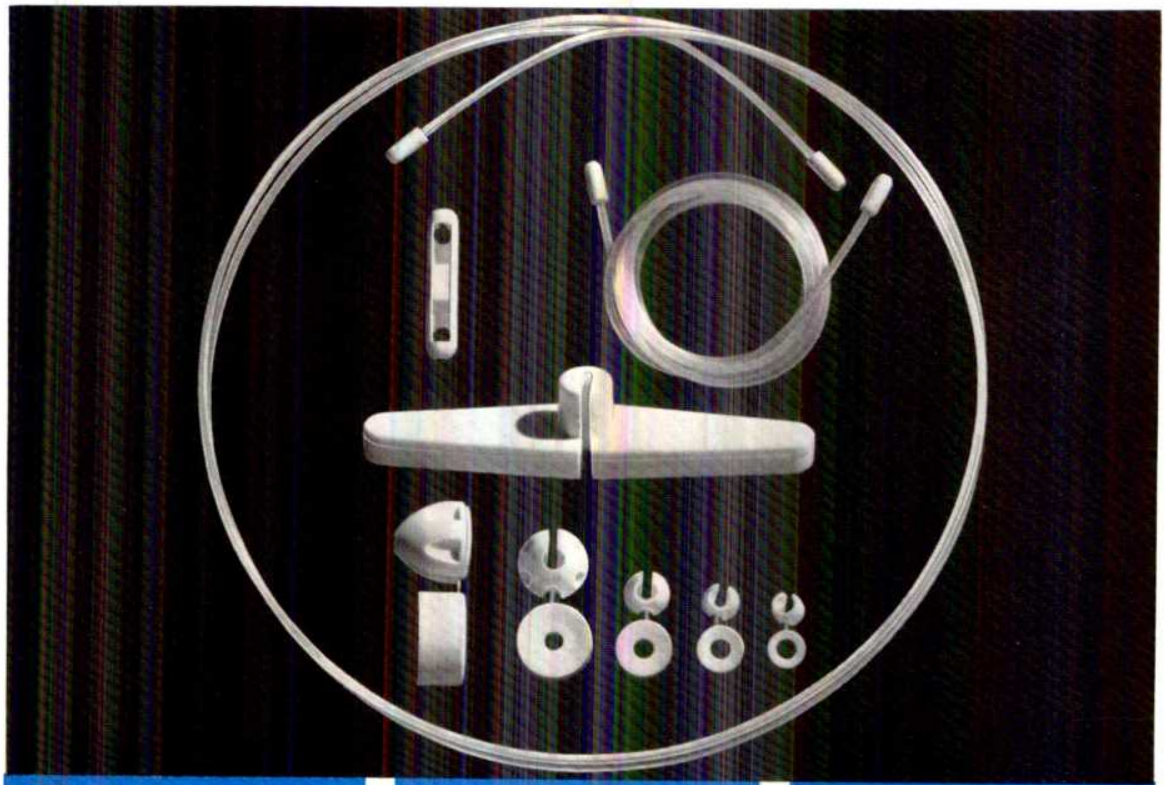

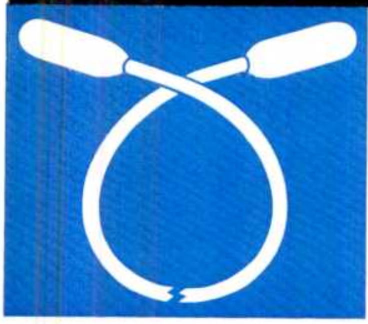

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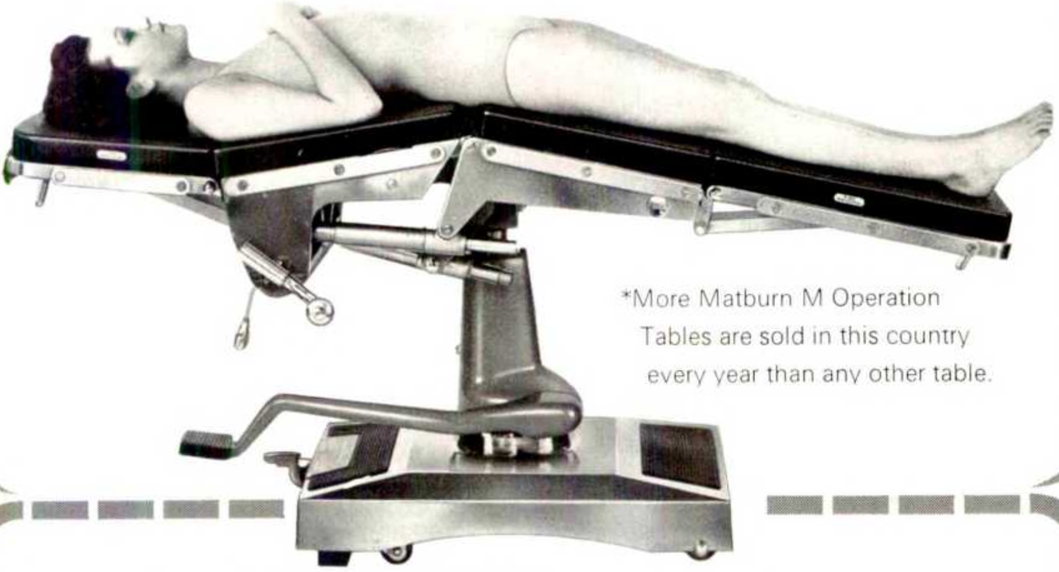

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3. Ladehoff, A. and Otte, E. (1963). Scand. J. Clin. Lab. Invest. **15**, 239.
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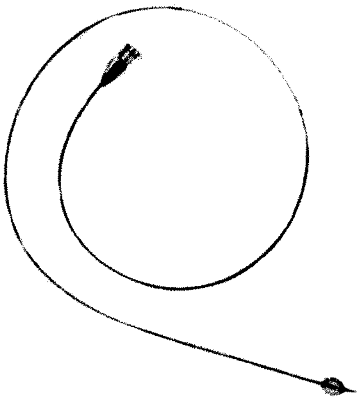

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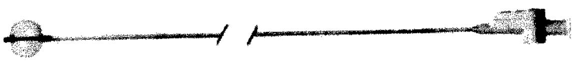

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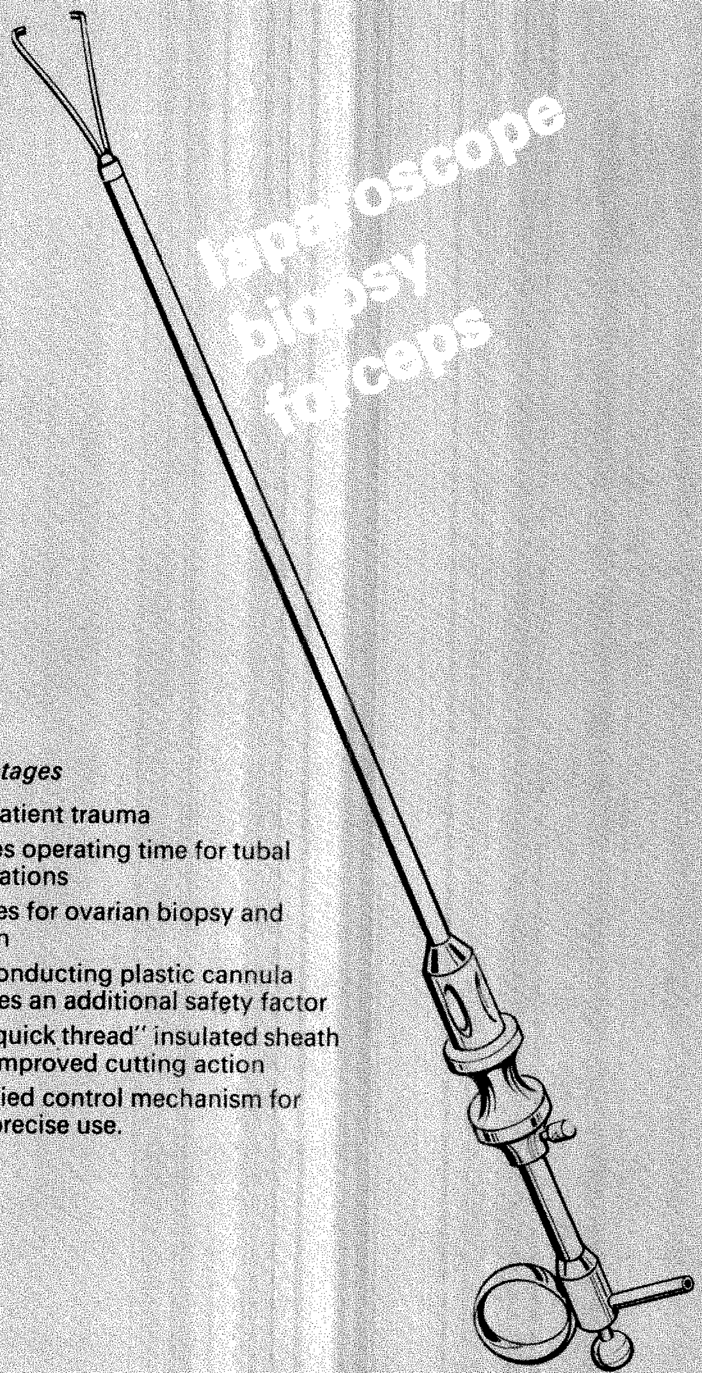

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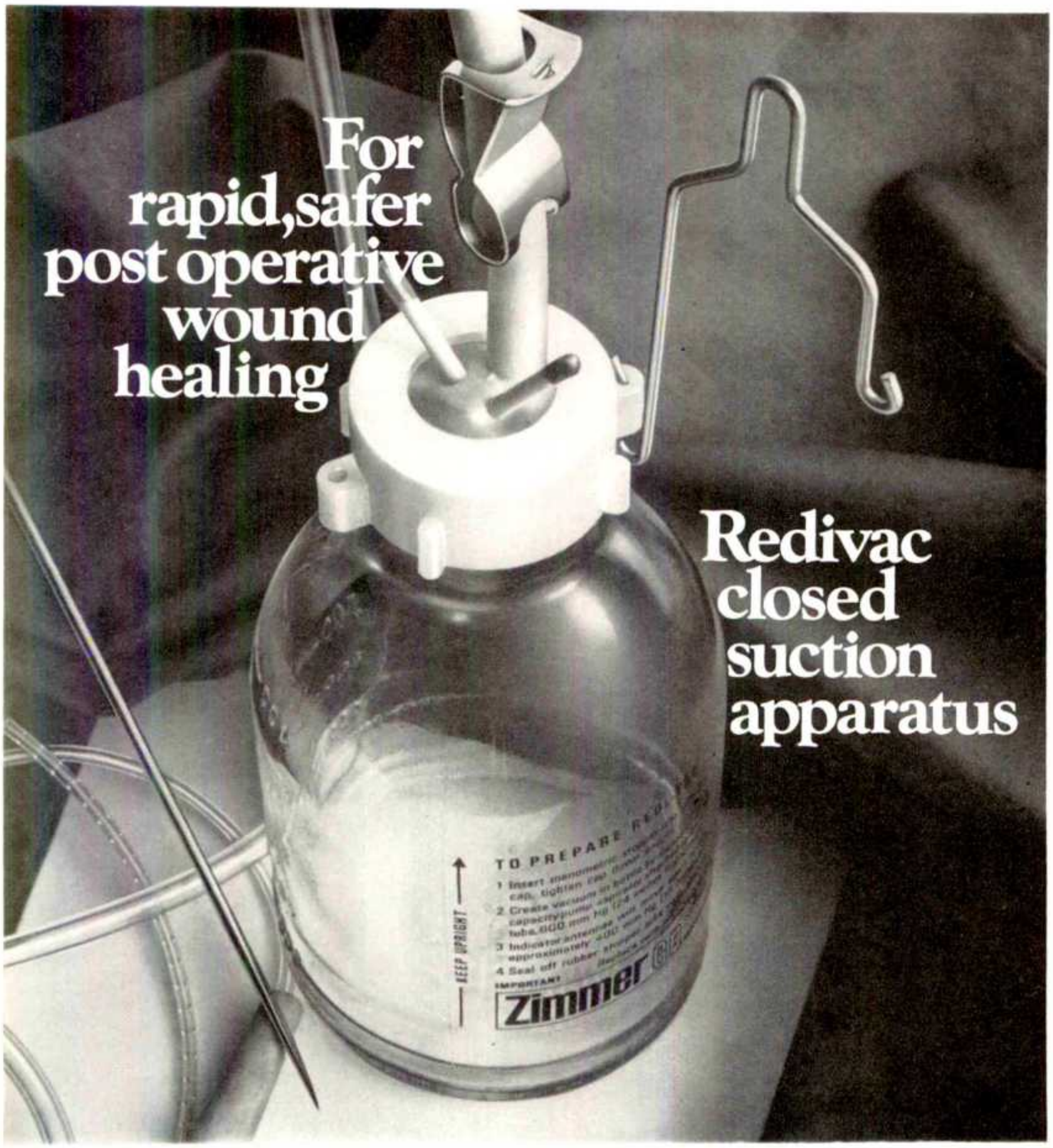
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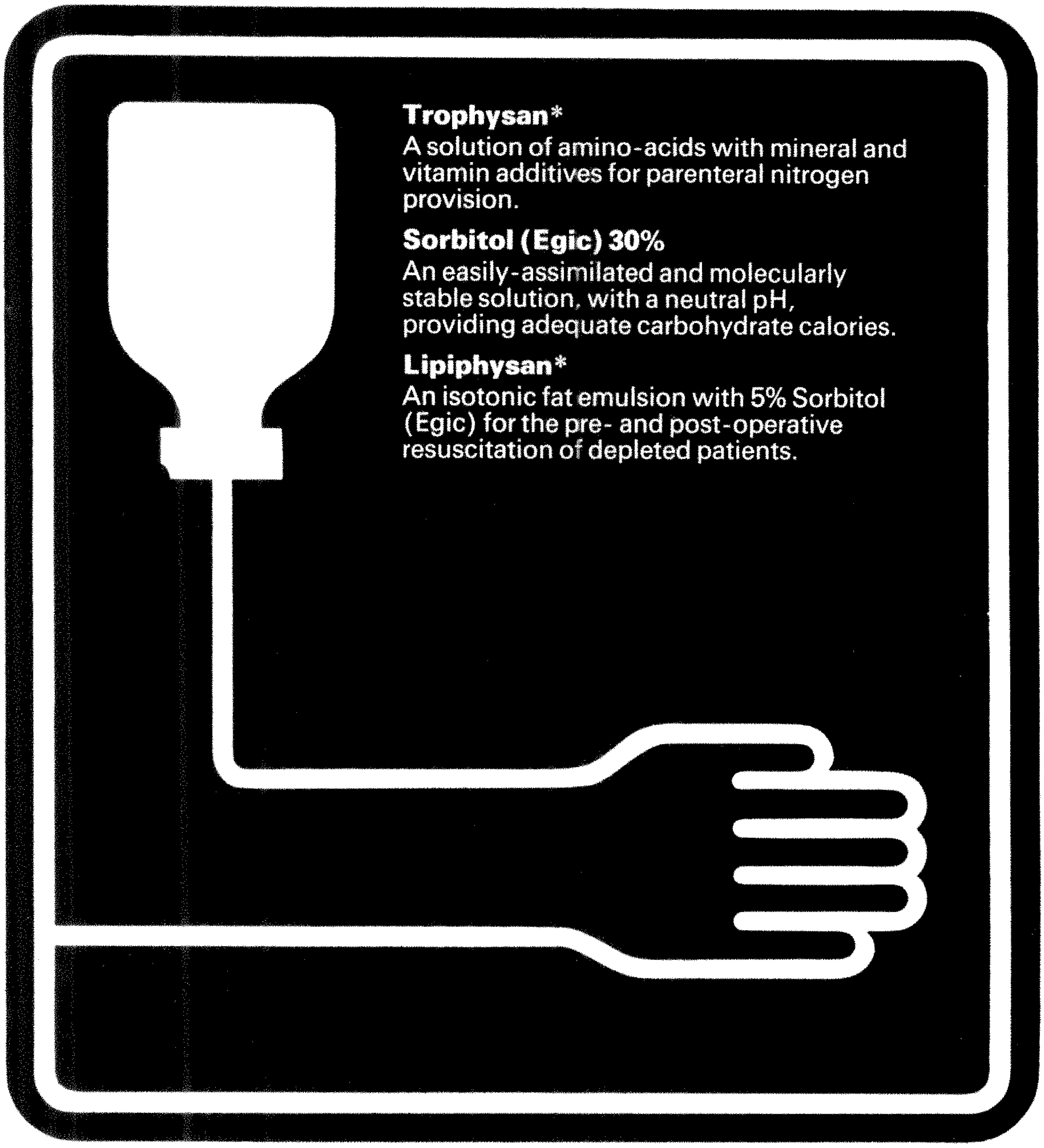

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BRITISH JOURNAL OF SURGERY

Vol. 59 MAY, 1972 No. 5

ORIGINAL PAPERS

THE SCOPE AND SAFETY OF SHORT-STAY SURGERY IN THE TREATMENT OF GROIN HERNIAE AND VARICOSE VEINS

A REPORT ON 705 CASES*

By F. S. A. DORAN, MARY WHITE, and M. DRURY

BROMSGROVE AND KIDDERMINSTER HOSPITALS, WORCESTERSHIRE

SUMMARY

Between 1948 and 1968 the number of surgical patients treated in England and Wales increased by 38·6 per cent. In 1968, 267,300 more surgical patients were admitted to hospital than in 1948. During the same period of time the increase in the number of beds was less than 1 per cent.

Faced with a steadily growing demand to treat patients suffering from cancer and other serious diseases it is difficult to find the beds and the operating time to treat patients with hernia and varicose veins. Even so the operations performed on patients suffering from these two complaints amount to nearly one-third of all the operations performed annually. There are 231 other operations in general surgery.

As a result the average time patients with ruptures and varicose veins languish on hospital waiting lists is up to 2 years, and often for longer than that.

At the present time in England and Wales the average time a patient stays in hospital after a herniorrhaphy or an operation for varicose veins is 10·5 days. This is an expensive waste of beds; 75 per cent of all patients can safely be sent home 48 hours after both these types of operation. The number of patients who develop an acute post-operative complication and cannot go home is only 5·4 per cent and the number who need readmission for a delayed complication is less than 1 per cent.

Being discharged home 48 hours after having their hernia repaired or their varicose veins operated on is popular both with the great majority of patients and also with their relatives. Moreover it is accepted by the general practitioners concerned. Proceeding in this way the time such patients have to wait for their operation is reduced to an average of 3–6 months.

It is important to realize, however, that short-stay surgery will increase the total number of operations performed each year. They are additional operations and, as such, need extra theatre time and extra theatre staff, otherwise they cannot be done.

The present series of 705 cases could not have been operated on if an additional theatre and staff had not been provided.

FACED with a steadily growing demand to treat patients suffering from cancer and other serious conditions most surgeons find it difficult to provide enough beds and theatre time to treat patients with hernia, varicose veins, piles, and subacute appendicitis. As a result such patients tend to languish on the waiting list for up to 2 years.

The facts are straightforward. In 1948 the number of general surgical patients admitted in England and Wales was 691,700. By 1968 the number had risen to 969,000, an increase of 267,300 and a growth of 38·6 per cent in 20 years. In the same 20 years the number of beds available only increased from 453,000 to 465,000, a growth of only 12,000 or 0·26 per cent (Lees, 1969).

It is likely that under the modern conditions of life in this country the numerical growth of patients seeking surgical treatment for ruptures, varicose veins, piles, and subacute appendicitis has increased more rapidly than it has for more dangerous conditions. This is suggested by the fact that at present there are 117,000 herniorrhaphies performed a year, 150,000 operations for varicose veins, 22,000 haemorrhoidectomies, and 25,000 operations for subacute appendicitis (Lees, 1969). These four conditions add up to one-third of all operations undertaken in general surgery. In addition to these four operations there are 231 other operations (Rob and Smith, 1956) and it takes them all to make up the rest of the annual total. Moreover, these four operations take half a million bed days and keep 10 per cent of all the available beds in continuous use.

---

* Based on a paper read at the Symposium on Short-stay Surgery organized by the Birmingham Regional Hospital Board and held at Dudley Road Hospital, Birmingham, on 22 Nov., 1969.

SHORT-STAY SURGERY

In the past surgeons believed that a wound would not heal strongly unless the patient was kept resting in bed for at least 14 days. To get a patient up sooner than that if he had had a groin hernia repaired was asking for a recurrence. During the last war the Army order was that after an inguinal herniorrhaphy the patient must stay in bed for 21 days (Farquharson, 1955).

The truth of this belief has now been challenged. Because of the high cost of hospital care in the United States of America patients have for some time been forced to leave the hospital early (Stallworthy, 1960). In Britain Farquharson (1955), owing to shortage of beds and operating sessions in Edinburgh, successfully repaired 485 inguinal herniae as out-patients, doing the operation under local anaesthesia in the out-patients' theatre. He argued, persuasively, that strict bed-rest in hospital was not essential to the secure healing of a surgical wound. However, he did not prove whether the herniorrhaphy healed as safely. His claim that the healing of the wound took place just as well at home as in hospital has been confirmed by Stephens and Dudley (1961), who treated 54 herniae and 112 varicose veins as out-patients, and by Williams (1969), who operated on 127 cases, of which 65 were ruptures, as out-patients.

Up to now it would appear that most surgeons do not find the policy of out-patient surgery for hernia and varicose veins attractive. Patients who have been operated on for either of these two conditions in England and Wales stay in hospital, on average, for 10·5 days (Lees, 1969). In 34 of the Birmingham Regional Board Hospitals the average time a patient is kept in hospital after a herniorrhaphy is 10·2 days, and after an operation for varicose veins 10·3 days.

It is evident that although surgeons in the main keep their patients in hospital for 10 days, they no longer believe that strict bed-rest is needed to obtain wound healing. All these patients are up and about in the ward. Farquharson (1955) has suggested that patients are kept in hospital because most surgeons are afraid that a complication developing at home would result in litigation. To minimize the risk of such complications Stephens and Dudley (1961) examined each patient and so did the anaesthetists. In addition to the physical examination the patient had a chest radiograph and, if indicated, an electrocardiogram and a forced expiratory volume test. No endotracheal tubes or relaxants were used and prompt recovery of consciousness was aimed at (Sutherland and Horsfall, 1961). The operations were done in the main theatre with strict aseptic precautions, not in the out-patients' theatre. At the beginning of practising short-stay surgery the patient was visited at home by a member of the hospital staff, but this was found to be unnecessary and the practice was discontinued.

Aldridge (1965), in an attempt to get the best of both worlds, carried out a trial on 136 patients admitted for herniorrhaphy. Instead of transferring them to a convalescent hospital 48 hours after the operation they were sent home at this time. The operations were all done under a general anaesthetic in the main theatre. Care at home was given by the district nurse with the backing of the patient's own doctor. Provided that the scheme was explained to the patient no objection was raised, and when asked afterwards all the patients said they liked it.

In 1968 an interesting trial was reported by Morris, Ward, and Handyside, in which 185 men, each with a unilateral inguinal hernia, were divided into two groups: one group was kept in hospital 5 or 6 days after the herniorrhaphy, the other group being discharged home after 24 hours. Complications developed in 43 patients or 23 per cent. Two-thirds of these complications were detected within 48 hours, the majority being apparent within 24 hours. Only 15 occurred on the third or subsequent postoperative day. Adding these facts to the patients' complaints about the immediate postoperative discomforts and the way that these were aggravated by an ambulance journey within 24 hours of the operation, the authors concluded that while it was unnecessary for the patients to be kept in hospital for 5 or 6 days they ought to stay there for 48 hours. This supports the period selected by Aldridge (1965).

The present report is concerned with 705 patients discharged home 48 hours after the operation.

GROIN HERNIAE

The evidence already published (Farquharson, 1955; Stephens and Dudley, 1961; Aldridge, 1965; Morris and others, 1968; Williams, 1969) leaves little serious doubt that after the repair of an inguinal or femoral hernia most patients can safely be discharged home in 48 hours. The material contained in this report confirms this opinion.

From the beginning of this short-stay scheme 345 patients with groin hernia attended the out-patients' department. Of this total, 266 or 77 per cent were accepted and only 79 were rejected and dealt with in the conventional manner. Of the 266 patients accepted, the great majority had an inguinal hernia.

No strict rule regarding age was enforced. The range was from 15 to 84 years, but the majority were between 30 and 59 years (*Fig.* 1). In most of the other reports it would seem that patients with double ruptures have not been accepted, and the Mansfield trial was undoubtedly restricted to men with a unilateral inguinal hernia (Morris and others, 1968). In the present series double ruptures have been accepted.

The operations performed on the 266 groin herniae were as follows:—

If the hernia was an oblique inguinal with a neck of 10 cm. in circumference or less a simple Lytle's repair of the deep ring was carried out, but frequently a rectus flap was added to protect the posterior wall of the inguinal canal or, alternatively, a nylon darn was used for the same purpose. The large oblique and the direct inguinal herniae were treated by either a Bloodgood-Keynes operation, an aponeurotic patch to the posterior wall of the canal, or a rectus flap sewn to Cooper's ligament. This last operation was used for all the femoral herniae. A certain number of the large oblique and the direct inguinal herniae was also treated with a nylon darn. The overall figures for each type of operation are set out in *Table I*.

Table I.—DETAILS OF THE OPERATIONS PERFORMED ON 266 GROIN HERNIAE

Operation	*No. of Cases*
Lytle's repair of the deep abdominal ring, with or without a rectus flap	125
Nylon darn operation	58
Bloodgood-Keynes	30
Aponeurotic flaps to repair the posterior wall of the canal	32
Rectus flap operation for femoral herniae	21
Total	266

Table II.—DETAILS OF THE OPERATIONS PERFORMED ON 244 PATIENTS WITH UNILATERAL VARICOSE VEINS

Operation	*No. of Cases*
Long saphenous strip	150
Short saphenous strip and dissection of popliteal fossa	36
Long saphenous strip and tie to leg perforating veins	36
Long and short saphenous strip	9
Long and short saphenous strip and tie to leg perforating veins	10
Tie to Hunter's canal perforating vein	3
Total	244

Table III.—DETAILS OF THE OPERATIONS PERFORMED ON 195 PATIENTS WITH BILATERAL VARICOSE VEINS

Operation	*No. of Cases*
Long saphenous strip	123
Short saphenous strip and dissection of popliteal fossa	4
Long saphenous strip and tie to leg perforating veins	30
Long and short saphenous strip	25
Long and short saphenous strip and tie to leg perforating veins	13
Total	195

Up to now no evidence has been published on the incidence of recurrence after herniorrhaphies managed as short-stay cases. This, as Morris and others (1968) said, is the 'acid test', and although they admit that their evidence is incomplete they took the optimistic view that early discharge did not increase the risk of a recurrence. We agree with this opinion. No obvious deterioration in the follow-up results of the 266 patients discharged home after 48 hours has been detected. The final answer to this question will have to wait until a properly conducted clinical trial arranged as a random series has been carried out. So far this has not been done. On the available evidence it is doubtful if a full clinical trial would be worth while.

VARICOSE VEINS

This report differs from all but one of its predecessors in that the majority of the patients—439 out of the total of 705—were cases of varicose veins. The series reported by Farquharson (1955), Aldridge (1965), and Morris and others (1968) were confined to patients with a hernia; no varicose veins were included. In the other series varicose veins were included. They amounted to 112 out of the 166 patients treated by Stephens and Dudley (1961), but there are only 5 patients with varicose veins in the list of 127 patients treated by Williams (1969).

As with the herniae, no strict rule with regard to age was enforced. The ages of the patients ranged from 14 to 71 years, but again most were between 30 and 59 years old (*Fig.* 1).

Another way in which the present series differs from its predecessors is that patients needing extensive below-knee operations have been included. Cases of this type were rejected by Stephens and Dudley (1961). The only patients we have excluded for surgical reasons have been those with an open varicose ulcer on the leg when they first attended the out-patients' department. Patients with perforating leg veins and varicose eczema were accepted provided that there was no ulceration. The proportion accepted was, as with the ruptures, 77 per cent or 439 out of a total of 570.

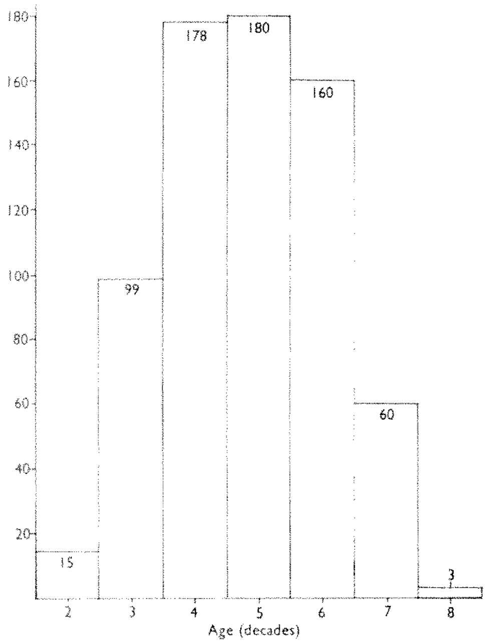

FIG. 1.—Age distribution of the 705 patients included in this series.

The extent of the operations carried out on these 439 patients with varicose veins is set out in *Tables II* and *III*. Some of the operations on the patients with bilateral varicose veins took over 2 hours to do, especially in those who were obese, or who had such tortuous saphenous veins that the stripper would not go up them swiftly. This was especially the case in those patients who had incompetence of the short as well as of the long saphenous vein, because they had to be turned over during the operation. Even if the incompetence was confined to one limb, having to turn the patient over and reapply paint and towels lengthened the time of the operation considerably.

Although clinical observation does not suggest that sending a patient home 48 hours after a herniorrhaphy increases the risk of a recurrence, the remote possibility that it does has not yet finally been excluded. With varicose veins, however, it is very difficult to invent any reason for suspecting that the final result of the operation is, in any way, damaged by this practice. It would seem, therefore, that after undergoing an operation for varicose veins, sometimes a prolonged and extensive one, it is quite safe to discharge a patient home after 48 hours.

IMMEDIATE POSTOPERATIVE COMPLICATIONS PREVENTING THE DISCHARGE OF THE PATIENT IN 48 HOURS

With regard to numbers, the occurrence of immediate postoperative complications is not a serious problem and does not threaten to undermine the short-stay system as a whole.

Out of the 705 patients in this report, only 38, or 5·4 per cent, were unfit to be discharged home 48 hours after operation. The reasons why these patients had to stay on in hospital are set out in *Table IV*. This shows that the most common cause has been acute chest infection with elevation of temperature. This corresponds with the findings of Morris and others (1968). Except for a few of these patients, the delay in their discharge home was only about 3 or 4 days.

Table IV.—THE IMMEDIATE POSTOPERATIVE COMPLICATIONS WHICH PREVENTED 38 PATIENTS FROM BEING DISCHARGED HOME IN 48 HOURS

Complication	*No. of Cases*
Upper respiratory infection	15
Extensive bruising and haematoma	5
Pain in the wound	4
Acute domestic collapse—relatives ill	4
Acute wound infection	2
Profuse bleeding at operation (varicose veins)	2
Prolonged postoperative apnoea	1
Prolonged operation (varicose veins)	1
Prolonged postoperative tachycardia	1
Persistent nausea and vomiting	1
Persistent abdominal discomfort	1
Violent drug reaction (massive urticaria)	1
Total	38

DELAYED POSTOPERATIVE COMPLICATIONS

The development of complications after the patient had been discharged home was not a serious problem numerically, occurring in 62 patients (9 per cent), of whom only 6 (0·9 per cent) had to be readmitted.

By far the most common complication was inflammation of the wound. It was more common in the patients who had been operated on for varicose veins than for a hernia, but even where there were multiple incisions on the limbs usually only one of the wounds was involved. In those patients who suffered an infection of the incision in the leg for perforating veins the portal of entry was often a small area of skin necrosis on one of the flaps.

In half of the infected cases the presence of sepsis was obvious between the seventh and the thirteenth postoperative days. In the remainder it did not show itself until the fourteenth to the twentieth days, and there was a small group in which the onset was delayed until the third or fourth week. Except for 3 cases who had to be readmitted, all the others were cleared up by out-patient treatment, but final wound healing sometimes took 4 weeks, and in a few it dragged on for 8 weeks, while one sinus took 4 months to dry up.

Often, in spite of obvious clinical signs of infection, some inflamed wounds did not discharge. The exudate cultured from those which did discharge contained *Staphylococcus pyogenes* in most instances. Quite a number of these exudates were reported as being sterile.

Of the 6 patients who were readmitted, 3, as mentioned above, had developed a septic wound. The other 3 patients comprised a woman who had a pulmonary embolus 8 days after a right long saphenous stripping, and 2 women who were found to have a deep-vein thrombosis in the left calf 6 days after returning home following long saphenous stripping. All were given a full course of anticoagulant therapy and made a satisfactory recovery.

GENERAL PRE- AND POSTOPERATIVE MANAGEMENT

On attending the out-patients' department for the first time, as well as clinically assessing the patient's general health and ordering a routine chest radiograph and haemoglobin estimation, each patient is questioned about his home conditions. It is obvious that the patient must have a satisfactory house to go to, which is reasonably equipped, and with a close relative willing to look after the patient. Usually a decision can be reached quickly and easily. If there is any doubt a telephone call to the patient's own doctor solves the problem one way or the other. Patients living alone, or in hostels, boarding houses, lodgings, etc., were always rejected for short-stay surgery.

In the West Midlands the general standard of housing is satisfactory. As witness to this is the fact that 77 per cent of all the patients who were sent to hospital with a hernia or with varicose veins have been treated as short-stay cases, and most of those who were rejected were turned down on surgical rather than on domestic grounds.

Fortunately nearly all of our patients live within a radius of 10 miles, but occasionally a patient living 20 miles away has been sent home in 48 hours if the domestic arrangements were good and the general practitioner was prepared to take a special interest.

Keeping the patient in for 48 hours before being discharged has the advantage that the ambulance journey is tolerated better and there is no need to administer perferozine to combat sickness on the return journey home as is necessary with 'day-surgery' (Dudley, 1961). Nevertheless, there have been numerous complaints about the discomfort of the ambulance journey home, particularly about the circuitous route taken in the discharge of other duties and of prolonged stops at other hospitals.

Once home the patient is instructed to go to bed for 2 days, except for essential purposes, and a letter is sent to the general practitioner before the patient leaves the hospital asking him to call on the patient. On the third day the patient is told to get up and move about the house. A normal diet is usually taken.

On the seventh postoperative day the patient is brought back to the out-patients' department by ambulance, examined, and half of the sutures are removed. Seven days later the ambulance brings the patient back again and the rest of the sutures are taken out. By then most patients are walking normally and their convalescence is well advanced. They are seen once or twice more, and if recovery is complete they are transferred to the follow-up system.

This, in outline, is how the present series has been conducted.

DISCUSSION

Provided that the patients are wisely selected, there remains no serious doubt that it is safe to send the majority of the patients home 48 hours after a herniorrhaphy or an operation for varicose veins.

However, it does not follow automatically that just because a thing can be done it ought to be done. It is only justifiable if it is to the patient's advantage, if it meets with the general practitioner's approval, and if it helps the hospital. To clarify this point a detailed survey was carried out on the last 200 patients who were treated as short-stay cases, and the general practitioners concerned were also questioned.

1. Patients and their Relatives.—The most important result of this survey is that 160 patients (80 per cent) liked the scheme unreservedly, 10 (5 per cent) liked it with reservations, and 26 (15 per cent) disliked it. The patients who disliked going home so soon after the operation gave a variety of reasons. One complained of 'feeling really ill' and another suffered with 'anxiety' and also said it was difficult to climb stairs. The rest of the patients who disliked their short stay in hospital all complained of domestic problems, usually with regard to the care of young children in the case of women, and 'making life difficult for my wife' in the case of men.

Turning now to the patients' relatives who had to look after them after their return from the hospital, 167 (83·5 per cent) said they liked the scheme without reservations, 11 (5·5 per cent) liked it but had reservations, and 21 (11 per cent) disliked it. Usually it was the patient's nearest relative who was concerned (128 cases or 64 per cent), but more distant relations were involved in 48 cases (24 per cent) and neighbours were called in to help with 24 (12 per cent) patients. Only 55 people had to take time off work to look after the patient and the length of time they lost varied from a half to one whole day. One of the reasons why so few people had to stay away from work is that when the operations are performed on a Wednesday, as in this series, the patients arrived home on the Friday afternoon, and as many people work a 5-day week they would be at home for the week-end anyway. If patients were operated on during a Monday or a Tuesday, being discharged home 48 hours later, then it is likely that their relatives and neighbours would have to stay away from work longer in order to help.

Lastly, a patient ought not to be discharged home 48 hours postoperatively unless the surgeon is satisfied that, in addition to there being a relative available to receive the patient, the place in which the patient lives is satisfactory. Fortunately in the West Midlands, as mentioned earlier, this problem seldom arises as the amount of slum property is very small. The type of accommodation in which the 200 patients included in this special survey lived is shown in *Table V*: 108 (54 per cent) lived in houses or bungalows which they owned or were buying, 63 (31·5 per cent) lived in council houses or flats, and only 29 (14·5 per cent) were in rented accommodation (house, cottage, flat, and 1 caravan).

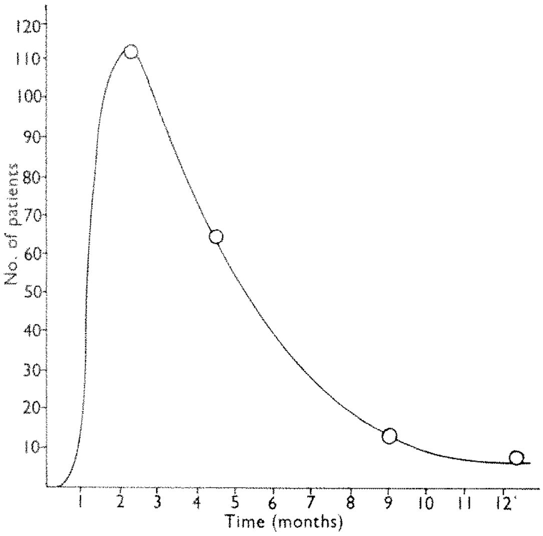

FIG. 2.—Time spent on the waiting list of the last 200 patients treated in this series.

Table V.—TYPE OF ACCOMMODATION IN WHICH THE LAST 200 PATIENTS IN THIS SURVEY LIVED

Accommodation	*No. of Cases*
House owner/occupier	99
Council house	55
Council flat	8
Bungalow	9
Rented	
House	17
Cottage	2
Flat	2
Caravan	1
Other accommodation	7
Total	200

It is fortunate that the great majority of the patients and their relations liked short-stay surgery because it at least halved the length of time they were on the waiting list. In this group patients who are unsuitable for short-stay surgery have to wait at least a year for treatment, but as shown in *Fig.* 2, of the patients who were accepted, 112 (56 per cent) were treated within 3 months, 65 (32·5 per cent) were treated in 6 months or less, and only 13 (6·5 per cent) had to wait more than 6 months. However, there were 9 (4·5 per cent) who were not admitted for more than a year.

The reasons for the varying lengths of waiting time shown in *Fig.* 2 were mainly to do with hospital staffing, but it should be noted that at all levels some of the delays were entirely due to the patients, and that out of the 22 patients who waited more than 6 months, the delays were of the patient's own making in 8. The rest of these long delays were caused by administrative errors, with two exceptions: 1 patient who deliberately delayed admission for over 1 year and another who delayed it for 3½ years.

2. The General Practitioners.—As well as inquiring closely of the last 200 patients with regard to short-stay surgery, the doctors who referred these patients to the hospital were also questioned to find out if the system was burdensome from their point of view.

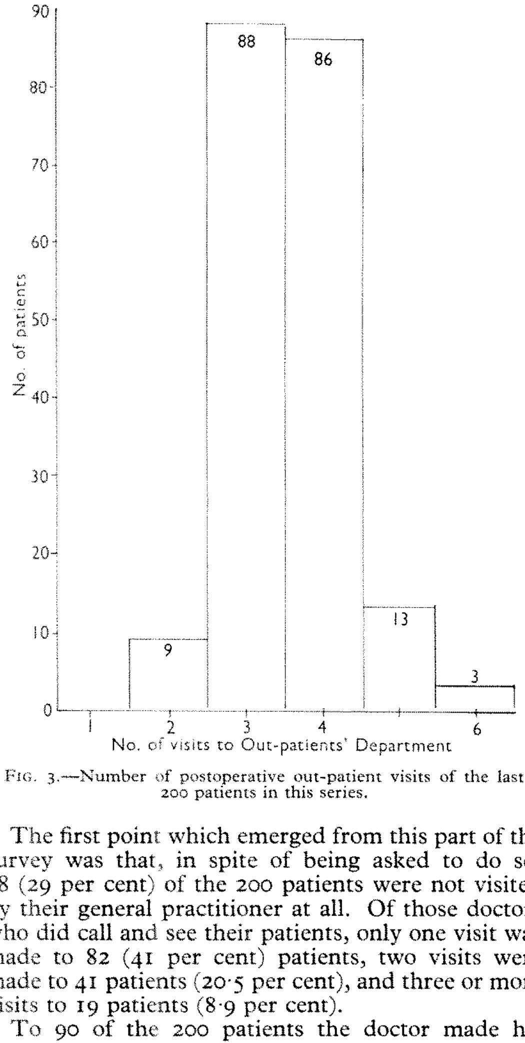

FIG. 3.—Number of postoperative out-patient visits of the last 200 patients in this series.

The first point which emerged from this part of the survey was that, in spite of being asked to do so, 58 (29 per cent) of the 200 patients were not visited by their general practitioner at all. Of those doctors who did call and see their patients, only one visit was made to 82 (41 per cent) patients, two visits were made to 41 patients (20·5 per cent), and three or more visits to 19 patients (8·9 per cent).

To 90 of the 200 patients the doctor made his visit as a routine because the hospital had requested him to do so. In 28 cases he called because the dressings needed changing, 17 patients simply wanted to be reassured, and the reasons for the visits paid to the other patients were not given.

Out of a total of 162 patients visited, the general practitioners thought their visit was worth while in 100 cases (61·7 per cent), but that it could equally well have been done by a nurse in the other 62 cases (38·3 per cent). On 26 occasions the general practitioners arranged for the district nurse to call, on 23 they prescribed dressings, in 18 instances they prescribed drugs, and three times they arranged transport to take the patient back to the hospital. On 82 (51·2 per cent) occasions they issued a certificate.

No evidence has been collected to suggest that the general practitioners whose patients have been subjected to short-stay surgery are opposed to the scheme. On the contrary, there is some evidence that they like it.

3. The Hospital.—Up to now it has been established that most of the patients and their relatives like short-stay surgery in the treatment of groin ruptures and varicose veins, and that their general practitioners accept the method.

From the hospital point of view the reduction of the time that patients remain untreated on the waiting list is to be welcomed. Short-stay surgery has little, if any, effect on the main wards because 90 per cent of their beds are full of more seriously ill patients anyway. There is, however, some increase in the work of the out-patients' department. If a patient is kept in the ward for 10 days postoperatively the sutures will have been taken out before the patient is discharged home. If the wound has become inflamed the patient will be kept in until it is clean or very nearly so.

After short-stay surgery the removal of sutures has to be done by the out-patients' staff. Asking the patient's own doctor to do the removal was considered, but for the present this step has not been taken. Moreover, of the patients who developed an inflamed wound after going home, none of them was readmitted, so that the treatment of those infected wounds was added to the other duties of the out-patients' nursing staff. Three patients with wound sepsis were readmitted but that was before the special survey now being discussed.

For these reasons the number of visits each patient makes to the out-patients' department tends to be rather more than would be the case if at least 10 days were spent in the ward. This point was examined particularly in the last 200 patients. The length of time that the patients attended the out-patients' department averaged 4–6 weeks, ranging from 2 weeks to 4 months for 1 patient with a persistent wound infection who had to continue attending until a sinus dried up. The actual number of visits the patients made is set out in *Fig.* 3, which shows that 174 patients (87 per cent) attended three or four times, that 9 (4·5 per cent) only attended twice, and that 16 (8 per cent) attended at least five times.

With regard to the hospital there is one final point, a point of vital importance. Short-stay surgery is a method of increasing the number of patients with groin ruptures and varicose veins who are operated on each year without reducing the number of patients suffering from more serious conditions to make way for them. It is extra work. This extra work cannot be done unless extra theatre time is provided. The present series of 705 patients have been treated because an extra theatre and an extra theatre staff were produced; otherwise it could not have been done.

CONCLUSIONS

1. With the housing conditions and the standard of living which exists in the West Midlands it is safe to treat 75 per cent of the patients who are referred to the hospitals with groin ruptures and varicose veins on a short-stay basis, discharging them home 48 hours after the operation.

2. The degree of safety can be judged from the facts that out of 705 patients, only 38 (5·4 per cent)

were unfit to go home 48 hours after the operation had been carried out, and only 6 (0·9 per cent) needed to be readmitted. In other words, the safety of the short-stay system is such that in practice it is over 90 per cent efficient.

3. It greatly reduces the length of time patients with groin hernia and varicose veins remain on hospital waiting lists.
4. As short-stay surgery increases the total number of operations performed per year, extra theatre facilities must be provided, or longer hours worked by existing theatre staff.
5. Short-stay surgery somewhat increases the amount of work that has to be done by the out-patients' nursing staff.
6. This scheme is liked by the great majority of the patients and by the relatives who have to look after them.
7. The general practitioners whose patients have been treated in this way do not object to the method.

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A CLINICAL TRIAL TO DETERMINE WHETHER A LYTLE'S REPAIR OF A PRIMARY INDIRECT INGUINAL HERNIA NEEDS THE ADDITION OF A RECTUS FLAP

AN EXERCISE IN SCIENTIFIC METHOD

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Summary

It is a paradoxical fact that although surgeons have discovered how to carry out organ transplants they have not discovered what is the best way to treat such very common conditions as early carcinoma of the breast and primary indirect inguinal hernia.

The reason for this failure is that when surgeons talk of their dedication to scientific methods they refer to an archaic, fallacious, and discredited method; a method discarded by the physical sciences a very long time ago. It is called 'Baconian empiricism'.

The time is long overdue for this archaic method to be rejected and replaced in all surgical work by properly constructed clinical trials leading to an approved mathematical scrutiny of the observed results. The trial must be conducted in a way which eliminates bias for or against the rival methods being tested, otherwise the important mathematical tests of validity cannot be applied to the observed results.

Evidence is submitted to show that more valid information can be obtained from a series of 155 cases of herniorrhaphy arranged in a scientific clinical trial than can be obtained from 2000 cases mechanically collected and tabulated in accordance with the rules of Baconian empiricism.

This clinical trial is used as an example of the new scientific approach to the problem of the primary indirect inguinal hernia, but it applies equally well to the treatment of early carcinoma of the breast.

The question asked was whether, having repaired the deep abdominal ring, a rectus flap ought to be added. The mathematical scrutiny of the observed results of the trial prove that this additional step would not improve the results obtained by a simple suture of the deep ring on its own.

In view of their recent progress in transplant surgery it is a curious paradox that surgeons have not solved problems which are so common that they are confronted by them nearly every day of their lives. For example, they do not know what is the best way to treat an early carcinoma of the breast. They do not agree on which, if any, operation should be performed, whether deep X-ray treatment is helpful or harmful, or on the place of cytotoxic drugs and hormones. They do not know whether a vagotomy ought to be truncal, selective, or highly selective. They do not know whether the best way to treat varicose veins is by operation or by injection. Most surprisingly of all they do not know which is the correct way to repair a primary indirect inguinal hernia in a man. In 1927 Keynes was astonished that the correct method of treating an inguinal hernia was then a matter of dispute. He thought that the operative technique should, already, have reached the point of final standardization. Thirty years, and several thousands of published cases, later Koontz (1956) reported that there was more difference of opinion about the correct way to repair an inguinal hernia than there was about the treatment of any other surgical condition.

The explanation of this paradox is quite simple.

Scientific medicine is now taken for granted by patient and surgeon alike. In recent years scientific medicine has become such an overworked phrase that it has been reduced to a cliché. All surgeons pay lip-service to it. However, when their writings are examined a surprise is in store. The scientific method they use is archaic, fallacious, and discredited, a method which the physical sciences discarded as useless in practice a long time ago.

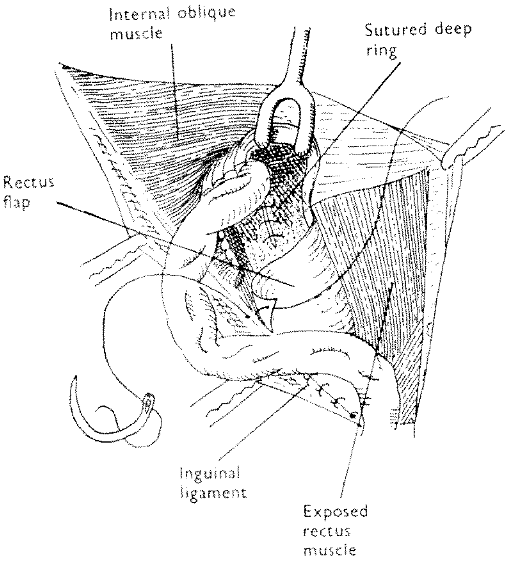

FIG. 1.—Aponeurotic flap cut from the rectus sheath hinged over and sutured to the inguinal ligament behind the cord.

The scientific method used by most surgeons today is termed 'Baconian empiricism'. Impressed by the failure of scholastic philosophy to advance men's knowledge of, and power over, Nature, Francis Bacon (1561–1626) put forward a theoretical basis for the experimental science introduced during the Renaissance (Dampier-Whetham, 1929).

Bacon held that the true connexion between natural phenomena would emerge *almost automatically* provided that (1) all available facts were recorded, (2) all possible observations were made, (3) all feasible experiments were performed, and (4) all the results were collected and tabulated.

Dampier-Whetham (1929) points out that the defect in the method is that it fails to appreciate the huge number of observations that complicated phenomena could call for, that the number of experiments possible would be enormous, and that the rules Bacon laid down for the collection and tabulation of the results were useless. Bacon seems to have had little or no influence on those who were actually performing scientific experiments.

From our point of view as surgeons it is important to realize that advances in science have seldom been achieved by the pure Baconian method (Dampier-Whetham, 1929). Therefore we have no alternative but to cut our losses in time, endeavour, and clinical material and to make a fresh start. Luckily there is an up-to-date scientific method suitable for use on biological problems such as ours ready to hand. All we need to do is to use it.

The present clinical trial is intended as an illustration of the way in which this modern scientific method should be applied to a surgical problem. The problem chosen is whether, when repairing a primary indirect inguinal hernia in man, the posterior wall of the inguinal canal can be strengthened by adding a rectus flap after the deep abdominal ring has been repaired.

The method could equally well be applied to deciding whether deep X-ray therapy in early carcinoma of the breast is helpful or harmful.

THE REASON FOR THIS CLINICAL TRIAL

A few years ago the author made a fresh start on the problem of finding out what was the best way to treat a primary indirect inguinal hernia. It was decided to accept Occam's principle and to cut away all the complex steps in the techniques of existing herniorrhaphies and to start again from the simplest form of repair.

In 1871 Marcy described his operation, which consisted of removing the hernial sac and then repairing the expanded deep abdominal ring through which it had come (Lytle, 1954). This type of repair was the obvious choice as the place to begin again with the new scientific approach.

Theoretically a simple suture of the deep abdominal ring, provided that it had not been stretched too much, might be enough in itself. Both Edwards (1943) and Lytle (1945) had suggested that this was so. Neither, however, had proved the point.

A scientifically conducted clinical trial was therefore carried out on 150 men, between the ages of 20 and 60 years, to discover if the result of a simple suture of the deep abdominal ring could be improved on by adding a fascial sling, similar to Ogilvie's 'levator annuli interni' (1959), or a tense fascial patch from the aponeurosis of the external oblique muscle. The trial proved that these technical additions were both useless and, being redundant, objectionable (Doran, 1962).

In a 2-year follow-up in which 146 patients were examined 5 recurrences were found. In 3 of these patients the groin was explored by the author, and in each the recurrent sac was direct in type and close to the pubic spine. The repair of the deep ring was sound in all of them.

The next step was to carry out another clinical trial to find out if these failures could be avoided by covering the back wall of the inguinal canal from the sutured deep ring to the pubic spine with a flap of rectus sheath placed behind the cord and sutured to the inguinal ligament (*Fig.* 1).

THE STRUCTURE OF THIS CLINICAL TRIAL

The old method stated that all facts must be recorded and all possible observations should be made. Even today this is impossible. It is easy to establish the fact that one billiard ball is black and another is white. It is easy to establish the fact that one patient weighs 57 kg. and another weighs 60 kg. because their weights can be measured. On the contrary, many of the clinical 'facts' cannot be measured: How heavy is heavy work? When is recreation strenuous? When is bronchitis chronic? When is the straining of constipation a danger? Can strong inguinal muscles always be distinguished from those which are less strong? Therefore the presence of many clinical facts cannot be established without doubt or dispute in every individual patient in the series.

Secondly, the instruction to make all possible observations is vain. Many of the complicated biophysical and biochemical factors of wound healing cannot be observed.

The new method admits all these shortcomings. It also admits that there is no way of finding out if the healing factors which cannot be observed are evenly distributed throughout the patients in any particular series. It escapes from this tangle of dilemmas by pointing out that provided accidental, or subconscious, bias in favour of operation A as against operation B can be eliminated a valid comparison of their relative merits can be made.

The new set of rules are as follows:—

1. Bias in favour of one of the rival techniques being compared must be eliminated by deciding by 'lot' which operation is to be performed in each individual case. This ensures that each technique is applied evenly to those patients who are a poor risk and those who are not, because there cannot be any causal connexion between the 'lot' and the non-surgical determinants of the strength of the repair.

2. The patients in the two groups must be followed up for the same length of time. As the risk of recurrence lasts throughout life gross bias in favour of operation A would be introduced if those cases were followed up for only half as long as those treated by operation B. Any comparison of recurrence rates in these circumstances would be invalid and worthless.

3. The patients in the two groups must be followed up and examined physically. As untrained laymen are incompetent clinically compared with surgeons, postal surveys introduce a gross bias in favour of the operative technique concerned to the detriment of any group in which the patients were both traced and examined.

4. The observed results must be subjected to an accredited mathematical scrutiny. This is needed to avoid the mistake of attributing to technical superiority a difference in the number of recurrences caused by the chance interplay of non-technical factors.

The present clinical trial has been conducted according to these new scientific rules (Fisher, 1947; Hill, 1966).

THE MATERIAL

The series consists of 155 indirect inguinal herniae.

Only male patients over the age of 20 years were used. No upper age limit was imposed but, as *Fig.* 2 shows, only 15 patients were more than 60 years old.

Following the example of the previous clinical trial (Doran, 1962) patients were only included if the circumference of the deep abdominal ring was 10 cm. or less (10 cm. happens to be the circumference of the author's right index and middle fingers at the level of the middle phalanx), and the size of the ring was measured from inside the hernial sac.

LENGTH OF FOLLOW-UP

Guided by previous experience the follow-up was limited to 2 years. With benign conditions it is difficult to keep the efficiency of the system in the region of 95 per cent for longer periods. Even at 2 years some patients have to be tracked down and examined in their homes on Sunday mornings.

In the previous clinical trial an efficiency of 97·3 per cent was achieved, but in the present one it was only 95 per cent. Out of the 155 cases of hernia, 7 herniae have been lost. A patient with bilateral herniae died of a ruptured aortic aneurysm; a diabetic patient also died of his disease; a third man was killed in a colliery accident; an Italian returned to his native land, and 2 other patients left the district and could not be traced. Therefore, out of 155 repaired inguinal herniae, 148 (95 per cent) were followed up for 2 years and were examined by the author.

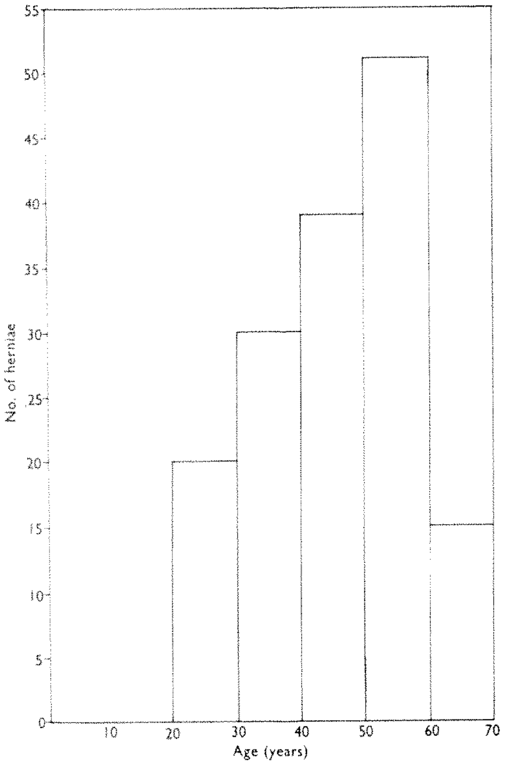

FIG. 2.—Age distribution of the patients in the present clinical trial. Only 15 were over 60 years.

THE OBSERVED RESULTS

Using this new method, time is not wasted trying, vainly, to draw a definite line between a 'bulge' and a 'recurrence'. As this method does not depend on the confrontation of absolute numbers, all that is needed is for each patient on follow-up to be examined by the same person. Provided the assessment error is constant for the patients in both of the groups that is enough.

The results are set out in *Table I.*

1. Lytle's Operation (Suture of the Deep Abdominal Ring).—Out of the total of 155 herniae, 86 were treated by a simple suture of the deep abdominal ring. Of these 86 repairs, 80 were successfully followed up for 2 years and 6 were lost

Only 1 recurrence was found in the 80 who were examined.

The 6 cases which were lost, and therefore not examined, raise a very important point. In Nature there is no valid principle of uniformity known. As a result it would be scientifically improper to make the flattering assumption that all these 6 repairs were sound and free from recurrence. In fact this might be true, but conversely, as none of them was examined, every one might be a recurrence. Or again the truth could lie at some intermediate point between these two extremes.

Table I.—RESULTS OF 155 REPAIRS OF PRIMARY INDIRECT INGUINAL HERNIA

OPERATION	TOTAL NO. OF HERNIAE	NO. OF HERNIAE FOLLOWED UP	KNOWN RECURRENCES		POSSIBLE RECURRENCES	
			No.	Per cent	No.	Per cent
Lytle's operation	86	80	1	1·16	7	8·02
Lytle's operation with rectus flap	69	68	1	1·45	2	2·90
Total	155	148	2	1·30	9	5·80

Table II.—CHI² (χ^2) TEST CALCULATED FOR THE MINIMUM AND MAXIMUM NUMBERS OF RECURRENCES POSSIBLE

CALCULATION OF χ^2	MINIMUM POSSIBLE NO. OF RECURRENCES		MAXIMUM POSSIBLE NO. OF RECURRENCES	
	Type of Operation		*Type of Operation*	
	Lytle	Lytle + Flap	Lytle	Lytle + Flap
No. of successes	85	68	79	67
Expected No. of successes	84·89	68·11	81·01	64·86
Successes observed − expected	+0·11	−0·11	−2·01	+2·14
$\frac{(\text{Observed} - \text{expected})^2}{\text{Expected}}$	0·00014	0·00018	0·0499	0·0706
No. of recurrences	1	1	7	2
Expected No. of recurrences	1·11	0·89	4·99	4·14
Recurrences observed − expected	−0·11	+0·11	+2·01	−2·14
$\frac{(\text{Observed} - \text{expected})^2}{\text{Expected}}$	0·0109	0·0136 $\chi^2 = 0·02482$	0·8096	0·6738 $\chi^2 = 1·6039$
	Where $n = 1$, $P = 0·90$: Not significant		Where $n = 1$, $P = 0·20$: Not significant	

The correct way to report this, and similar results, is to say:—

a. The minimum number of recurrences possible is 1 or 1·16 per cent.

b. The maximum number of recurrences possible is 7 or 8·02 per cent.

As stated above the real result could be at either extreme or at some intermediate point.

2. Lytle's Operation with Rectus Flap added.—Of the total of 155 herniae, 69 had a rectus flap added to the suture of the deep abdominal ring. Sixty-eight of the herniae treated in this way were successfully followed up for 2 years. In this group also only 1 recurrence was found, but unlike the other group only 1 case was lost, so the efficiency of its follow-up was 98·5 per cent as compared with 93 per cent for the other group.

With the rectus flap added, therefore, the minimum number of recurrences possible is again 1 (1·45 per cent), but as only 1 case was lost the maximum possible is only 2 (2·9 per cent).

Taking the series as a whole the rate of recurrence ranges from a minimum of 1·3 per cent to a maximum of 5·8 per cent.

As the defects in the follow-up occurred almost entirely in the group treated by a Lytle's operation alone an interesting situation exists. If the minimum figures of the two groups are compared then there is nothing to choose between them: 1·16 per cent for the Lytle's operation on its own, and 1·45 per cent with a rectus flap added. But the maximum figures, owing to the loss of 6 cases in the Lytle group as compared with 1 in the other group, show an apparent superiority in the group treated by the addition of a rectus flap: 2·9 per cent as opposed to 8·02 per cent.

Fortunately, as this test has been a properly conducted clinical trial this awkward situation can be unravelled by the application of a suitable mathematical test to find out whether or not a difference of this magnitude could have occurred by chance alone.

A MATHEMATICAL SCRUTINY OF THE OBSERVED RESULTS

Quite apart from the present situation it would be very lax to accept the observed results of a clinical trial on their face value. An observed difference ought only to be accepted if it is too large to be accounted for by chance alone. It is usual to demand that the difference should be such that it could only have occurred by chance once in 22 trials of equal size. There are numerous ways of making this calculation, but the χ^2 test is simple and convenient and therefore has been used here. It is set out in *Table II.* Two sets of calculations have been made, first to test the figures for the 'minimum possible' number of recurrences and then for those representing the 'maximum possible' number of recurrences. In this trial the second group of figures are of particular importance. The result of this essential calculation shows that even the difference of 5 between the number of recurrences in the two groups could well have occurred by accident. Therefore on both counts, 'minimum possible' and 'maximum possible', *the correct verdict is that both methods of treatment are of equal value.*

Without this mathematical scrutiny it would have been very difficult to know what verdict to reach in the present trial, and it is important to realize that the ability to apply a mathematical test depended entirely on the fact that the trial had been correctly planned from the outset as a random series.

Having proved that these two methods are of equal value, the decision which of them to use in practice is resolved, as in all trials which end in a tie, by the application of Occam's razor. The most simple solution to the problem must always be preferred. There are cogent practical reasons for this policy.

DISCUSSION

Having described the new scientific method and having given an illustration of its practical application, it will be interesting to turn back for a moment to its discredited rival, Baconian empiricism, and to examine the way its four rules worked in practice.

1. All Available Facts must be recorded and 2. All Possible Observations must be made.—As no facts except facts of observation can be made with regard to a patient with an inguinal hernia these two rules can be taken together.

Table III.—Size of 13 Major Series published since 1900

Author	*Total No. of Cases in Series*
Bull and Coley (1907)	1,525
Davis (1916)	1,756
Hoguet and Coley (1918)	5,525
Taylor (1920)	2,230
Erdman (1923)	1,093
Coley (1924)	1,155
Gibson and Felter (1930)	1,618
Fallis (1936)	1,600
Grace and Johnson (1937)	1,115
Skinner and Duncan (1945)	1,126
Garner (1947)	2,643
Hagan and Rhoads (1953)	1,082
Palumbo, Paul, and Mighell (1954)	1,375
Total	23,843

No one is going to pretend that all facts with regard to every patient with an inguinal hernia, now and in the past, have been observed and then recorded. Nevertheless, a very large number have been. For example, in 13 major series published in the United States alone the grand total is 23,843 cases of inguinal herniorrhaphy (*Table III*). If European and smaller series are added the number would rise to at least 50,000 cases.

Obviously it can be said that our experience is too limited and that the Baconian method needed far larger numbers, but the published numbers are big, and if still more are required then the method can be criticized as being insensitive, clumsy, and very dilatory.

In addition to the thousands of patients who have been operated on, observations have been made and recorded about their sex, age, bodily configuration, length of time prior to operation that the hernia had been present, whether its first appearance had followed an injury or not, what social class the patient belonged to, whether they did sedentary, light, or heavy work, whether they suffered from chronic bronchitis, chronic constipation, urinary obstruction, or any other defect likely to produce straining, whether complications, such as wound sepsis, occurred, and so on *ad infinitum*. It does not flatter the method that all this effort in trying to make the factual observation of patients with inguinal hernia complete should have been in vain.

3. All Feasible Experiments must be made.—Surgeons have obeyed this rule with alacrity and zeal.

It is 100 years since Marcy published his first article on the simple suture of the deep abdominal ring (Lytle, 1954). Bassini performed his operation for the first time 13 years later in 1884. Marcy's simple repair was so deeply buried by the proliferating complexity which followed that it was completely forgotten until it was rescued by Lytle.

Table IV.—Edwards's (1943) Selection of Eponymous Operations for Primary Indirect Inguinal Hernia

Author	*Operation*
Andrews (1895)	Conjoined tendon sewn to Poupart's ligament behind the cord, external oblique muscle imbricated to make tunnel for cord
Bassini (1889)	Conjoined tendon sewn to Poupart's ligament behind the cord
Bates (1913)	Closure of internal ring and transversalis fascia through 5-cm. incision with purse-string suture
Bloodgood (1898)	5-cm. incision of rectus sheath allowing rectus muscle and conjoined tendon to meet Poupart's ligament behind the cord
Brenner (1898)	As Bassini but using cremaster muscle to reinforce internal oblique muscle
Downes (1911)	Behind the cord the exposed edge of the rectus is sewn to Poupart's ligament and imbricated flaps of internal oblique muscle
Fergusson (1899)	Narrowing of internal ring and the external oblique muscle imbricated superficial to the cord
Fowler (1897)	Division of back wall of canal, cord placed inside the peritoneum to emerge by pubic spine, canal obliterated
Gallie (1921)	Fascial darn to back wall of canal
Halstead (1889)	Suture of conjoined tendon and cremaster muscle to Poupart's ligament superficial to cord, imbrication of external oblique muscle
Hull (1913)	Herniotomy through 1·3-cm. skin incision
Kirschner (1910)	Free graft of fascia lata
La Roque (1919)	Intraperitoneal inversion of sac and transperitoneal herniotomy above the internal ring
McArthur (1904)	As Bassini but using two pedicle flaps of external oblique aponeurosis as sutures
McEwan (1886)	Sac freed to above internal ring, folded into pad, and sutured into the deep ring as a plug
McGavin (1909)	Two filigrees inserted into posterior wall behind cord
Marcy (1871)	Herniotomy—suture of internal ring with kangaroo tendon displacing cord upward and laterally
Scott (1905)	Conjoined tendon sewn to Poupart's ligament behind cord, relaxing cut in rectus sheath, obliteration of external ring
Stein (1939)	Herniotomy—flap of fascia covering internal oblique sewn to Poupart's ligament
Stetten (1923)	Suture of conjoined tendon to Poupart's ligament and imbrication of external oblique muscle behind the cord
Torek (1906)	As Bassini but the vas deferens is separated from the vessels and is sutured to keep it so
Watson (1916)	Cord thinned and sewn high on the internal oblique muscle, conjoined tendon sewn to Poupart's ligament and imbrication of external oblique muscle

Bacon would have been proud of the number of technical experiments performed by surgeons working in this field. Not all these experiments will be listed, but it will suffice to make the point if Edwards's (1943) selection of eponymous operations, 22 in number, is given (*Table IV*).

One of the main criticisms levelled at the Baconian method by the practitioners of the experimental sciences has always been that it grossly underestimated the complexity of natural events. Moreover the method does not specify how many instances of each particular experiment are needed to allow the triumph of the correct one to stand out as self-evident truth.

Evidence that this criticism is well founded has been provided by the failure of the Liverpool registration scheme to solve the problem. Given a finite quantity of clinical material, the larger the number of technical experiments, the smaller will be the number of patients available to each particular technique. If the number of technical experiments is too large then, inevitably, *fragmentation occurs* and there are not enough examples of each technique to satisfy the demands implicit in rule 1 and rule 2 of the method.

Table V.—RESULTS OF THE LIVERPOOL SERIES (MARSDEN, 1958, 1961), ILLUSTRATING THE PHENOMENON OF FRAGMENTATION WHICH RESULTS FROM INDISCRIMINATE REGISTRATION

TYPE OF REPAIR	1958		1962		1958 AND 1962 RECURRENT
	Primary Indirect	Primary Direct	Primary Indirect	Primary Direct	
McArthur-Morrison	168	54	265	75	15
Bassini (with nylon)	91	39	235	101	31
Bassini (with mersaline)	25	0	46	9	2
Bassini (with catgut)	47	14	104	19	3
Bassini and Wyllys Andrews III (nylon)	56	45	97	56	12
Bassini and Wyllys Andrews III (mersaline)	20	12	47	12	1
Bassini and Wyllys Andrews III (catgut)	2	1	11	16	2
Wyllys-Andrews III (catgut)	15	5	15	5	2
Wyllys-Andrews III (nylon)	0	0	0	0	2
Wyllys-Andrews II (catgut)	36	9	61	19	5
Wyllys-Andrews II (nylon)	5	0	9	1	2
Wyllys-Andrews II (mersaline)	1	0	1	0	0
Bassini and Wyllys Andrews II (catgut)	8	4	37	9	1
Bassini and Wyllys Andrews II (nylon)	0	1	5	5	0
Closure of canal	30	1	55	6	15
Cooper's	2	3	4	4	0
Gallie	4	3	4	5	2
Nylon tricot	27	7	43	16	8
Excision of sac	16	0	32	0	0
Closure of the internal ring	12	0	24	0	0
Fascia transversalis	4	1	6	1	0
Bassini (with wire)	0	0	3	2	3
Polyvinyl sponge	0	0	0	0	1
Rectus sheath flap	0	0	1	2	0

Table V shows how the process of fragmentation destroyed the Liverpool series, which added up to 1000 patients by 1958 and to 2000 patients by 1961 (Marsden, 1958, 1961). It will be seen that twenty-four technical methods were involved. Evenly distributed that ought to have meant 83 patients out of the total of 2000 for each method of repair. This should be compared with the present clinical trial of 155 hernia repairs (*Table I*) in which the two contending groups included 86 and 69 cases respectively.

In fact, the methods tested at Liverpool were not evenly distributed, as *Table V* demonstrates. Of the forty-eight groups in the 1962 results for primary hernia forty-two contain less patients than either of the two groups tested in the present clinical trial.

4. All the Results must be collected and tabulated.—Surgeons have been obeying this rule for more than 50 years. Because the method is useless the collection and tabulation of thousands of observed clinical and technical facts have been a waste of time and material. All it has done is to bury the solution to the problem in a large pseudo-statistical slagheap.

If anyone has any doubts on this point let him reflect on the failure of the Baconian method to teach us the best way to treat early carcinoma of the breast. The collection, tabulation, and recording of observed clinical facts have been much more intense and efficient in this field than it has been with regard to inguinal hernia. Much interesting and useful information has been accumulated, but it has not solved the problem at which it was aimed. In the Birmingham region alone, between 1936 and 1960, 15,700 cases of carcinoma of the breast were registered. Out of this total, 6489 were 'early' carcinomas, that is, Stages I and II. These cases were analysed on the basis of an efficient 5-year follow-up (Bond, 1967). This analysis did not solve the problem of the way in which we ought to treat an early carcinoma of the breast. On the contrary, it confused the issue even further by suggesting that no operation, with the possible exception of removing the primary from the breast, was any use, and by claiming that deep X-ray therapy was harmful not helpful. This may be true but it cannot be known to be true until it has been scientifically and mathematically tested.

It is to be hoped, at long last, that surgeons will realize that Francis Bacon is a false prophet and that it would be a mistake to try to solve our problems, whether they be the correct way to treat an early carcinoma of the breast or to repair a primary indirect inguinal hernia, by the further application of this ineffectual, discredited, and scientifically discarded method.

This warning is a serious one because already it is being said that the method can be saved by the computer. This is the gross fallacy of thinking that a method which is wrong can be corrected by mechanizing its application.

CONCLUSIONS

1. The correct method of repairing a primary indirect inguinal hernia with a neck 10 cm. in diameter or less is by a simple suture of the deep abdominal ring (referred to as Lytle's operation).

2. It is unnecessary to protect the posterior wall of the canal by the routine addition of a rectus flap placed behind the cord and sewn to the inguinal ligament.

3. All additional technical steps and all new methods of repair should be scientifically tested by a properly conducted clinical trial using Lytle's operation as the standard for comparison before they are introduced into routine practice.

4. Surgeons should follow the example of practitioners in the experimental sciences and reject Baconian empiricism with its mistaken belief that biological problems can be solved with punch-cards, programs, and computers.

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ULCERATIVE COLITIS TREATED BY ILEOSTOMY AND EXCISIONAL SURGERY

FIFTEEN YEARS' EXPERIENCE AT ST. MARK'S HOSPITAL

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SUMMARY

The results of excisional surgery with the establishment of a permanent ileostomy in 246 patients with ulcerative colitis operated on in the years 1955–69 at St. Mark's Hospital, London, are presented. The overall mortality of the primary surgery was 8·1 per cent, being 9·3 per cent in the years 1955–9, 10·6 per cent in the years 1960–4, and 5·3 per cent in the years 1965–9. This mortality was 1·6 per cent in 128 patients treated electively, 10·7 per cent in 75 cases coming to urgent surgery, and 23·3 per cent in 43 patients undergoing emergency operations. The mortality in this third group fell from 36·4 per cent in the years 1955–9 to 25 per cent in the years 1960–4 and 15 per cent in the years 1965–9. The incidence of major postoperative complications for patients treated by total proctocolectomy or colectomy and ileostomy was also clearly related to the preoperative severity of the disease, being 18·8 per cent in the elective cases, 31·3 per cent in the urgent cases, and 40 per cent in the emergency cases.

Late complications of surgery were, with the exception of intestinal obstruction requiring surgery, infrequent in this series and showed a marked fall in the last 5 years of the study. With the possible exception of urolithiasis, this investigation revealed no increased susceptibility to diseases or conditions of a general nature in the long-term study of these patients (average length of follow-up 7 years) and emphasized the excellent life expectancy in patients in whom radical surgery had been carried out in the absence of malignant change.

THIS paper presents the short- and long-term results in patients with ulcerative colitis treated at St. Mark's Hospital over a 15-year period by surgery involving the establishment of a permanent ileostomy. Using the criteria outlined below, there were 246 patients in whom this surgery had been carried out in the years 1955–69.

The criteria for inclusion in the series were as follows:—

1. All major primary surgery including the ileostomy must have been undertaken at St. Mark's Hospital. Three patients in whom the rectum was excised elsewhere (abroad in 2 cases) provide the exception and have been included in the figures for

colectomy and ileostomy and follow-up but have been excluded from those for rectal excision and perineal wound healing.

2. The ileostomy must have been permanent, which is defined as present up to the concluding date for this study (1 Jan., 1970) or until the date of death.

Table I.—AGE AND SEX DISTRIBUTION

AGE-GROUP (YEARS)	MALE		FEMALE		TOTAL	
	No.	Per cent	No.	Per cent	No.	Per cent
10–14	2	1·7	4	3·2	6	2·4
15–19	9	7·5	4	3·2	13	5·3
20–24	16	13·3	7	5·6	23	9·3
25–29	14	11·7	9	7·1	23	9·3
30–34	11	9·2	14	11·1	25	10·2
35–39	13	10·8	10	7·9	23	9·3
40–44	8	6·7	14	11·1	22	9·0
45–49	17	14·2	13	10·3	30	12·2
50–54	12	10·0	13	10·3	25	10·2
55–59	7	5·8	17	13·5	24	9·8
60–64	7	5·8	12	9·5	19	7·7
65–69	2	1·7	7	5·6	9	3·7
70–74	1	0·8	1	0·8	2	0·8
75–79	1	0·8	1	0·8	2	0·8
Total	120	100·0	126	100·0	246	100·0

Table II.—PREOPERATIVE GRADING

YEARS OF SURGERY	GROUP								TOTAL	
	A		B		C		D			
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
1955–9	10	11·6	30	34·9	35	40·7	11	12·8	86	100·0
1960–4	9	13·6	27	40·9	18	27·3	12	18·2	66	100·0
1965–9	12	12·8	40	42·5	22	23·4	20	21·3	94	100·0
Total	31	12·6	97	39·4	75	30·5	43	17·5	246	100·0

Table III.—TYPE OF SURGERY

YEARS OF SURGERY	TOTAL PROCTO-COLECTOMY		COLECTOMY AND ILEOSTOMY		OTHER OPERATIONS		TOTAL	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
1955–9	10	11·6	65	75·6	11	12·8	86	100·0
1960–4	38	57·6	24	36·4	4	6·0	66	100·0
1965–9	69	73·4	19	20·2	6	6·4	94	100·0
Total	117	47·6	108	43·9	21	8·5	246	100·0

3. The availability of a pathological report. Two patients undergoing ileostomy as the only surgery and for whom no such report existed were excluded.

4. The pathological diagnosis must have been ulcerative colitis, and all cases of Crohn's disease and 'unclassified' colitis were excluded. Histological review to ensure accuracy of the diagnosis was undertaken in any doubtful cases.

CLINICAL DETAILS

The age and sex distribution of the 246 cases is shown in *Table I*, where age, defined as the age last birthday, is that at the time of the establishment of the ileostomy. There were 120 males in the series and 126 females. The mean age for the male cases was 38·3 years, for the female cases 43·6 years, and for all patients 40·7 years.

All the patients were graded according to their immediate preoperative clinical condition using the criteria of Ewart and Lennard-Jones (1960). This classification is comprised of the following groups:—

Group A: Good general condition; inactive colitis.

Group B: Good general condition; mild active colitis.

Group C: Poor general condition and/or severe active colitis.

Group D: Critically ill patients treated by emergency operations.

The preoperative grading is shown in *Table II*. The percentage of cases treated electively (groups A and B) rose slightly over the 15 years, the cases coming to urgent surgery (group C) showed a definite fall from 40·7 per cent in the years 1955–9 to 23·4 per cent in the period 1965–9, while there was a slight increase in the incidence of those undergoing emergency surgery (group D).

SURGERY AND RESULTS

Table IV.—OTHER SURGICAL PROCEDURES IN 21 CASES

Surgery	*No. of Cases*
Colectomy and ileorectal anastomosis; subsequent ileostomy (12) and rectal excision (10)	12*
Total proctocolectomy in two or more 'non-standard' stages	5
Ileostomy and subsequent colectomy	1*
Right hemicolectomy and ileostomy	1*
Ileostomy only (+ suture of perforation in 1)	2†

* One patient died postoperatively.
† Both patients died postoperatively.

Type of Surgery.—The operations carried out are shown in *Table III*. The incidence of total proctocolectomy and ileostomy increased markedly over the three 5-year periods of the study, rising from 11·6 per cent in the years 1955–9 to 73·4 per cent in the years 1965–9. Total or subtotal colectomy and ileostomy showed a corresponding decreasing incidence, falling from 75·6 per cent in the first 5-year period to 20·2 per cent in the third. Other surgical procedures carried out in 21 cases are shown in *Table IV*.

Postoperative Mortality of the Primary Surgery.—The overall postoperative mortality of the primary surgery over the 15 years of the study was 8·1 per cent, there being 20 deaths in 246 cases. Primary surgery includes all operations directed to the treatment of the disease, while postoperative mortality is defined as death following surgery while the patient was still in hospital. Analysed in the three quinquennia 1955–9, 1960–4, and 1965–9, the operative mortality was 9·3 per cent (8 out of 86), 10·6 per cent (7 out of 66), and 5·3 per cent (5 out of 94).

Table V relates the number of postoperative deaths to the preoperative grading of the patient. It will be seen that the mortality for cases treated electively (groups A and B) was 1·6 per cent (2 deaths in 128 cases) and there was no death in these groups after the year 1962. For group C, cases coming to urgent surgery, the mortality was 10·7 per cent, while for group D, cases treated as emergencies, the mortality was 23·3 per cent overall. The postoperative mortality in this group fell from 36·4 per cent (4 deaths in 11 cases) in the years 1955–9 to 25 per cent (3 deaths in 12 cases) in 1960–4 and 15 per cent (3 deaths in 20 cases) in 1965–9.

Table V.—Postoperative Mortality of the Primary Surgery related to Preoperative Grading and Year of Surgery

Group	Years of Surgery						Total		Percentage Operative Mortality
	1955–9		1960–4		1965–9				
	No.	No. died	No.	No. died	No.	No. died	No.	No. died	
A	10	1	9	0	12	0	31	1	3·2
B	30	0	27	1	40	0	97	1	1·0
C	35	3	18	3	22	2	75	8	10·7
D	11	4	12	3	20	3	43	10	23·3
Total	86	8	66	7	94	5	246	20	8·1

Table VI.—Postoperative Mortality of the Primary Surgery related to the Type of Surgery

Type of Surgery	Years of Surgery						Total		Percentage Operative Mortality
	1955–9		1960–4		1965–9				
	No.	No. died	No.	No. died	No.	No. died	No.	No. died	
Total proctocolectomy	10	0	38	1	69	4	117	5	4·3
Colectomy and ileostomy	65	6	24	2	19	1	108	9	8·3
Other operations	11	2	4	3	6	0	21	5	23·8
Rectal excision alone	60	0	19	1	13	0	92	1	1·1

Table VII.—Postoperative Mortality of the Primary Surgery related to the Age of the Patients

Age-group (Years)	No. of Cases	No. of Postoperative Deaths	Percentage Postoperative Mortality
10–19	19	3	15·8
20–29	46	2	4·4
30–39	48	3	6·2
40–49	52	3	5·8
50–59	49	5	10·2
60–69	28	4	14·3
70–79	4	0	0
Total	246	20	8·1

The operative mortality related to the type of surgery undertaken is shown in *Table VI.* Total proctocolectomy which was carried out in 117 cases was followed by 5 deaths, all in patients graded in groups C or D preoperatively. Nine patients out of 108 treated by colectomy and ileostomy died postoperatively; all but 1 of these deaths were in patients coming to urgent (group C) or emergency (group D) surgery. Five patients (all but 1 of whom were emergency cases) died following other surgical procedures, and the details of the surgery in these cases is shown in *Table IV.*

The operative mortality related to the age of the patient is shown in *Table VII*, where it is seen that the highest mortality was in the youngest age-group and in patients over 50 years of age. There were 134 cases aged 10–44 years and in this group there were 8 deaths (6 per cent). In the 112 patients aged 45 years or over there were 12 deaths (10·7 per cent).

Emergency Surgery.—Emergency operations were undertaken in 43 cases (17·5 per cent), 13 of these patients having been transferred to St. Mark's Hospital specifically for this surgery. In 15 patients the colon had perforated preoperatively (sealed in 4 cases, with abscess formation in 1, and 'free' in 10 cases) and 6 patients in this group died postoperatively (40 per cent). The indications for emergency surgery in the 28 non-perforated cases were acute deterioration in the general condition in 7 patients, very severe disease failing to respond to intensive medical treatment in 10 cases, severe colonic dilatation in 8 cases, and haemorrhage in 3 patients. The mortality in the non-perforated group was 14·3 per cent (4 deaths in 28 patients). The surgery undertaken in these 43 patients was total proctocolectomy in 8 cases, with 3 deaths, colectomy and ileostomy in 28 patients, with 3 deaths, and other surgical procedures in 7 cases, with 4 deaths (the last 4 patients shown in *Table IV*).

Causes of Postoperative Deaths.—Twenty patients died postoperatively. The main causes of death, verified by post-mortem examination in 14 cases, were as follows: general peritonitis in 7 cases, acute haemorrhagic enteritis in 1, systemic infection in 3, superior mesenteric artery thrombosis in 2, pulmonary embolus in 2, coronary embolus in 1, electrolyte imbalance in 1, and bronchopneumonia in 3. Among the 7 patients dying from general peritonitis were 2 who developed prestomal ileitis postoperatively, and these cases have already been reported (Knill-Jones, Morson, and Williams, 1970).

Postoperative Complications.—Only patients undergoing total proctocolectomy or colectomy and ileostomy are considered in this section. Complications were classified into major, i.e., potentially life-threatening, or minor, i.e., any other condition which interrupted the course of convalescence, and these figures together with the number of postoperative deaths are given in *Table VIII*.

Table VIII.—INCIDENCE OF POSTOPERATIVE COMPLICATIONS IN PATIENTS UNDERGOING STANDARD SURGERY

SURGERY	NO. OF CASES	NO. OF POSTOPERATIVE DEATHS	COMPLICATIONS		
			Major	Minor	None
Total proctocolectomy	117	5	21	37	54
Colectomy and ileostomy	108	9	33	18	48
Total	225	14	54	55	102

Major complications occurred in 54 patients: intra-abdominal infection in 16, intestinal obstruction in 14 (13 patients required laparotomy), other abdominal complications including ileostomy dysfunction in 8, deep venous thrombosis in 4 patients, and pulmonary embolism in 2, chest infection in 7, and miscellaneous complications in the remaining 3 patients.

When the operative deaths are excluded then it is found that for patients treated by total proctocolectomy, 21 cases (18·8 per cent) developed major complications, 37 (33 per cent) had minor complications, and 54 (48·2 per cent) had no setbacks during convalescence. For patients treated by colectomy and ileostomy, the respective figures were 33·3, 18·2, and 48·5 per cent.

If the figures are analysed according to the preoperative severity of the disease then, with the postoperative deaths excluded, it is found that 18·8 per cent (22 out of 117) of patients treated electively (groups A and B) by either proctocolectomy or colectomy and ileostomy had major complications; for group C this figure was 31·3 per cent (20 out of 64) and for group D 40 per cent (12 out of 30).

The duration of convalescence may also be used as a measure of postoperative complications. For groups A and B the average length of postoperative in-patient stay was 29·9 days, for group C 36·6 days, and for group D 48·6 days.

Excision of the Rectum.—Rectal excision was carried out in 101 cases excluding patients treated by total proctocolectomy: in 92 patients the rectum was excised alone and in the remaining 9 cases rectal excision was carried out with other surgery.

Excision of the rectum alone in 92 patients was followed by 1 death; 14 patients had major postoperative complications, 19 had minor complications, and 58 had an uninterrupted convalescence.

At the end of the follow-up period there were 11 patients alive in whom the rectum had not been excised.

The Perineal Wound.—Two hundred and four patients left hospital with a perineal wound and survived for more than 1 year. The date of healing of the wound was known in 157 of these cases. Healing was complete in less than 6 months in 80 patients (51 per cent) and in less than 1 year in a further 41 cases. Thus, in 77·1 per cent of cases where the information was available the wound had healed in 1 year or less.

There was little difference in the rate of perineal wound healing between patients treated by total proctocolectomy and those undergoing rectal excision following colectomy and ileostomy. In the former group, out of 81 cases where the time was known, wound healing was complete in 1 year or less in 65 patients (80·2 per cent) and in less than 6 months in 43 cases (53·1 per cent). In the latter group, in 66 cases where there was adequate information the respective figures were 72·7 and 48·5 per cent.

Between the date of surgery and the end of 1970 (thus allowing at least 1 postoperative year to elapse in all cases to assess perineal wound healing) 16 patients with a total of 19 admissions required in-patient treatment for an unhealed perineal wound. The patient readmission rate was therefore 7·8 per cent, and the average stay in hospital was 27·3 days.

Intestinal Obstruction.—Complete small intestinal obstruction or incomplete obstruction requiring surgery occurred in 32 patients between the date of operation and the concluding date for this study (1 Jan., 1970). This gives an overall patient reoperation rate for this complication of 13 per cent. This rate was 19·9 per cent for patients operated on in the years 1955–9, 9·1 per cent for the years 1960–4, and 9·6 per cent for the years 1965–9. In all, a total of 35 operations was carried out in these 32 patients, giving a total reoperation rate of 14·2 per cent.

Table IX.—INCIDENCE OF SURGICALLY TREATED OBSTRUCTION RELATED TO TYPE OF PREVIOUS SURGERY

SURGERY	NO. OF CASES	POSTOPERATIVE OBSTRUCTION	NO. OF CASES LEAVING HOSPITAL	READMISSIONS FOR OBSTRUCTION
Total proctocolectomy	117	5	112	6
Colectomy and ileostomy	108	8	99	2
Colectomy and ileostomy and excision of rectum	88	2	87	8*
Other primary surgery	21	0	16	2

* Includes 1 patient with a previous laparotomy following colectomy and ileostomy.

Table IX relates the incidence of surgically treated obstruction to the type of previous surgery and shows both the postoperative incidence and the late incidence. The average stay in hospital for patients readmitted to St. Mark's Hospital with obstruction was 19·2 days.

The cause of the obstruction was known in 34 of the 35 laparotomies, and was adhesions in 24 instances, a volvulus in 2, a strangulated para-ileostomy hernia in 2, miscellaneous causes in 4, and lateral space obstruction in 2 patients operated on prior to 1958.

The time of obstruction relative to the date of the last surgery for the 24 patients with adhesion obstruction was as follows: in the postoperative period, 11; after discharge but within 1 year of surgery, 9; between 2 and 3 years after surgery, 3; and at an interval of 10 years after surgery, 1. Seventeen of these 24 patients had had only one operation, the remaining 7 more than one.

Episodes of incomplete intestinal obstruction were responsible for 14 patients being readmitted, with an average duration of hospital stay of 6·1 days. Conservative treatment was successful in all cases although 1 patient required laparotomy at a later date.

Reconstruction and Resiting of the Ileostomy.—Reconstruction of the ileostomy was required in 7 patients and resiting was necessary in 1, giving a total patient reoperation rate for these complications of 3·5 per cent.

One patient required reconstruction in the postoperative period; the other 6 were readmitted specially for this surgery, with an average stay in hospital of 11·1 days. Two patients required reconstruction on two occasions, and the reasons for these 9 operations were instability of the ileostomy in 1 instance, stenosis in 1 case, and retraction on the other 7 occasions.

Other Complications requiring Readmission to Hospital.—

Gastro-intestinal upsets usually with symptoms of nausea and vomiting, abdominal pain, and increased ileostomy effluent were responsible for the readmission of 9 patients with a total of 13 admissions. The condition settled with conservative treatment in all cases. The average in-patient stay for these conditions was 5·5 days.

Local ileostomy complications were very uncommon. Only 2 patients were readmitted for this reason, in each case for the treatment of skin excoriation.

Abdominal wound complications were uncommon; 5 patients were admitted on 6 occasions for treatment to abscesses or sinuses related to the abdominal wound. One patient underwent repair of an incisional hernia. The patients in this group spent an average of 14·6 days in hospital.

Other complications related to the previous surgery occurred in 9 patients; the most serious of these were late retroperitoneal abscess formation in 2 cases.

Table X shows the number of patients readmitted for these various complications up to the end of the follow-up period. Allowing for multiple readmissions of the same patient, the total number of patients readmitted for the first 7 complications shown in *Table X* was 49 (21·7 per cent) of the 226 who left hospital. Fifteen patients who had not previously been admitted for complications required in-patient treatment for an unhealed perineal wound. Therefore, in all, 64 patients (28·3 per cent) were readmitted for complications referable to the previous surgery.

THE FOLLOW-UP

During 1970, follow-up information was obtained about all patients (with the exception of 4 who lived abroad) who no longer regularly attended the hospital. The concluding date for this study has therefore been taken as 1 Jan., 1970, for all purposes except for the assessment of perineal wound healing (*see above*). Thus, patients were followed up for varying periods up to 15 years after surgery, and the average length of follow-up for the 205 patients known to be alive on 1 Jan., 1970, was 7 years.

The main conditions of a general nature that occurred during the years of follow-up, together with the number of patients with these conditions preoperatively, are shown in *Table XI*.

Table X.—READMISSIONS FOR VARIOUS COMPLICATIONS

CAUSE	NO. OF PATIENTS RE-ADMITTED	PATIENT RE-ADMISSION RATE (per cent)	NO. OF RE-ADMISSIONS	TOTAL RE-ADMISSION RATE (per cent)
No. of patients at risk: 226				
Complete intestinal obstruction	18	8·0	20	8·9
Incomplete intestinal obstruction	14	6·2	14	6·2
Reconstruction of the ileostomy	6	2·7	8	3·5
Gastro-intestinal upsets	9	4·0	13	5·7
Local ileostomy complications	2	0·9	3	1·3
Abdominal wound conditions	6	2·7	7	3·1
Other related complications	9	4·0	9	4·0
No. of patients at risk: 204				
Perineal wound	16	7·8	19	9·3

Table XI.—DISEASE IN THE FOLLOW-UP PERIOD

Disease	*No. of Cases in the Follow-up Period*	*No. of Cases Pre-operatively*
Peptic ulcer	1	4
Gall-stones	3	3
Pulmonary tuberculosis	0	6
Other pulmonary disease	3	4
Cardiovascular disease	5	7
Urinary-tract calculi	6	5
Thyroid conditions	3	3
Diabetes mellitus	0	5
Mental illness	2	0
Musculoskeletal affections	5	3
Gynaecological conditions	4	5
Other complaints not requiring surgery	5	9
Other complaints requiring surgery	5	6
Malignant tumours	8	2

Calculi in the Urinary Tract.—Five patients are thought to have had urinary-tract calculi preoperatively and 6 patients are known to have had such stones postoperatively. In the former group the stones occurred at intervals varying from 2 to 30 years after the onset of colitic symptoms, but in 2 patients other factors may have been involved in stone formation. One patient passed a stone, in another a renal calculus was an incidental finding on radiology, and in the other 3 cases there was a history of surgery for renal calculi.

Two patients were found to have ureteric calculi approximately 6 weeks postoperatively. In both cases the calculi (single in 1 case and multiple in the other) were later passed spontaneously.

Calculi were found in 4 patients at varying intervals from 6 to 12 years after surgery; 1 patient passed a calculus but in the other 3 patients operation was required. The chemical composition was known in 3 of the cases where stones arose after surgery: this was reported as carbonates in 1 case, calcium oxalate in the second, and calcium oxalate and urate in a patient with multiple bladder calculi.

Deaths in the Follow-up Period.—Seventeen patients are known to have died in the interval between their discharge from hospital and the end of the follow-up period. The causes of death are summarized in *Table XII*, where the relationship to the complications of the disease or its treatment is shown.

Table XII.—CAUSES OF LATE DEATH

Cause	*No. of Patients*
Related deaths	
Metastases from carcinoma in ulcerative colitis	4
Abdominal lymphosarcoma (primary lesions in the sigmoid and rectum and ulcerative colitis)	1*
Serum hepatitis	1
Possibly related death	
Suicide	1
Unrelated deaths	
Malignant tumours	5†
Bronchopneumonia	2
Coronary thrombosis	1
Congestive cardiac failure	1
Rheumatoid arthritis	1

* Case reported by Cornes, Smith, and Southwood (1961).

† Carcinoma of the ovary, 1; postcricoid carcinoma, 1; carcinomatosis—unknown primary, 1; carcinomatosis, double primary—nostril and prostate, 1; reticulosarcoma, 1.

Expected and Observed Mortality.—Eighty-nine males and 103 females fitted the criteria for the calculation of expected mortality. These criteria were: (*a*) complete removal of the colon and rectum, (*b*) the survival for 1 postoperative year from the completion of this surgery, and (*c*) absence of malignant change in the excised specimen. This calculation, taking into account the age and sex of the patient, was made using the 1961 English Life Tables (No. 12). The expected deaths to the end of the follow-up period in the 89 males were 5·1, and the observed deaths 1; for the 103 females the respective figures were 3·9 and 4.

DISCUSSION

Excisional surgery with the construction of a permanent ileostomy is now a well-established procedure as the operative treatment for ulcerative colitis. The present series of 246 patients undergoing such surgery in the years 1955–69 demonstrates some important points in the evolution of this surgery which will be discussed in detail.

Type of Surgery.—Colectomy and ileostomy as the initial operation was undertaken in 75·6 per cent of cases in the years 1955–9, but in the last 5 years of this study the incidence had fallen to 20·2 per cent; total proctocolectomy, undertaken in only 11·6 per cent of cases in 1955–9, was the operation carried out in 73·4 per cent of patients in the years 1965–9. This rising incidence of a one-stage procedure has been reported before, both from this hospital (Lockhart-Mummery, 1970) and from a group of hospitals (Ritchie, 1971), and the present figures show that it continues to be the operation most frequently undertaken for ulcerative colitis at this centre.

Preoperative Condition of the Patient.—The surgical treatment of patients operated upon electively (groups A and B) carried a very low mortality-rate in this series, i.e., 1·6 per cent in 128 cases, an even lower figure than that reported in other large series, e.g., 3·4 per cent (Daly and Brooke, 1967), 3·8 per cent (Watts, de Dombal, and Goligher, 1966), and 4 per cent (Hughes, 1964). In addition, elective surgery was followed by a low major postoperative complication rate and a rapid convalescence. By contrast, the operative mortality for emergency surgery (group D) was 23·3 per cent, the major complication rate being over twice that for elective surgery and the duration of postoperative in-patient stay 19 days longer on average. Results intermediate between these two groups were obtained in those cases coming to urgent surgery (group C).

Emergency surgery carries a high mortality in reported series, e.g., 15 per cent (Hughes, 1964), 17·4 per cent (Boxall, 1966), 24 per cent (Daly and Brooke, 1967), 26·7 per cent (Watts and others, 1966), 31 per cent (Lennard-Jones and Vivian, 1960), and 44·4 per cent (Ritchie, 1971), and the figures for the present series are no exception. The figure of 15 per cent for the years 1965–9, although as low as any of those referred to above, highlights one of the main contemporary problems in the treatment of colitis, which is the management of the severe attack. Ideally, surgery should not be undertaken in these circumstances and every effort should be made to induce remission by full-scale medical treatment and to operate later, if necessary, under elective conditions. However, in a proportion of cases this remission will not occur, or only to a limited extent, and it is in these patients especially that expert assessment is required on the optimum timing for surgery. A strong plea for earlier surgery substantiated by a fall in operative mortality from 20 per cent in 40 patients coming to urgent or emergency surgery in the years 1952–63 to 7 per cent in 71 similar cases in the period 1964–9 has been made recently by Goligher, Hoffman, and de Dombal (1970).

Twenty-eight of the 43 emergency cases were treated by colectomy and ileostomy; the 3 deaths in this group were in patients operated on in the earlier years, and no deaths occurred in 18 emergency cases treated in this way from 1962 onwards. Total proctocolectomy undertaken as an emergency in 8 patients between 1960 and 1969 was followed by 3 deaths, all in the last 3 years of the study. Findings at operation may dictate the more extensive procedure, but the figures perhaps suggest that colectomy and ileostomy, where practicable, remains the treatment of choice for patients undergoing emergency surgery.

Complications of Surgery.—Small intestinal obstruction requiring surgical intervention occurred in 32 patients up to the end of the follow-up period, the incidence falling from 19·9 per cent for patients operated on in the years 1955–9 to 9·6 per cent for the years 1965–9. This latter figure, which is very similar to that reported in other series, e.g., 9 per cent (Daly and Brooke, 1967) and 9·3 per cent (Ritchie, 1971), suggests that obstruction, especially if due to adhesions, is a non-preventable complication even with present-day surgical technique. However, it was not a fatal late complication in this series, there being no deaths following surgery in the 18 patients readmitted with this condition.

Delayed healing of the perineal wound was the only other specific complication with an appreciable incidence in this series and readmissions for this reason showed no tendency to fall over the years of the study. It seems probable that the high readmission rate was the result of a policy designed to accelerate perineal wound healing, laying open of a sinus and curettage being considered as the quickest way to effect this.

Considered collectively, readmissions for complications (with the exception of those for an unhealed perineal wound) showed a considerable fall over the 15-year period, from 32·1 per cent of 78 patients operated on in the years 1955–9 to 9 per cent of 89 patients in the years 1965–9. This lower figure may be due partially to the shorter follow-up in these cases, but a continuing decline in complications is to be expected with increasing experience of this surgery.

The Follow-up.—Consideration of the diseases encountered during the years of follow-up shows no conditions occurring with any frequency. With the exception of urinary-tract calculi, this has been the finding in another large series (Ritchie, 1971). Almost 600 patients have been followed up in these two series and no other specific diseases following surgery have been discovered. The supposition is, therefore, that no such diseases exist except, perhaps, for this increased tendency to urolithiasis. The incidence of this condition in the present series was only 1·9 per cent in the 226 patients who left hospital with an ileostomy; excluded from this number are the 2 patients in whom stones were found some 6 weeks after surgery, as it seems possible that the calculi were present preoperatively. In the absence of exact figures for the incidence of such calculi in the general population the figure of 1·9 per cent cannot be said to be significant. However, when it is considered in conjunction with the figures of Ritchie (1971), i.e., 4·3 per cent in 371 patients leaving hospital with an ileostomy, the possibility remains that ileostomists may be more prone to develop urinary-tract calculi than the normal population.

Expected and Observed Mortality.—There are now three sets of figures available giving the number of expected and observed deaths in groups of ileostomists: these are Daly's (1968) series of 358 ileostomists from Birmingham, the present author's (Ritchie, 1971) series of 267 patients drawn from 37 hospitals of the North East Metropolitan Hospital Region, and the group of 192 patients from St. Mark's Hospital presented in this paper. All the cases in these three series were subject to the same criteria of selection; the only difference in the samples being that the second series included 20 patients with Crohn's disease. In Daly's (1968) figures for patients operated on in the years 1947–66 and followed up until 1966 the expected deaths were 17·66 and the observed deaths 19; in the second series (Ritchie, 1971) for patients undergoing surgery in the years 1955–66 and followed up until the end of 1967 the respective figures were 11·6 and 18, and in the present study for patients treated in the years 1955–69 and followed until the end of 1969 the respective figures were 9 and 5. Thus, there is a small excess mortality in Daly's series, a rather higher figure in the second group, and no excess mortality in the present series. It is not obvious why this somewhat unlikely result should have been obtained for the patients in the present study, but it is possible that the sample was not large enough or the follow-up not long enough. A more accurate assessment of the position with regard to life expectancy in these patients can be obtained by the addition of the figures in these three series to obviate errors due to smallness of the samples. Then it is found that in 817 patients the expected deaths were 38·3 and the observed deaths 42, i.e., only 4 excess deaths in 817 cases, and it appears probable that these figures give a more accurate picture than any one of the series considered alone.

The conclusion, therefore, from the figures presented in this paper, particularly when considered with those from the other series, must be that the life expectancy of patients with ulcerative colitis, in the absence of malignant change, is normal when 1 postoperative year has elapsed following radical surgery.

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DEVELOPMENT OF RIGHT INGUINAL HERNIA FOLLOWING APPENDICECTOMY

A 10-YEAR REVIEW OF CASES

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SUMMARY

The incidence of right inguinal hernia in patients who have undergone appendicectomy is significantly greater than that in the general population. It is suggested that the most likely cause is injury to the segmental nerve-supply to the inguinal musculature.

It is suggested that the sequela of right inguinal hernia following appendicectomy may be decreased, if not prevented, by proper understanding of the anatomy of the region and care during surgery, but 'in spite of the tempting simplicity of aetiologic reasoning, a cause-and-effect relationship cannot yet be confirmed'.

HOGUET in 1911 first described the frequent development of right inguinal hernia following appendicectomy. He found 8 right inguinal herniae out of 190 patients who had previously had an appendicectomy, the time interval between appendicectomy and the appearance of a hernia in his cases being from 2 weeks to 4 years.

In 1951 Lichtenstein and Isoe reviewed 567 patients with inguinal hernia. In 67 of these the appendix had been removed (40 were right-sided, 12 bilateral, and 15 left-sided), but it was Seulberger and Pefers (1951) who suggested: 'Lateral abdominal incisions predispose to inguinal herniae, especially on the right side.' Walker in 1954 also found 100 post-appendicectomy patients with right inguinal hernia out of 1357 inguinal herniae.

The present study examines the incidence of right inguinal hernia following appendicectomy during the past decade in a regional hospital.

MATERIALS AND METHODS

This is a retrospective study based on the records of all cases of inguinal hernia operated on at Worcester Royal Infirmary between 1959 and 1969. Infant herniae have been excluded. The age range was from 13 to 82 years, only 2 patients being below the age of 16 years. The type of hernia repair was of a standard Bassini type using either silk or tantalum wire as the suture material.

RESULTS

A total of 701 herniae were operated on, 51 of these having previously undergone appendicectomy. Of these 51 patients, 41 developed right inguinal hernia, 7 left inguinal hernia, and the remaining 3 were bilateral. Out of the 41 cases, there were only 3 females.

In the group of 41 patients with right inguinal hernia the appendicectomy had been through a lower paramedian incision in 6 and via a McBurney's approach in the remainder. The type of hernia was indirect in 26 cases and direct in 15 cases. There have been no recurrences in this group to date.

The incidence of right inguinal hernia after appendicectomy has been compared with the incidence in cases who had not undergone appendicectomy in *Table I*.

In the 650 patients who had not had a previous appendicectomy the ratio of right-sided hernia to left-sided was approximately 2 : 1, whereas in the post-appendicectomy group the ratio was 6 : 1. This difference is statistically significant (χ^2 test: significant at a 5 per cent level).

Table I.—THE INCIDENCE OF INGUINAL HERNIA IN 51 CASES WHO HAD UNDERGONE APPENDICECTOMY COMPARED WITH THAT IN 650 CASES WHO HAD NOT HAD AN APPENDICECTOMY

	AFTER APPENDICECTOMY			NO APPENDICECTOMY		
	Right Hernia	Left Hernia	Bilateral Herniae	Right Hernia	Left Hernia	Bilateral Herniae
No. of cases	41	7	3	306	144	200
Percentage	80·3	13·7	5·8	40·07	22·1	30·7
Ratio of right to left	6 : 1			2 : 1		

DISCUSSION

The results show that appendicectomy predisposes to the development of right-sided inguinal hernia.

Approximately 5 per cent of the population of Britain have inguinal hernia and the repair of these accounts for 10 per cent of general surgical operations. Sixty per cent of these herniae are right-sided, 20 per cent are bilateral, and 20 per cent are left-sided (Ellis, 1970). These figures are similar to the overall distribution of herniae in the present study.

To understand the possible iatrogenic causes and the aetiological relationships in the development of right inguinal hernia following appendicectomy, one needs to refer to the anatomy of the internal ring, which was beautifully illustrated by Lytle (1970): 'The internal ring is "U" shaped; composed of thickened transversalis fascia, is suspended by its two pillars, medial and lateral to the posterior aspect of transversus abdominis muscle. The curve of the "U" lies at or just above the lower border of aponeurosis of the transversus muscle. This aponeurosis forms the floor of the ring and is supported in front by the internal oblique muscle.' An efficient valve is thereby provided which closes when the intra-abdominal pressure is increased. Injury to the transversus abdominis muscle and posteriorly adherent transversalis fascia can damage the shutter mechanism of the internal ring and also weaken the posterior wall of the triangle of Hesselbach.

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Incomplete approximation and healing of the fascial layers (transversus muscle and aponeurosis with posteriorly adherent transversalis fascia) after appendicectomy is one of the important factors in the subsequent development of inguinal hernia (Scott, 1960). This can easily happen, owing to the protrusion of peritoneum and extraperitoneal fat through the open transversus muscle and its posteriorly adherent transversalis fascia. Scarring of this layer with fixation to the other abdominal wall muscles, as occurs after prolonged drainage of an appendix abscess, has also been suggested as a cause of weakness leading to the development of inguinal hernia (Hoguet, 1911).

Observations from the present study suggest that damage to the segmental nerve-supply of the internal oblique and transversus muscles leads to the weakening of the posterior wall of the inguinal canal and the internal ring. In addition, the shutter mechanism of the canal must be compromised by the denervation. Examination of some of the patients in this series showed generalized bulging in the inguinal region, and in some cases the muscles have been found to be atrophic at operation. Electromyographic studies to confirm the denervation would be of value.

In the present series there were only 2 patients under 16 years of age, and it would seem that post-appendicectomy hernia occurs less in the younger age-group. This may well be due to restoration of the damaged structures in the abdominal wall by the growing body.

It is felt that this study emphasizes that nerve injury should be avoided during surgery and also that the structures of the right lower abdominal wall should be preserved during McBurney's or right lower paramedian incisions. The following technical suggestions may help to lessen the incidence of hernia in patients undergoing appendicectomy. The skin incision is not thought to be of much significance, but incisions much below the anterior superior iliac spine are to be avoided if possible, as segmental nerves pierce at this level and course downwards. The external oblique muscle should be opened between its parallel fibres. Importance is given to the opening of the internal oblique and transversus muscles with the adherent transversalis fascia posteriorly at the level of the anterior superior iliac spine and not below. It is advisable to split the transversus muscle and its aponeurosis as a separate layer which includes, of course, the transversalis fascia on its posterior surface. The peritoneum then bulges into the wound. This avoids injury to the internal ring and the triangle of Hesselbach. Separate suture of the transversus aponeurosis with the attached transversalis fascia is advisable to avoid bulging of the peritoneum through this layer. The internal oblique muscle is approximated with one light suture so as not to strangulate the muscle. Alternatively, just the thin fascia over it may be sutured.

Thus, one should avoid injury to the important structures in the inguinal region, especially below the horizontal line extending from the anterior superior iliac spine to the rectus muscle.

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TUBERCULOUS PERIPHERAL LYMPHADENITIS

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SUMMARY

Tuberculous peripheral lymphadenitis is still a common and often poorly treated manifestation of tuberculosis. One hundred and eighteen cases are reviewed, and the problems of diagnosis and management are considered together with the causes of failure of treatment.

IN 1968 tuberculosis caused 2091 deaths in England and Wales—more than any other infectious disease. In the same year there were 12,974 new cases of the disease. Although the incidence of new cases of respiratory tuberculosis has diminished dramatically during the past decade, that of non-respiratory disease has decreased little and so forms an increasing proportion of the total tuberculosis problem (*Table I*).

Superficial lymph-node involvement is the most common presentation of non-respiratory tuberculosis, accounting for about 40 per cent of the cases reported in this paper, and yet it is the least adequately diagnosed and treated form of the disease. As superficial lymph-node involvement is an early manifestation and is often unaccompanied by gross

Table I.—NOTIFICATIONS OF NEW CASES OF TUBERCULOSIS FOR ENGLAND AND WALES*

Type of Tuberculosis	1960	1968
Respiratory tuberculosis	21,117	10,681
Meninges and central nervous system	199	92
Other forms	2,661	2,181
Total	23,977	12,974

* Registrar General's *Statistical Review* (1961, 1968).

disease elsewhere, clinicians are often tempted to treat it less rigorously than the more notable forms of the disease. Tuberculosis, however, is a disease of long duration, characterized in many patients by periods of quiescence without cure followed by local reactivation or evidence of dissemination. This is well illustrated by the following case (not derived from the material which is analysed later).

Mrs. C. M. T., born on 27 June, 1903. In 1907 this patient had tuberculous nodes excised from the left neck. A left ureteronephrectomy for tuberculosis was carried out in 1924, and in 1929 tubercle bacilli were again recovered from the urine. In 1932 tuberculous cystitis was diagnosed. Examination of the patient in 1948 revealed a small fibrotic bladder, with no evidence of active infection. In 1960 tuberculosis of the left breast was diagnosed and the breast was excised. The patient was treated for 1 week with para-aminosalicylic acid (PAS) and isonicotinic acid hydrazide (INAH) which were then stopped because the patient had a convulsion. In 1965 a vesical calculus was removed and a urethral caruncle showing on biopsy a granulomatous reaction containing Langhans giant cells was found. The patient was treated for 5 months with PAS and INAH. Further urinary symptoms occurred in 1968, a small caruncle on biopsy showing typical features of a caruncle only.

PRESENT STUDY

Two hundred and thirty-eight cases of extrapulmonary tuberculosis obtained from three general hospitals in the decade 1960–9 have been analysed (*Table II*). Of these, there were 103 individuals in whom 118 episodes of lymph-node tuberculosis were treated. Of the recurrent cases the original episode occurred before the 10-year period in 8 cases; this has been included in the analysis but where it would bias the results it has been listed separately.

Table II.—SITE OF LESION IN 238 CASES OF EXTRAPULMONARY TUBERCULOSIS

Site of Lesion	*No. of Cases*
Superficial lymph-node	103
Urogenital tract	52
Bone and joint	37
Intestine	5
Abdominal lymph-nodes	2
Tuberculous peritonitis	6
Soft-tissue lesions without underlying bone or joint disease	11
Breast	5
Liver and spleen	7
Lupus vulgaris	3
Thyroid	1
Adrenals	6
Coexisting pulmonary tuberculosis	49

Table III.—AGE DISTRIBUTION IN 118 CASES OF LYMPH-NODE TUBERCULOSIS

Age-group (years)	*No. of Cases*
0– 9	7
10–19	12
20–29	26
30–39	28
40–49	14
50–59	12
60–69	6
70	9
Unstated	4

Age Incidence.—The age distribution in this series is markedly different from that in most reported series (Dowd, 1916; Barrington Ward, 1937; Miller and Cashman, 1955; Wimot, James, and Reilley, 1957; Jones and Campbell, 1962; MacKellar, Hilton, and Masres, 1967), where children largely predominate. In the present series the maximal incidence occurs in the age-group of 20–40 years (*Table III*).

Place of Birth.—A disproportionate number of the cases in this series were born outside England, Scotland, and Wales. This is no doubt due to the fact that cases were collected from areas with a high immigrant population as well as to the known susceptibility of Asians to this disease (*Table IV*).

Clinical Presentation.—Eighty-four out of 118 cases of tuberculous peripheral lymphadenitis presented with a swelling in the neck alone or accompanied by only minor constitutional symptoms (*Tables V, VI*). Group *e* (*Table V*), cases with a particularly acute presentation, represents one of the variants of so-called 'Asian tuberculosis'; this picture may also, though less commonly, be seen in native-born English.

Table IV.—PLACE OF BIRTH IN 118 CASES OF LYMPH-NODE TUBERCULOSIS

Place of Birth	*No. of Cases*
England, Scotland, and Wales	50
Ireland	8
Indian subcontinent	27
East African Indian	6
West Indian	5
Others	9
Not known	11

Table V.—SYMPTOMS AND OTHER FINDINGS IN 118 CASES OF LYMPH-NODE TUBERCULOSIS

Symptoms and Findings	*No. of Cases*
a. Swelling in neck without other symptoms	39
b. Swelling in neck with mild general symptoms, e.g., malaise, lethargy, anorexia, weight-loss, mild fever	34
a or *b*. Not stated	11
c. Swelling in neck accompanying past or present pulmonary infiltration	16
d. Swelling in neck with evidence of lymph-node enlargement elsewhere	6
e. Acute presentation often with high fever, disseminated lymph-node enlargement, and sometimes hepatosplenomegaly	6 6
f Lymph-node enlargement accompanying tuberculosis in other systems	6

Table VI.—SITE OF INVOLVED NODES IN 118 CASES OF LYMPH-NODE TUBERCULOSIS

Site of Involved Nodes	*No. of Cases*
Cervical	106
Pre-auricular	1
Submental	1
Submandibular	13
Upper deep cervical	89
Lower deep cervical	28
Occipital	2
Axillary	5
Inguinal	6
Epitrochlear	1
Unstated	4

PHYSICAL SIGNS OF INVOLVED NODES

The natural history of physical signs of tuberculous superficial lymph-nodes is widely accepted (Jones and Campbell, 1962; Clain, 1968). The classification of Jones and Campbell (1962) is as follows:—

Stage 1: Enlarged, firm, mobile, discrete, slightly tender nodes showing non-specific reactive hyperplasia.

Stage 2: Nodes larger, rubbery, and fixed to surrounding tissues owing to periadenitis showing histological caseation.

Stage 3: Central abscess formation.

Stage 4: Collar-stud abscess formation.

Stage 5: Sinus formation.

Stage 1 is not diagnosable as tuberculous except by indirect means or in retrospect. Since periadenitis and caseation occur early in the disease process, clinical diagnosis should be relatively easy and accurate. However, in the present series the diagnosis of tuberculosis was thought unlikely in about 1 in 3 cases.

Confusion occurs mainly in cases in clinical stages 1–3 (and only 8 out of 118 cases did not fall into stages 2 and 3), because the physical signs may not be as clear cut as this staging would suggest. Abscess formation when present is difficult to detect clinically in nodes lying deep to the deep fascia. Periadenitis is often not marked even in the presence of gross caseation.

A number of nodes pass through a stage of solid enlargement histologically characterized by a non-caseating granulomatous picture, which in the absence of acid–alcohol-fast bacilli is indistinguishable from that of sarcoidosis or other non-caseating tuberculoid granuloma. These nodes seldom show fixity owing to periadenitis. In this series no less than 1 in 10 of the excised nodes were macroscopically solid, without caseation or showing microcaseation and so were erroneously not submitted for culture. Solid nodes may occasionally reach a considerable size, in 1 case measuring 3 × 2 × 2 cm.

DIFFERENTIAL DIAGNOSIS OF CERVICAL TUBERCULOUS LYMPHADENITIS

1. From Other Causes of Lymph-node Enlargement.—

a. Non-specific inflammatory.

b. Lymphoma.

c. Leukaemia.

d. Secondary carcinoma.

e. Infectious mononucleosis.

f. Various other causes dealt with under histological differentiation.

2. Other Swellings in the Neck.—

a. Parotid and submandibular salivary gland enlargement.

b. Bronchial cyst.

c. Carotid-body tumour.

d. Extension of abscess from cervical vertebra.

The provisional diagnoses in the 43 cases in the present series which were thought not to be tuberculous are listed in *Table VII.*

Diagnostic lymph-node biopsy is frequently necessary in the elucidation of illness accompanied by lymph-node enlargement. In adults secondary carcinoma is the commonest cause of lymph-node enlargement, but tuberculosis is the next most common cause, being as frequent as lymphoma and leukaemia (*see Table VIII* for a 5-year review of lymph-node biopsies from one general hospital and also Matzker, 1967).

MICROSCOPIC DIFFERENTIATION

Tuberculosis of lymph-nodes produces a granuloma characterized by epithelioid and giant cells of the Langhans type, usually with marked, though occasionally minimal or absent, caseation. Acid–alcohol-fast bacilli may be demonstrated by the Ziehl-Neelsen or by the Auramine-Rhodamine technique (Jones and Campbell, 1962).

Table VII.—CLINICAL DIAGNOSIS IN THE 43 CASES OF THIS SERIES NOT DIAGNOSED AS TUBERCULOUS LYMPHADENITIS

Diagnosis	*No. of Cases*
Lymphoma	18
No diagnosis	7
Pyogenic abscess	6
Bronchial cyst	4
Pyrexia of unknown origin with lymphadenopathy	3
Carcinoma of thyroid	2
Carcinoma of bronchus	1
Lipoma	1
Aneurysm of subclavian artery	1

Table VIII.—DIAGNOSIS AT LYMPH-NODE BIOPSY IN 192 CASES DURING THE 5-YEAR PERIOD 1965–9

Diagnosis	*No. of Cases*
Secondary carcinoma	67
Lymphoma and leukaemia	34
Tuberculosis	32
Reactive hyperplasia	37
Sarcoid reaction	6
Other or no diagnosis	16

1. Caseating or Non-caseating Granuloma in which Acid-fast Bacilli are seen.—

a. Anonymous or Atypical Mycobacterial Infection.—This is distinguishable only on culture from *Mycobacterium tuberculosis* infection. Many anonymous mycobacteria, unlike *Myco. tuberculosis*, are not guinea-pig pathogens, so that culture of tuberculous material should always be performed on Lowenstein-Jensen medium as well as by guinea-pig inoculation.

b. Lepromatous Leprosy.—Mycobacteria may be seen intracellularly but within large mononuclear 'lepra cells'. The granulomatous reaction is diffuse and without caseation.

2. Granulomatous Reaction with Central Necrosis in which Acid-fast Bacilli are not seen.—

a. Catscratch Disease.—Catscratch disease is probably a virus, although an anonymous mycobacterium has recently been suggested (Jones and Campbell, 1962). This is an irregular-shaped granuloma with a marked tendency to suppuration.

b. Lymphogranuloma Venereum.—Lymphogranuloma venereum is usually found in the groin nodes and is characterized by a small, solid granuloma composed of large mononuclear cells which break down centrally with polymorphonuclear leucocyte infiltration to form a stellate abscess. The patient gives a positive Frei test.

c. Syphilis.—Primary and secondary syphilis may produce a giant-cell granuloma with or without central necrosis. There is a marked tendency for endarteritis and new vessel formation around the periphery. Treponemes are demonstrable by suitable staining (Hartsock, Halling, and King, 1970).

d. Tularaemia.—The histological picture may be indistinguishable from tuberculosis but the causative *Pasteurella tularensis* can be grown by guinea-pig inoculation or agglutinating antibodies are detectable in the serum.

e. Fungus Granuloma.—The causative fungus can be seen, blastomyces and coccidioides in haematoxylin and eosin preparations, and *Histoplasma capsulatum* by periodic acid Schiff reagent. *Actinomyces israeli* does not involve lymph-nodes.

3. Granulomatous Reaction without Necrosis—Sarcoid Reaction.—

a. Sarcoidosis.—Sarcoidosis in which the sarcoid lesion can be found in more than one site in the body (Scadding, 1967) and in such patients the Kveim test is usually positive.

b. Brucellosis.—Brucellosis may present a sarcoid picture. This may be diagnosed on guinea-pig inoculation or by the presence of serum agglutinins.

c. Hodgkin's Disease.—A granulomatous reaction may occur as an integral part of the reaction in a lymph-node involved by the disease, which is, however, characterized by the presence of Reed-Sternberg cells.

d. An isolated sarcoid picture may be seen in lymph-nodes adjacent to some malignant and benign conditions including carcinomas (Nickerson, 1937; Nadel and Ackerman, 1950; Symmers, 1951; Revfem, 1954), malignant melanoma (Nadel and Ackerman, 1950), Hodgkin's disease, and other lymphomas (Revfem, 1954).

TECHNIQUE OF DIAGNOSIS

Clinical methods as noted above are inaccurate in establishing the cause of lymph-node enlargement. In this series a non-tuberculous clinical diagnosis was made in 1 in 3 cases (*Table VII*).

Tuberculosis may coexist with carcinoma or lymphoma. Since all three are not uncommon conditions (*Table VIII*) the presence of one elsewhere in the body will not establish the cause of subsequent lymph-node enlargement. Furthermore, in lymphoma, immunity may well be depressed, making the patient more susceptible to intercurrent infection. In the present series a lymphoma was found subsequent to tuberculous lymphadenitis in 3 cases. Sarcoidosis may supervene in a patient with proved tuberculosis or vice versa (Scadding, 1967).

To establish the tuberculous aetiology of lymph-node enlargement the node should show typical histology, preferably with acid–alcohol-fast bacilli visible. Most importantly the organism should be isolated by culture on Lowenstein-Jensen medium and by guinea-pig inoculation.

Caseous material is a poor source of tubercle bacilli. The lack of infectivity of tuberculous pus is well attested (Dowd, 1916). It probably contains a bacteriostatic substance (Soltys, 1953). The solid part of the lesion rather than pus should be submitted fresh for culture. Indeed, solid as well as caseating nodes should be routinely submitted for culture before being immersed in fixative, as should other biopsy material when there is doubt about the diagnosis. The opportunity of adequate culture may occur only once.

In this series standards of bacteriological diagnosis were low (*Table IX*), for in less than 1 in 3 cases was an attempt made to culture the biopsied node.

Surgical excision of the largest available lymph-node for examination is mandatory; this is a procedure normally requiring general anaesthesia. Excision of a small superficial node under local anaesthesia frequently results in a failure to establish a diagnosis, showing histologically a normal architecture, reactive hyperplasia, or a sarcoid reaction; all these features may be seen in nodes adjacent to carcinoma, lymphoma, tuberculosis, sarcoidosis, and some benign tumours (Revfem, 1954) in nodes that are almost certainly sterile. The practice of aspirating pus to establish a diagnosis is not a good one, as it has a low success rate (*Table IX*) and a high complication rate.

Table IX.—BACTERIOLOGICAL DIAGNOSIS

Bacteriological Diagnosis	*No. of Cases*
Acid–alcohol-fast bacilli seen but not cultured	25
Acid–alcohol-fast bacilli seen and cultured	23
Tubercle bacilli not seen but cultured	3
Caseous material only cultured	23
Positive culture	9
Organism isolated	
Myco. tuberculosis	24
Anonymous mycobacterium	2

TREATMENT OF CERVICAL TUBERCULOUS LYMPHADENITIS AND ITS RESULTS

In the pre-chemotherapeutic era the two bases of treatment were the sanatorium régime and radical surgical excision of all affected nodes. It was the failure and the time-consuming nature of the former that led to the adoption of the latter treatment. It is important to note that radical surgery involved the excision of all palpably involved nodes, however small in size, with or without an excision of the supposed site of the primary focus by tonsillectomy (Dowd, 1916; Barrington Ward, 1937; Mason Browne, 1957; Wimot and others, 1957). Dowd noted in 1916 that lesser operations were attended by poor results, and this has remained the consensus since (Mason Browne, 1957; Bluhm, 1964) and is confirmed by this study. Dowd (1916) further noted that the presence of pus or the incision of a cold abscess was no bar to going on to complete excision of the involved nodes. Surgical treatment on this radical basis has not been performed in any of the patients in this series, but has been restricted to obtaining material for diagnostic purposes. Even when disease was restricted to the upper cervical nodes unilaterally and clean excision of the main involved node has been performed, radical surgery has not been attempted.

1. Results of Local Excisional Surgery alone.—In 1937 Barrington Ward claimed only a 1 per cent recurrence rate needing treatment following surgery for cervical tuberculous lymphadenitis, though he noted that a further 11 of his 95 cases had persisting asymptomatic enlargement of nodes in the neck. In the previous year Thompson (1936) claimed gross local recurrence in 50 of 55 cases who had been treated surgically. He stands alone in claiming such a high local recurrence rate after surgery, so it is probable, though not stated, that lesser surgical procedures were used. In the present series inadequate surgery without chemotherapy was accompanied by a high recurrence rate. Aspiration or incision of abscesses without excision of the diseased node resulted in sinuses in almost every case in which such treatment was used despite concomitant chemotherapy.

Dowd (1916) analysed the results of adequate excisional surgery in the treatment of 687 cases of cervical tuberculous lymphadenitis. He showed that the prognosis following adequate surgery depended on the extent of the disease present at the time of surgery. He divided his cases into three groups:—

Group 1.—Involvement of the primary focus in the oropharynx, plus ipsilateral upper cervical node enlargement alone.

Group 2.—Node involvement along the entire ipsilateral jugular chain.

Group 3.—Massive node involvement in the neck, often running a rapidly progressive course, with or without evidence of tuberculosis outside the neck.

Furthermore Dowd noted that the disease that he was treating was predominantly a disease of childhood, and that, in general, tuberculous cervical adenitis in children runs a more favourable course than does the disease in adults. His results are important in demonstrating the natural history of the disease when treated by the best non-chemotherapeutic means and are reproduced in *Table X*. Unfortunately, in his figures he did not differentiate between local and distant recurrence. Clearly, mortality at least must be due to disease in a site other than the lymph-nodes. From these figures it is clear that whilst surgery can reasonably be used to cure local disease in one site, it cannot be expected to cure generalized lymphadenitis or disease which has spread to other systems.

Table X.—DOWD'S (1916) RESULTS FOR SURGICAL TREATMENT OF CERVICAL TUBERCULOSIS (687 CASES FOLLOWED FOR 1–20 YEARS)

GROUP	NO. OF CASES	AVERAGE AGE (years)	CURE RATE (per cent)	RECURRENCE RATE (per cent)	MORTALITY (per cent)
1	452	8	99	1	0
2	185	15·9	68	24	5·5
3	50	12·7	34	43	20·0

Nearly all discussions of this disease assume that the primary focus in relation to cervical lymph-node disease is in the oropharynx. In fact, as shown by Wimot and others (1957), in at least 50 per cent of cases a healed primary focus is visible in the lungs. Also, at least 10 per cent have coexistent post-primary pulmonary infiltration (Jones and Campbell, 1962; Gillam and Knowles, 1963; Bluhm, 1964; Kent, 1967). In the present series there was a roughly similar proportion of cases in each group as in Dowd's (1916) series, but of the group 1 cases, 1 in 4, although clinically group 1, on radiography had evidence of disease outside the neck. In all, 1 in 2 patients had disease which if treated by radical surgery alone would have had a high risk of recurrence (*Table XI*).

2. **Tonsillectomy.**—In combination with excision of the affected nodes tonsillectomy has been considered important (Barrington Ward, 1937; Miller, 1956; Wimot, 1957; Wimot and others, 1957). However, as pointed out above the primary complex is not in the oropharynx in at least 50 per cent of cases (Wimot and others, 1957). When the primary focus is in the oropharynx it may not be in the tonsil, but if it is in the tonsil this often appears normal (Wimot and others, 1957).

Tonsillectomy was not performed as a part of the treatment in this series. Success or failure does not appear to be influenced by the procedure.

3. **Lesser Surgical Procedures.**—Aspiration, incision and expression, and curettage have been condemned as techniques in the treatment of lymph-node tuberculosis. Mason Browne (1957) noted high recurrence rates, and his figures are quoted in *Table XII*. Aspiration and incision of a cold abscess are likely to lead to sinus formation. The appearance of tuberculous sinuses in the neck is quite uncommon now. In the present series, of the 13 cases in which sinuses appeared, 9 followed aspiration or incision of caseating nodes. In no case in which excision of one or more whole nodes was performed did a sinus result.

Table XI.—THE DISTRIBUTION OF THE CASES WITH CERVICAL NODE INVOLVEMENT IN THE PRESENT SERIES ACCORDING TO THE CLASSIFICATION OF DOWD (1916)

Group	*No. of Cases*
1	50
1 (3)*	17*
2	18
3	20

* Cases clinically group 1 but showing evidence of disease, active or quiescent, on radiography.

Table XII.—RECURRENCE RATES FOLLOWING SURGICAL TREATMENT OF CERVICAL TUBERCULOUS LYMPHADENITIS IN THE SERIES OF MASON BROWNE (1957)

Technique	*Recurrence Rate* (per cent)
Aspiration of pus	86
Incision and expression	40
Incision and curettage	34
Primary excision when abscess present	14
Primary excision when no abscess present	3
Secondary excision	0

The treatment of a sinus should be its excision together with the excision of the underlying nodes from which it arose, and appropriate chemotherapy. Sinuses so produced in this series when not excised persisted for 3–6 months despite chemotherapy.

Curettage of a tuberculous cavity is not acceptable on theoretical grounds, in that it is likely to cause haematogenous dissemination of the disease.

4. **Chemotherapy.**—Adequate chemotherapy in most forms of tuberculosis is now taken to involve the concomitant continuous administration for a sufficient length of time of two antituberculous drugs to which the organism cultured from the patient has been shown to be sensitive. (Recently, treatment with drugs given twice weekly only has been tried successfully in pulmonary tuberculosis (Poole and Stradling, 1969; Pande, 1970). This has not been used in any case in the present series.)

The drugs most usually used in combination have been streptomycin, isonicotinic acid hydrazide (INAH), and para-aminosalicylic acid (PAS). Rifampicin and thiacetazone are newer first-line drugs. Second-line drugs include ethionamide, cycloserine, and viomycin. In those cases in which the organisms were found to be sensitive, and in those in which no sensitivities were known, the most usual pattern of treatment has been to give INAH and PAS together throughout the course of treatment accompanied by daily injections of streptomycin for the first 3 months.

The length of treatment accepted as adequate for most forms of tuberculosis is now 2 years (Hanson, 1970). This has not been universally applied in lymph-node disease, and shorter courses of chemotherapy are still frequently used (Miller, 1956; Mason Browne, 1957; Gillam and Knowles, 1963). Gillam and Knowles in 1963 found a 25 per cent recurrence rate, half of which occurred after 12 months' chemotherapy. They recommended that cases with disease restricted to the upper one-third of the jugular chain on one side of the neck (Dowd group 1 cases) should be treated surgically, with chemotherapy continued only until surgery had been performed and the wound had healed. All other cases should be treated for 12 months or more.

Kent (1967) has advocated 24 months' treatment, finding only 1 recurrence in 36 cases so treated.

The results of treatment in the present series are detailed in *Table XIII*. Only cases followed for at least 12 months after treatment are included. Eighty-seven cases treated during the decade 1960–9 are detailed, the average follow-up period being 4·5 years. A further 8 episodes occurring before this decade in cases subsequently treated are included, the appropriate totals being indicated in brackets. These cases were treated by presumably adequate surgery 10–38 years before.

COMPLICATIONS OF TREATMENT

1. **Radical and Local Surgery.**—The incidence of peripheral nerve damage is very low in most reported series (Dowd, 1916; Barrington Ward, 1937; Bluhm, 1964; Kent, 1967), though the spinal accessory nerve and the cervical branch of the facial, the hypoglossal (Clain, 1968), and the recurrent laryngeal nerves (Hiranandani and Mulay, 1970) are all at risk according to the site of the node. In this series only the posterior auricular nerve was twice mentioned as being damaged. Nerve injury can be avoided as long as the anatomy of the region is well understood.

The occurrence of iatrogenic sinuses has already been discussed. In their absence scars produced by surgery will be unobtrusive (Barrington Ward, 1937).

2. **Chemotherapy.**—All the drugs employed have a high incidence of side-effects, some of which may be fatal. In this series chemotherapy had to be changed or discontinued in 10 cases because of side-effects, none of which was permament. In view of this and because of the need for adequately continued therapy, all drug therapy should be managed by a chest physician.

CAUSES OF FAILURE OF TREATMENT

Radical surgery excising all palpably involved nodes is successful in Dowd group 1 disease (Dowd, 1916) in preventing local recurrence in the decade after surgery in all but a very small number of cases (Dowd, 1916; Barrington Ward, 1937), though there is a late failure rate even in this stage of the disease. In the present series 8 cases recurred 10–38 years after adequate surgery (*Table XIII*).

The more restricted surgical excision used at present does not even remove all local disease and if unaccompanied by adequate chemotherapy has a high early recurrence rate. From Dowd's (1916) original figures it is obvious that radical surgery, however extensive, is incapable of extirpating all disease in an unacceptable proportion of stage 2 and 3 cases.

Table XIII.—RESULTS OF TREATMENT BY CHEMOTHERAPY WITHOUT RADICAL SURGERY IN THE PRESENT SERIES*

LENGTH OF CHEMOTHERAPY (months)	NO. OF CASES TREATED	NO. OF RELAPSES
Nil	8 (16)†	5 (13)†
1– 6	22	8
7–12	21	3
13–18	16	0
19–	20	1
Total	87 (95)†	17 (25)†

* Average length of follow-up, 4½ years.

† Figures in parentheses refer to cases included in the analysis but which are not strictly comparable as they occurred outside the stated decade (*see* text).

Failure of Chemotherapy.—

1. *Failure to use Two Drugs to which the Organism is Sensitive.*—In the present series in 4 out of 5 cases the organisms had not been cultured, so that its sensitivities could only be guessed at. Two INAH-resistant *Myco. tuberculosis* were encountered: 1 in a case of lymph-node disease and the other in urinary-tract disease.

2. *Disease caused by Mycobacteria other than* Myco. tuberculosis.—*Myco. bovis* occurred once in the series of extrapulmonary tuberculosis. It was, as is usual, INAH-resistant. The pathogenicity of some anonymous mycobacteria is now well attested (Chapman, 1960; Jones and Campbell, 1962; Corpe, Runyon, and Lester, 1963; Runyon, 1965), though whether they produce disease which always runs the same course as that due to *Myco. tuberculosis* is not definitely established. Group I, II, III, and IV organisms have all been implicated in cases of cervical lymphadenitis and in disease in other systems. Anonymous mycobacteria are well recognized as pathogens in America (Chapman, 1960; Runyon, 1965). They have been implicated in tuberculous cervical lymphadenitis of childhood in Australia, Jones and Campbell (1962) finding them in 1 in 10 of their cases, whilst MacKellar and others (1967) considered almost all their childhood cases as due to one of these organisms. In this country no comparable series has been published, though Marks (1970) states that only 142 cases of anonymous mycobacterial infection (all sites) have been found in Wales in the years 1953–68, though the incidence is rising. In the present series of 26 cases of lymph-node disease in which a bacteriological diagnosis was established 2 were due to anonymous mycobacteria, both of which were in adults.

Anonymous mycobacteria are not usually guinea-pig pathogens, so that suspect tuberculous material should always be cultured on Lowenstein-Jensen medium as well as by guinea-pig inoculation. Anonymous mycobacteria are largely insensitive to the usual antituberculous drugs, even in combination.

3. *Failure to continue Chemotherapy for Long Enough.*—Chemotherapy should never be given for less than 12 months (*Table XIII*), but almost certainly for 24 months as in all other forms of tuberculosis.

4. *Failure of the Patient to take the Prescribed Therapy.*—In two recent articles from England (Poole and Stradling, 1969; Pande, 1970) a 16–25 per cent defaulting rate for long-term anti-tuberculous chemotherapy is described.

5. *Occurrence of Drug Resistance during Treatment.*—This should not occur if the patient is treated with two drugs to which the organism is known to be sensitive.

6. *Coexistence of Tuberculosis with Another Disease causing Lymph-node Enlargement, e.g., Lymphoma.*—Failure of regression of adequately treated lymph-node tuberculosis indicates the need for further lymph-node biopsy.

CONCLUSIONS

Tuberculous lymphadenitis, however extensive or localized, is best treated by adequate chemotherapy in the same way as all other forms of the disease.

Surgery is always indicated before treatment is started to establish a full and accurate diagnosis histologically and bacteriologically. At this stage surgery should be employed to excise all grossly enlarged and caseating nodes. Sinuses whether originally present or occurring during treatment are an indication for surgery, excising both the sinus and the associated underlying nodes. Abscesses should not be aspirated or incised; if one of these procedures is used because the abscess is not thought tuberculous the nodes involved should be excised as soon as possible after the mistake is discovered to prevent the otherwise prolonged morbidity and eventual disfiguring scarring associated with the production of tuberculous sinuses.

Radical surgery as used in the pre-chemotherapeutic days still has an important role to play in the treatment of anonymous mycobacterial infection which is insensitive to chemotherapy.

Post-treatment excision of a persistently enlarged node should always be performed for diagnostic purposes to exclude the possibility of coexistent malignancy and to eliminate walled-off foci of the tubercle bacilli and to establish their sensitivities. The thesis that disease involving the upper cervical chain on only one side (Dowd group 1 disease) can be treated successfully by radical surgery alone is dangerous; chemotherapy should always be used for these as for more advanced cases. Even in clinically Dowd group 1 disease there is radiological evidence of disease, active or quiescent, outside the neck in 25–50 per cent of cases, leading to a later danger of reactivation of the extracervical focus.

Extracervical tuberculous lymphadenitis is almost always part of a generalized disease and should be treated as such by chemotherapy.

To be adequate chemotherapy should be continued for 24 months.

Very late recurrence is a feature of tuberculosis, especially of disease of the lymph-nodes. It is impossible in a follow-up of 10 years' duration to know whether the treatment as outlined will affect the incidence of late recurrence, although it can virtually eliminate early recurrence.

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PNEUMOPERITONEUM AS AN AID IN THE SURGICAL TREATMENT OF GIANT HERNIAE

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SUMMARY

The management of giant hernia and eventration can be greatly facilitated and made safe by the use of preoperative pneumoperitoneum. Daily insufflation of air into the peritoneal cavity, starting with 500 ml. and increasing gradually to 2–3 litres a day for approximately 2 weeks, stretches the abdominal cavity and avoids respiratory and circulatory distress at the time of operation. This preoperative treatment converts a potentially dangerous operation into a fairly simple procedure.

CASES of giant abdominal hernia, either idiopathic or incisional, are not common in the practice of the individual surgeon, although they are seen quite frequently in certain areas of the world, such as Central Africa. When encountered, they are regarded as doubtfully curable, and certainly not to be accepted lightly for operation. Mansuy and Hager (1958) stated that many cases are considered inoperable because of feared complications following sudden changes in intra-abdominal pressure and technical difficulty in closure. This view is echoed by many authors, and is certainly justified when one thinks of the possible struggle involved in trying to push back into the already filled abdominal cavity a large mass of redundant abdominal contents which has existed outside the abdomen proper perhaps for years. The result all too often is either a very unsatisfactory closure of the abdominal wall under tremendous tension, with gross respiratory and cardiac embarrassment and possible death of the patient (Berlemont, 1952), or a breakdown of the repair sooner or later with recurrence of the hernia. Many patients attempt to support these large, unwieldy, and irreducible herniae by belts which excoriate the skin and produce superficial ulceration (*Fig.* 1A, B).

The induction of pneumoperitoneum before attempting definitive repair of a giant hernia was first suggested by Moreno (1940, 1947, 1951, 1964), who describes the advantages of this method as follows: the pressure of the pneumoperitoneum causes (1) stretching of the abdominal wall, creating a larger cavity for replacement of hernial sac contents; (2) reduction of the volume of hollow viscera to be replaced at the time of repair; (3) reduction of the oedema of the mesentery, omentum, and the subperitoneal tissues caused by the chronic hernia, creating less mass to be replaced; (4) stretching of the hernial sac causing elongation of adhesions and making dissection easier; (5) increased tone of the diaphragm; (6) preoperative respiratory and circulatory adjustments to the elevation of the diaphragm (Geffen and Maisel, 1966).

MATERIALS AND METHODS

Under local anaesthesia an epidural catheter is inserted through a long aspiration needle into the peritoneal cavity in the epigastrium or left hypochondrium. Alternatively, an intracath catheter can be used (Steichen, 1965). The site of the puncture should, however, be kept away from the immediate area of the hernia in order to avoid any bowel adherent to the anterior abdominal wall (Koontz, 1958). Successful penetration of the abdominal wall will be marked by a lessening of resistance to the pressure of the needle, and the catheter will be found to pass readily into the abdomen. A few ml. of Hypaque 45 per cent (sodium diatrizoate) are injected through the catheter and a radiograph is taken. While this is being developed the needle is withdrawn, leaving the catheter in situ. The catheter is then strapped to the skin (*Fig.* 2A, B). A three-way stopcock is attached to the catheter, and a Millipore filter is attached to the stopcock. The radiograph should show the contrast medium trickling down into the pelvis. Five hundred ml. of air are then injected, either by syringe or by a pneumothorax apparatus (Moore, 1961; Steichen, 1965). If the medium is shown to have pooled in the abdominal wall, or the catheter has not passed easily into the abdomen, then one or two further attempts may be made, but it is probably better to repeat the procedure on the following day than to distress the patient by repeated unsuccessful attempts.

After the initial injection of 500 ml. of air a similar amount is injected twice daily for 3–4 days. Thereafter, provided that there have been no untoward symptoms, each injection is increased by 250 ml., making a daily total of 1·5 litres of air. A further rise is made, again after 3–4 days, but at this point if progress has been satisfactory the increase can be of the order of 300–500 ml., thus bringing the daily total to between 2·1 and 2·5 litres of air. The patient gradually blows up like a balloon and may become alarmed, unless adequately reassured, at the enormous increase in size of the abdomen, having originally come for treatment for a swelling already considered too large. If at any time during the insufflation of air the patient feels any discomfort or dyspnoea or if tachycardia develops, the injection can be stopped and, if necessary, some air can be withdrawn. The next insufflation can be delayed for a day or so to allow the patient to settle down. No attempt is made to prevent the distension of the hernial sac by applying binders. This will allow any adhesions between the contents and the sac to elongate. Non-adherent contents of a previously irreducible hernia will frequently be found to have disappeared completely into the abdomen at the time of operation. Moreno (1964) has recommended the regular measurement of intra-abdominal pressure to determine the most appropriate day for operative repair of the hernia—when the pressure readings have become constant and the vital capacity stabilized—but I have not had any difficulties from the omission of this step. In practice the average patient is ready for operation in about a fortnight, the end-point being judged by the tension of the abdominal wall; this should feel as tight as a drum, especially on the flanks. If, however, the flanks feel too soft, then 2 or 3 days' extra air insufflation will usually suffice to prepare the patient fully for operation.

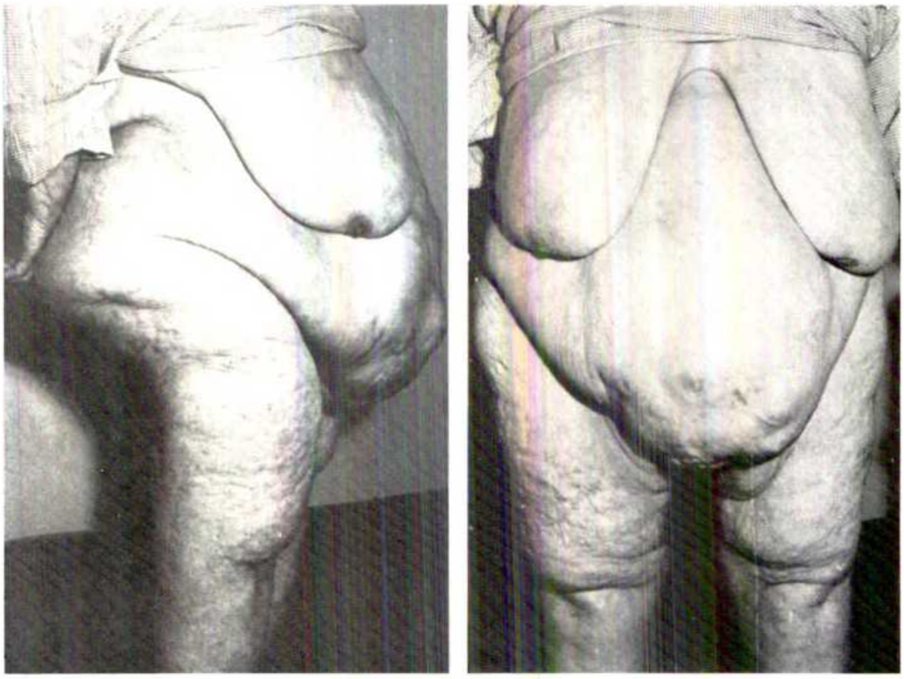

FIG. 1.—Mrs. S. before operation.

At operation excision of the redundant skin, fat, and stretched fasciae and tissues should be carried out as far as possible before the hernial sac is punctured. When this occurs, the air rushes out of the abdomen rather like a punctured car tyre, and the remainder of the excision and suturing is continued on a completely deflated and flaccid abdominal wall. I have rarely found it necessary to use any strengthening material such as tantalum mesh, but this should be available if the defect is too large to close naturally (Koontz, 1951, 1956) (*Figs.* 2C, D, 3).

PRESENT SERIES

Twenty-five cases of giant hernia have been treated by preoperative pneumoperitoneum over a period of 20 years. Although the earlier cases performed in the Sudan have not been adequately followed up, the early and late results have amply confirmed the views of the originator of the method, Professor Ivan Goni Moreno, and his colleagues that this is a safe method for dealing with this difficult problem.

An example of the value of this method is shown by the following case.

Case 1.—Mrs. E. B., aged 65 years, was admitted on 6 April, 1967, complaining of abdominal pain and vomiting for 4 days. She had had absolute constipation for the same period, together with oliguria. Twenty-eight years earlier an ovarian cyst had been removed which had been followed almost immediately by the development of an incisional hernia. The patient had worn a support for this since then, but the hernia had progressively increased in size and had suddenly become painful and larger 4 days before admission.

The patient was ill and dehydrated, but obese, weighing just over 127 kg. There was an enormous bilobed incisional hernia involving the lower half of the abdomen, approximately 38 cm. in diameter and rising to a height of 20 cm. from the abdominal wall. The abdomen itself was distended and tympanitic. There was gross intertrigo with patchy superficial ulceration over the hernia.

Following suction and correction of the electrolyte imbalance, the hernia fortunately became softer and the patient's condition improved, with passage of flatus after 48 hours.

The induction of pneumoperitoneum was started on 14 April and an operation was carried out on 1 May. Some slight wound infection occurred, but this settled quickly and the patient was discharged with an abdominal belt.

Four years later the patient reports that her life has been transformed by the hernia repair. She now weighs 105 kg. and is 160 cm. tall.

Another type of case which may require help is that of a patient with a terminal colostomy, perhaps following an abdominoperineal resection of the rectum. A massive incisional hernia may develop, with the bowel opening perched on top of a hillock and a length of colon lying subcutaneously together with a mass of small intestine. The colostomy belt gradually becomes more and more difficult to apply, while episodes of partial obstruction in the extruded small bowel may become frequent.

These cases can also be treated satisfactorily by preoperative pneumoperitoneum and subsequent repair. There were 2 such cases in the present series, and both required the resection of a further 45 cm. or so of colon, followed by the refashioning of the colostomy opening after dealing with the hernia.

In 2 cases of enormous hernia which had existed for many years a violent bout of coughing forced an extra loop of small intestine into the hernial sac and produced strangulation. Under local anaesthesia in 1 case, and general anaesthesia in the other, the constricting ring was incised and the trapped bowel

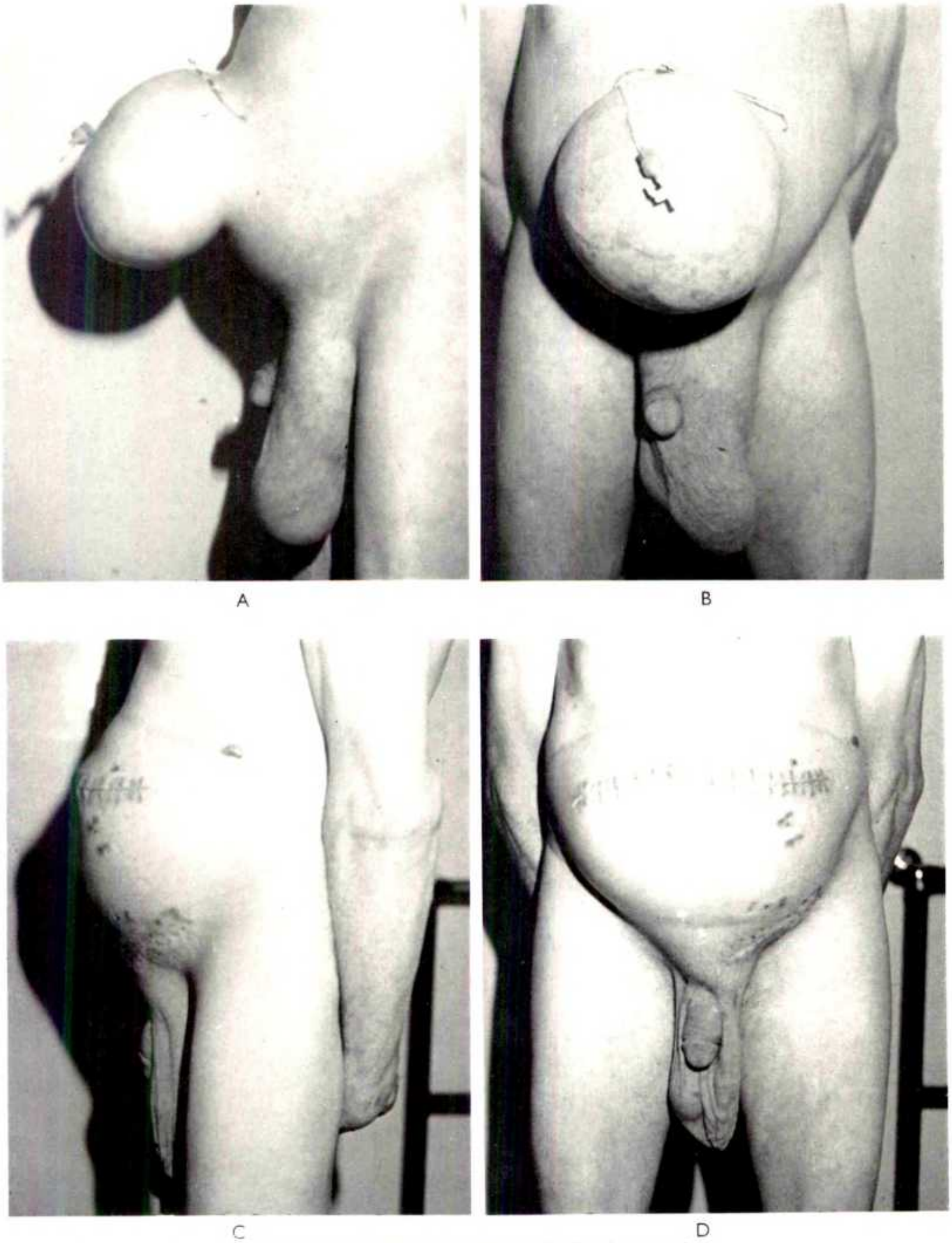

FIG. 2.—A, B, Mr. B. before operation. C, D, After operation.

freed and reduced, being viable in both cases. No attempt was made to deal with the hernia at that time. After a suitable interval for healing and convalescence, the régime of pneumoperitoneum was carried out and a definitive repair was performed in due course.

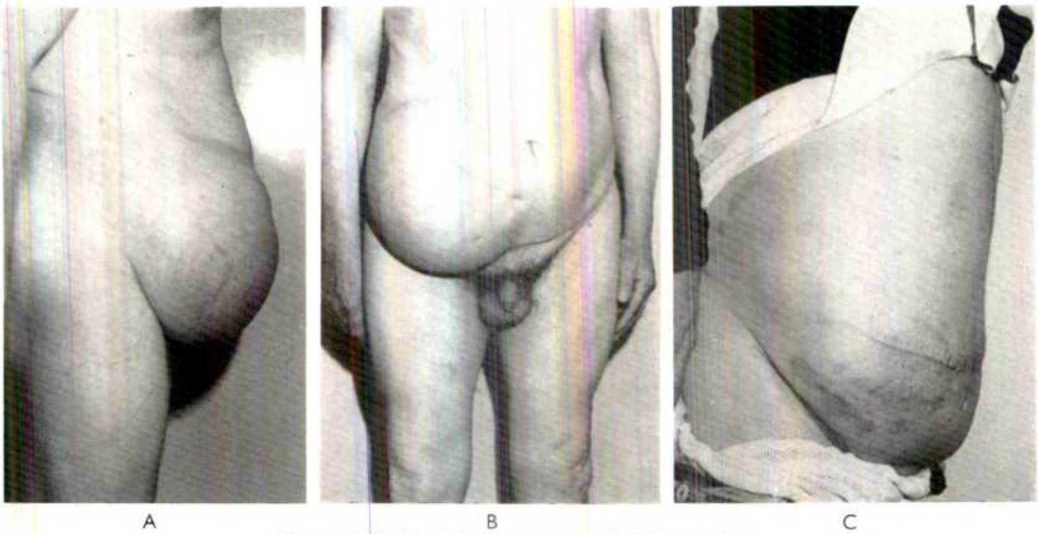

FIG. 3.—A, B, Mr. A. before operation. C, After operation.

DISCUSSION

The problem of dealing with giant herniae has brought a number of suggestions, such as resection of some of the intestine held in the hernial sac (Davey, 1968) or phrenic section (Touroff, 1954). Ziffren and Womack (1950) report the treatment of a case using a two-stage method, with incision of all the coverings down to the peritoneum initially and resuture of the skin, followed by repair of the hernia 12 days later.

The method described by Moreno (1940) has the merit of simplicity and safety. The distension of the abdominal cavity can be developed at any pace desired, and can be interrupted and restarted at any stage if the patient is disturbed. This plan is vastly superior to that of allowing oneself to be faced with a mass of tissue spilling out over an already crowded abdomen and wondering what to do with it. Berlemont (1952) describes the unfortunate sufferers as usually aged, obese, and emphysematous. There is often great difficulty in freeing the hernial contents. He records a series of 8 cases in the Sudan in which 5 patients died. The causes of death were long operations with brutal reduction, consequent pulmonary collapse, and cardiac insufficiency with diminution of intrathoracic volume. A second series of 18 cases using preoperative pneumoperitoneum produced 17 cures and 1 death.

Many reports have appeared from South America (Ottolenghi, 1944; Carpanelli, 1946; Iparraguirre, 1946; Aguirre, 1949; Goldin and Olmedo Diaz, 1960) and from America and Europe (Guellette, 1947; Koontz and Graves, 1954; Mason, 1956; Koontz, 1958; Moore, 1961; Galeano, Azulay, and Montoreano, 1962, 1965; Anagnostides and Kostopoulos, 1962; Moyer, 1964; Steichen, 1965; Unglaube and Gromoll, 1966; Pingree and Clark, 1968; Connolly and Perri, 1969) confirming the success of this method.

Galeano and others (1962, 1965) point out that the enormous swelling observed when one first sees a patient suffering from giant hernia may mask small additional herniations, and these, together with points of weakness which may presage but have not progressed to full herniation, will become very obvious during the course of air insufflation, and can then be brought within the scope of repair. Deep anaesthesia will not, of course, be necessary to achieve the profound relaxation usually demanded by the surgeon in dealing with these difficult cases.

Koontz and Graves (1954) stress that air should be injected slowly, as diffuse pain, nausea, or pain in the shoulders may appear. These symptoms soon disappear and later insufflations are well tolerated. They recommend using the linea semilunaris as the site for injection, as thick fascia is present and this gives a more positive indication of penetration of the peritoneal cavity. The use of a pneumothorax apparatus has been recommended by Moore (1961) in place of the more tedious syringe. He gives an initial 500 ml. and continues with 500–2000 ml. daily as an out-patient procedure, monitoring the insufflation by water-pressure and stopping at a level of 14 cm. The usual amount of air mentioned by most authors is 2–3 litres daily, but Anagnostides and Kostopoulos (1962) mention that Moreno has injected up to 6–8 litres of air at a session.

Connolly and Perri (1969) quoted 22 cases of adult hernia previously reported in the American literature who were treated in this way and added 3 cases of their own. They commented that the gradual expansion of the abdominal wall is physiologically similar to the stretching in pregnancy and in conditions producing large accumulations of ascitic fluid.

The absorption of oxygen from the peritoneal cavity has been found to be imperceptible after a few hours and it is safe to assume that the rate of absorption of air would be less than the rate of absorption of pure oxygen.

Several authors (Connolly and Perri, 1969; Galeano and others, 1962, 1965) mention contra-indications to the use of pneumoperitoneum. These include abdominal wall infection, decompensated cardiac conditions, the presence of a small ring, or strangulation. Certainly, strangulation would preclude the immediate application of pneumoperitoneum, while any attempt at immediate repair of a giant hernia which has had the added complication of strangulation would be extremely hazardous.

Moore (1961) warns that pneumoperitoneum may mask acute abdominal conditions such as perforating peptic ulcer, diverticulitis, and appendicitis. He also notes that when pulmonary tuberculosis was treated by therapeutic pneumoperitoneum some years ago there was an increase in the incidence of perforated peptic ulcer, possibly due to mechanical separation of the viscera from the parietal peritoneum and protective adjacent structures. Other possible complications mentioned by Galeano and others (1962, 1965) include respiratory syncope, puncture of a viscus, haematoma, and retroperitoneal and mediastinal emphysema, but these are regarded as rare. Faber and Harsanyi (1962) report a case of fatal air embolism due to therapeutic and diagnostic abdominal air insufflation, but this complication is regarded as extremely rare by Simmonds (1946), who records 5 cases of air embolism in 13,000 insufflations for pulmonary tuberculosis, and remarks that puncture of a viscus is even more infrequent. Koontz (1958) considers the occurrence of pneumonia in 1 of his patients as possibly due to air being injected too rapidly.

None of these complications has been seen in the present series and the only disturbance has been an occasional attack of tachycardia or dyspnoea in the first few days of the treatment.

Acknowledgements.—I should like to thank Professor J. C. Goligher for his valuable comments and guidance in the writing of this article, and also Miss W. Smith for her secretarial assistance and Mr. N. Wroe for the photographs.

I should also like to thank those junior colleagues of mine who undertook the, at times, rather tedious task of performing the daily air insufflations.

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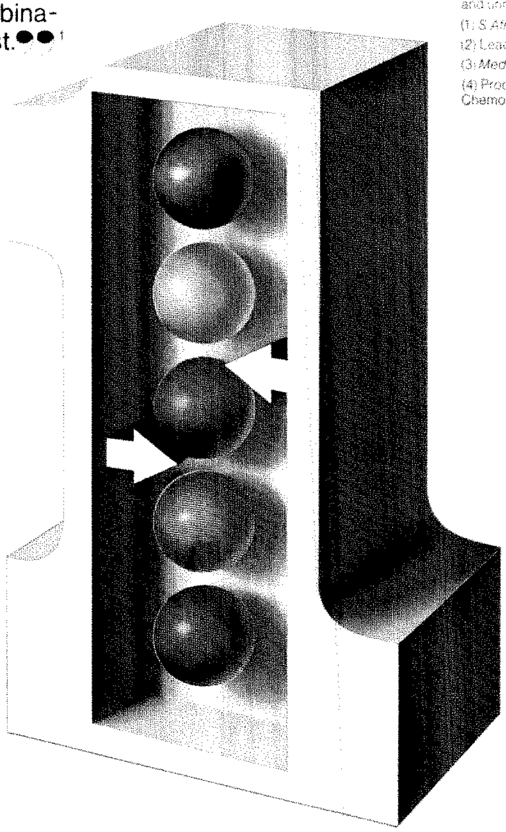

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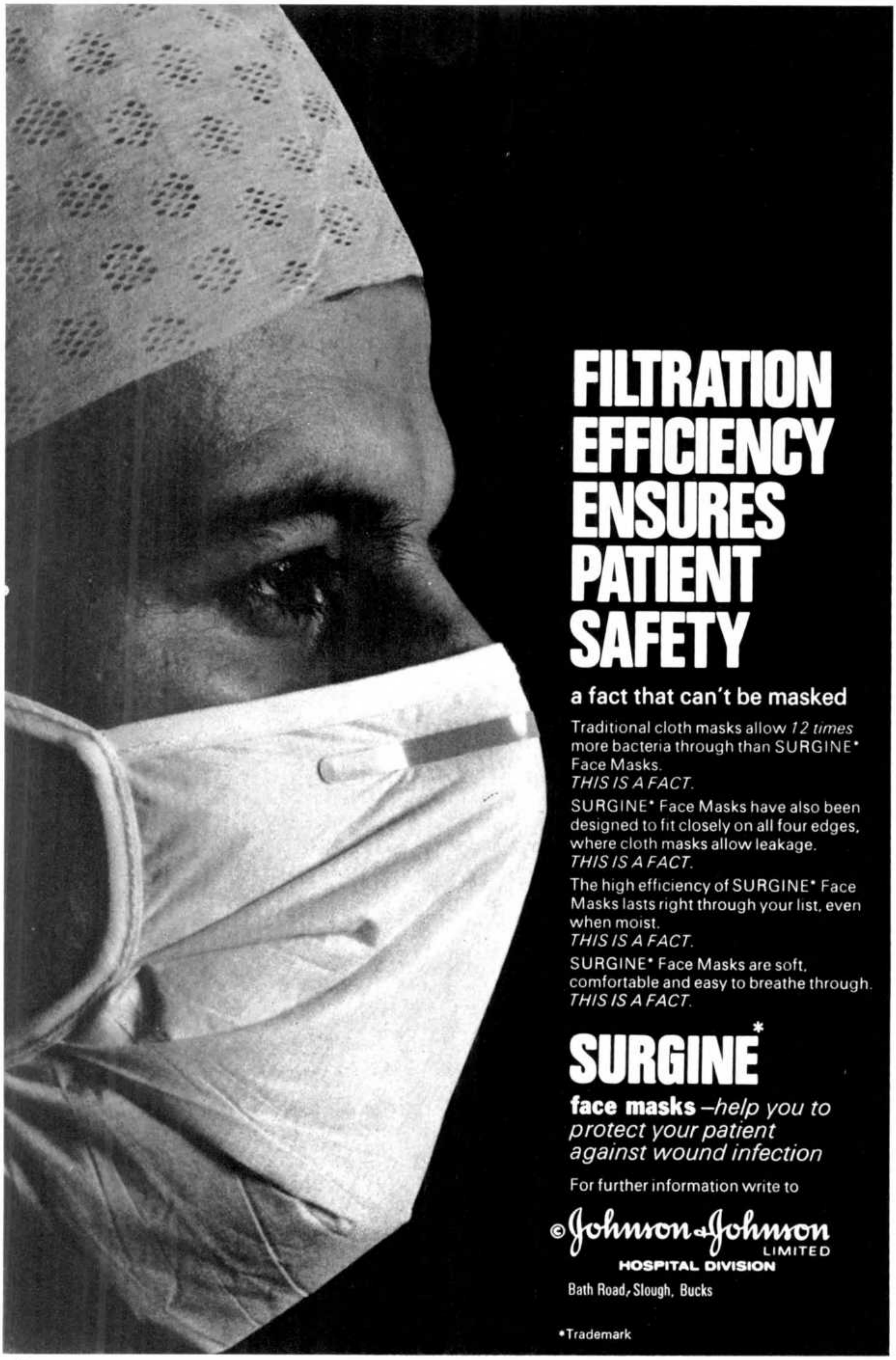

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THE LITHOGENIC EFFECT OF VAGOTOMY*

By A. G. A. COWIE and C. G. CLARK

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SUMMARY

The composition and the rate of flow of bile produced in response to a standard fatty meal in cholecystectomized dogs have been determined before and after vagotomy and pyloroplasty. The results presented support the view that vagotomy is potentially lithogenic, particularly after cholecystectomy.

FOR over 20 years since it was first suggested (Majoor and Suren, 1947) the possibility of a causal relationship between surgical procedures performed for peptic ulceration and the development of gall-stones has been considered. Much of the evidence for this has been clinical observation, and in a review of the literature in 1968 Fletcher and Clark, summarizing the evidence, concluded that the case for a lithogenic effect of surgery was as yet not proved. There has been little evidence since then either to support or to deny the hypothesis. Among the more important observations are those of Krause (1963), who showed that the incidence of gall-stones in patients with peptic ulceration but who did not undergo surgery was much the same as the incidence in the normal population. Many studies tend to implicate vagotomy as the common factor linking those operations which may be associated with an increased incidence of gall-stones. There is no increase in stone formation following selective vagotomy in which the vagal innervation of the biliary tree is preserved (Farris, 1969; Griffith, 1969).

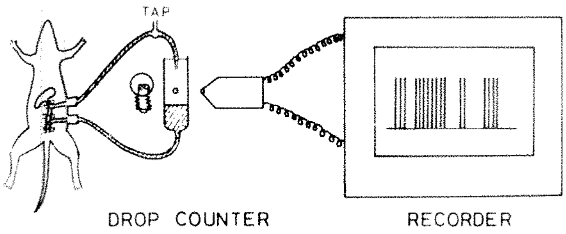

FIG. 1.—Diagrammatic representation of the experimental procedure.

The role of the vagus in the control of bile-flow and bile composition in the dog was reported by Fletcher and Clark (1969). Using animals with an intact gall-bladder they showed that a standard fatty meal provoked a flow of bile; the rate of flow was much less after vagotomy and the concentration of cholate was also lowered, thus changing the ratio of cholate concentration to cholesterol concentration in the bile. Both of these effects might predispose to cholesterol crystallization and thus promote stone formation. This work has now been extended to include studies on dogs after cholecystectomy.

MATERIALS AND METHODS

The biliary cannula of Fletcher and Corry (1968) was used. This requires the placement of latex tubes in the proximal and distal common bile-duct, the tubes being led to a surface-mounted cannula with a detachable 'U' cap so that between experiments, with the cap in place, the normal enterohepatic circulation of bile can be maintained with the sphincter of Oddi undisturbed. During experiments a drop chamber with an attached photo-electric cell is included in the still-intact enterohepatic circulation, and the flow-rate is measured by the drops recorded on a timed moving-paper recorder (*Fig.* 1). A tap is included in the system so that 0·6-ml. samples may be aspirated at 30-minute intervals for analysis. The dead space within the system amounts to 1·5 ml., which is insufficient materially to alter the enterohepatic circulation.

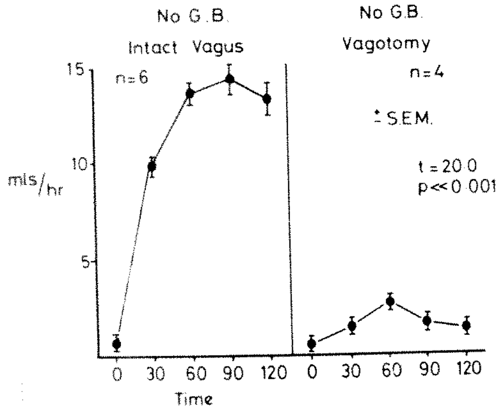

FIG. 2.—The bile-flow rate in response to a fatty meal before and after vagotomy.

Bile-flow and bile composition were determined in response to a standard fatty meal of 60 g. of Prosparol in 6 dogs before and in 4 dogs after a total abdominal vagotomy with a Mikulicz pyloroplasty. Each dog underwent cholecystectomy at the initial operation, and 2 weeks' convalescence was allowed following operation prior to measurement. In each case liver-function tests remained normal, and the completeness of the vagotomy was confirmed at autopsy. Total cholate concentration was determined by the method of Irvin, Johnston, and Kopala (1944), phospholipid concentration by a modification of the method of Fiske and Subbarrow (1925), and cholesterol concentration by a method derived from that of Babson, Shapiro, and Phillips (1962) and Leffler and McDougald (1963).

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* Based on a short communication which was presented at the Birmingham Meeting of the Surgical Research Society in July, 1971.

RESULTS

In each experiment a standard fatty meal of 60 g. of Prosparol was given and measurements were continued for 2 hours. With the vagus intact there was a brisk increase in the rate of flow from 0·5 ml. to between 10 and 14 ml. per hour (*Fig.* 2). After vagotomy the rise was small. Each value plotted is a mean shown with 1 standard error in each direction. The difference between each similarly timed pair, determined by a *t*-test appropriate for small numbers, is highly significant ($P < 0\cdot001$).

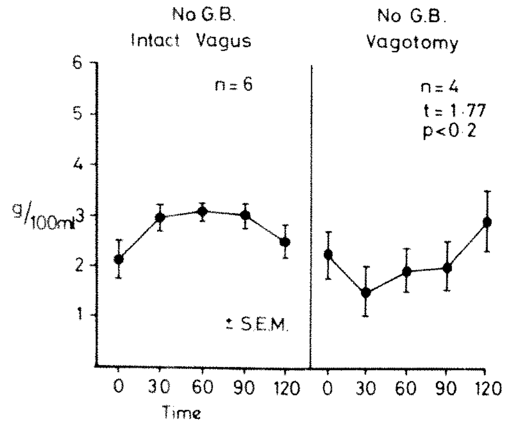

FIG. 3.—The effect of vagotomy on the concentration of cholate.

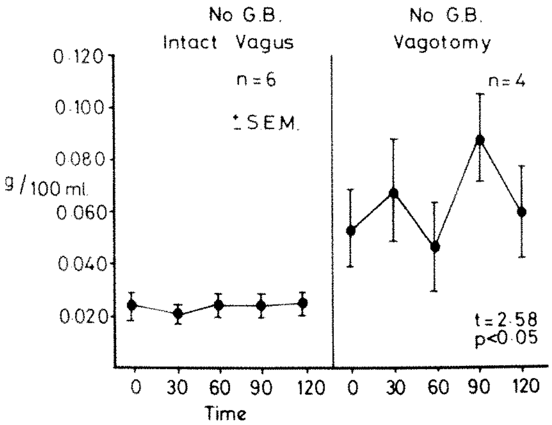

FIG. 4.—The effect of vagotomy on the concentration of cholesterol.

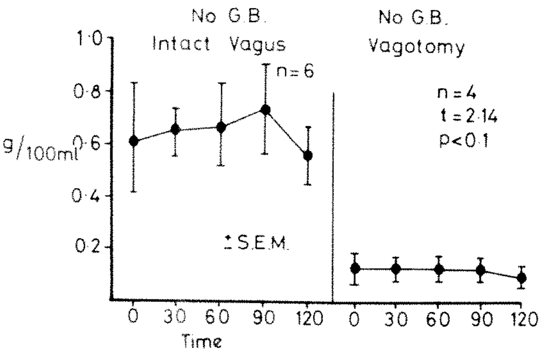

FIG. 5.—The effect of vagotomy on the concentration of phospholipid.

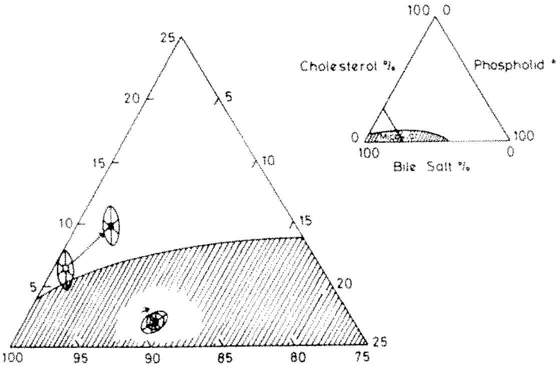

FIG. 6.—Triangular co-ordinates illustrating bile composition in dogs. ○, Vagus intact; fasting. ●, Vagus intact; after a meal. □, After vagotomy; fasting. ■, After vagotomy; after a meal.

The concentration of cholate (*Fig.* 3) shows a slight reduction after vagotomy, but this is not a statistically significant change. The concentration of cholesterol shows a small rise after vagotomy (*Fig.* 4), and this is significant ($P < 0\cdot05$). The concentration of phospholipid (*Fig.* 5) shows a reduction after vagotomy, but the significance is again of a low order ($P < 0\cdot1$).

These results can be interpreted as showing a change in bile composition likely to make the bile more lithogenic, but a better interpretation can be obtained by converting the data in relation to the known effects of cholesterol crystallization.

The chemical composition of bile, with reference to the relative concentrations of phospholipid, bile-salts, and cholesterol, can be expressed in such a way that it can be plotted on triangular co-ordinates as a phase diagram (Hoffman and Small, 1967). The smaller triangle in the upper right-hand corner of *Fig.* 6 is such a phase diagram for bile containing 5–10 per cent of solids. The shaded area in the lower part of this triangle is known as the micellar zone of the phase diagram. Within this zone cholesterol is solubilized in mixed micelles, but outside the zone cholesterol will inevitably crystallize for physicochemical reasons. The larger triangle in *Fig.* 6 is an expanded section of the phase diagram. To plot the present results on this diagram requires conversion of the concentrations measured from g. per 100 ml. to mmol. per litre, and each concentration is expressed as a percentage of the total molar concentration of the three substances involved. The figure for bile-salt is adjusted to allow for the fact that cholate only has been measured, and to do this it has been assumed that the cholate : bile-salt ratio remains relatively constant. This ratio is a species characteristic (Haslewood, 1955), and in dogs is 1 : 1·9.

The result of plotting the figures in this way can be seen in *Fig.* 6. Each point is shown with 1 standard error in each direction.

In the normal dog with intact vagi the results are within the micellar zone and are little affected by the stimulus of food. After vagotomy, however, the plot moves out of the micellar zone and this moves farther into the zone of cholesterol crystallization after a meal. The results previously reported (Fletcher and Clark, 1969) have been treated in the same way. In their experiments with vagotomy in dogs with an intact gall-bladder it was found that although the bile moved in the direction of the micellar boundary it did not move into the zone of cholesterol crystallization.

DISCUSSION

Bile-flow in the unanaesthetized cholecystectomized dog is stimulated by a fatty meal and this effect is virtually abolished by vagotomy. Similar results were obtained by Fritz and Brooks (1963), who used insulin and tolbutamide to stimulate bile-flow and then studied the blocking effect of anticholinergic drugs. Baldwin, Heer, Albo, Peloso, Ruby, and Silen (1966) found similar results on insulin stimulation in man with total biliary drainage, but both the latter experiments failed to maintain the enterohepatic circulation which is known to be important in the regulation of bile output (Thureborn, 1962).

The role of the vagus nerves in the secretion of bile is uncertain, and it has been suggested that the principal effect of vagal stimulation on bile-flow is mediated through the release of gastrin from the antrum (Sauberman and Silen, 1967).

There is a linear relationship between bile-flow and bile-acid secretion (Wheeler and Ramos, 1960), and in the fasting state spontaneous variations occur which can be blocked by anticholinergic drugs. Bile secretion can be stimulated by secretin (Bayliss and Starling, 1902), cholecystokinin–pancreozymin (Edholm, Jonson, and Thulin, 1962), and gastrin (Zaterka and Grossman, 1966), with marked similarity in the flow and composition of the bile. In the present studies bile-flow was reduced after vagotomy and pyloroplasty, which could theoretically impair the response to each of these secretagogues.

More important, however, was the observation that the composition of bile was altered. There was a significant increase in the concentration of cholesterol, a reduction in the concentration of phospholipid, but no real change in the cholate concentration. In an earlier study in dogs with intact gall-bladders vagotomy had a similar effect in reducing bile-flow, but it also reduced the concentration of cholates (Fletcher and Clark, 1969). The results in both experiments affected the ratio of bile-salt to cholesterol in such a way as to make the bile potentially more lithogenic. The phase diagrams of Hoffman and Small (1967) provide a better means of assessing the significance of these findings. When the results are examined in this way it can be seen that the previous observations of Fletcher and Clark (1969) do not suggest a significant change in the lithogenic effect of bile after vagotomy in dogs with intact gall-bladders. However, the results of the present experiments clearly indicate that following cholecystectomy in the dog, bile is already in the zone of cholesterol crystallization in the fasting state and it moves farther into the zone in response to feeding.

If these results have any relevance to the aetiology of gall-stones in man following gastric surgery, then vagotomy may only result in this complication in circumstances where gall-bladder function is already impaired. The results of these acute experiments, however, may require modification in the light of long-term experiments.

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SPONTANEOUS AORTODUODENAL FISTULA

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SUMMARY

Two further cases, 1 fatal and 1 with long-term recovery, of patients treated surgically for spontaneous aortoduodenal fistula are reported, bringing the total number of published operations to 20. Thirty-six further examples of the lesion which were not treated by operation have been reported since 1957.

Of a wide variety of causes for this lesion, the commonest is arteriosclerotic aneurysm of the aorta.

The association of recurrent gastroduodenal haemorrhage with severe pain and collapse may indicate this lesion, and the treatment should be surgical.

Control of the aorta proximal to the fistula is the essential first step in prosthetic grafting of the aorta and closure of the duodenum. Otherwise, spontaneous aortoduodenal fistula is uniformly fatal.

FISTULA formation between the aorta and the duodenum occurs most commonly as a complication of prosthetic grafting of the aorta. The condition can, however, occur spontaneously, and Cleland (1947) described such a spontaneous fistula as a 'necessarily fatal condition'. Since that time a number of successfully treated cases have been reported. The purpose of this paper is to bring up to date the list of published cases, adding 2 of our own, and to consider the aetiology, diagnosis, and surgical management of this condition.

HISTORICAL REVIEW

The first account in the literature of rupture of an aortic aneurysm into the gastro-intestinal tract appears to be that given by Cooper in 1837. Since then many case reports have been published, with review articles by Rottino (1943), Hunt and Weller (1946), and Scott, Maxwell, and Grimes (1949). The last comprehensive list of cases was made by Skromak, O'Neill, Ciccone, and Snyder (1957), who reported 42 examples of aortoduodenal fistula, including 2 of their own. Since then a further 56 cases have been reported, including the present 2 cases, and details of these are summarized in *Table I*. Some of these reports include additional cases of fistulae into other parts of the gastro-intestinal tract that are not being considered here.

CASE REPORTS

Case 1.—Mrs. M. C., aged 38 years, was referred for surgery in March, 1966, with a 6-month history of intermittent right-sided abdominal pain and pyrexia. Despite intensive investigation the only abnormality shown was a persistently raised E.S.R., which at no time during her illness fell below 80 mm. per hour. Although barium studies of the stomach and small bowel were negative on two occasions, it was thought that an inflammatory lesion of the small bowel was the most likely diagnosis.

Before an elective laparotomy could be performed, however, the patient had a moderate haematemesis, recovering after transfusion of 2 litres of whole blood. Thirty-six hours later a further severe haematemesis was accompanied by very severe pain and circulatory collapse, and she rapidly became exsanguinated and pulseless.

At immediate laparotomy, pulsating arterial blood was found coming from the duodenum, the source being a spontaneous fistula of the aorta into the third part of the duodenum. An 8-cm. length of woven Teflon graft was inserted to replace the damaged segment of aorta, and the duodenum was repaired. Transfusion of 17 litres of whole blood was required during the operation, and despite replacement of calcium and administration of epsilon aminocaproic acid an irreversible coagulation defect developed, leading to death from haemorrhage after 48 hours.

Because of the damage from extravasation of blood and surgical trauma, no abnormal tissue in the region of the fistula could be found at autopsy to explain the aetiology. The naked-eye appearances at operation did not suggest a peptic ulcer, and the aortic wall close to the fistula was normal.

Case 2.—Mr. W. C., aged 69 years, was admitted with recurrent attacks of epigastric pain and faintness, each attack being accompanied by profound collapse and subsequent melaena stools. During the fourth attack he began to pass bright blood per rectum, and laparotomy was performed through an upper midline incision.

At operation the third part of the duodenum was found to be adherent to what appeared to be a small aortic aneurysm, although its nature was never definitely established. Preliminary control was obtained by taping the aorta at the hiatus, enabling the fistula to be safely opened and the aorta reclamped below the renal arteries. A knitted Dacron bifurcation graft was inserted, the common iliac vessels being only slightly atheromatous. The duodenum was closed and the graft was covered with peritoneal flaps only, as there was insufficient aortic wall to sew over it.

Recovery was uneventful and the patient remains well 22 months later.

AETIOLOGY

As can be seen from *Table I*, by far the commonest cause of aortoduodenal fistula is arteriosclerosis of the aorta, usually with aneurysm formation. One aortic dissection has been incriminated (Roach, 1939) and one post-traumatic aneurysm (Sheldon, Leckie, and Mills, 1968). Infective aneurysms have been found —both syphilitic (Pratt-Thomas, 1944) and mycotic (Foa, 1895). Tuberculous para-aortic nodes have been described by Tozer (1914), Muendel and Pilpel (1954), Polk, Martiny, and De Castro (1956), and Eadie and Pollock (1968). An abscess cavity containing pus was found by Garzon, Wilson, and Gunter (1958), Voyles and Moretz (1958), and Dinapoli, Schirger, and Kirklin (1962). In 1 case (Ghaphery, Gupta, and Currie, 1966) the fistula was related to a carcinoma of the pancreas.

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Table I.—Details of the Cases of Aortoduodenal Fistula reported in the Literature since 1951

Author	Age and Sex	Aetiology	Site	Outcome
Hirst and Affeldt (1951)	66 F.	Arteriosclerotic aneurysm	Third part	Died 48 hours after admission
Hirst and Affeldt (1951)	67 M.	Arteriosclerotic aneurysm	Third part	Died 11 hours after admission
Hirst and Affeldt (1951)	65 M.	Arteriosclerotic aneurysm	Third part	Died 2 hours after admission
Hirst and Affeldt (1951)	80 F.	Arteriosclerotic aneurysm	Third part	Died 8 hours after admission. At autopsy two communications were found
Hirst and Affeldt (1951)	76 M.	Arteriosclerotic aneurysm	Third part	Died 46 hours after admission
Hirst and Affeldt (1951)	73 F.	Arteriosclerotic aneurysm	Third part	Died following haematemesis at home
Hirst and Affeldt (1951)	75 M.	Arteriosclerotic aneurysm	Third part	Died 5 days after admission. At autopsy four communications were found
Hirst and Affeldt (1951)	78 M.	Arteriosclerotic aneurysm	Third part	Died 6 days after admission
Muendel and Pilpel (1954)	63 M.	Arteriosclerotic aneurysm	Third part	Died 4 hours after rectal haemorrhage. Also had pulmonary tuberculosis
Polk, Martiny, and De Castro (1956)	63 F.	Arteriosclerotic aneurysm	Third part	Operation: Defects in aorta and duodenum sutured. Died 3 days later. Also had tuberculosis
Heberer (1957)	? M.	Arteriosclerotic aneurysm	Third part	Operation: Saccular aneurysm resected; aorta and duodenum repaired; alive and well 2 years later
Garzon, Wilson, and Gunter (1958)	52 M.	Arteriosclerotic aneurysm	Third part and colon	Operation: Defect in aneurysm sutured and packed. Died at the end of the operation
Voyles and Moretz (1958)	61 M.	Arteriosclerotic aneurysm	Third part	Operation: Resection and graft. Died after 1 month following further haemorrhage and resuture, using a thoracotomy for control of the aorta
Kubota and Moragues (1959)	69 M.	Arteriosclerotic aneurysm	Third part	Died 12 hours after admission
Kubota and Moragues (1959)	81 M.	Arteriosclerotic aneurysm	Third part	Died 3 days after admission
Szunyogh (1959)	68 M.	Arteriosclerotic aneurysm	Third part	Died 14 hours after haemorrhage
Montserrat and Naranjo (1960)	71 M.	Arteriosclerotic aneurysm	Third part	Died within a few hours
Baumler (1961)	74 M.	Arteriosclerotic aneurysm	Third part	Died 2 weeks after admission
Maclean and Couves (1961)	34 F.	Arteriosclerotic aneurysm	Fourth part	Operation: Resection and graft 6 hours after initial laparotomy and suture of fistula, allowing time for preparation. Well at 30 months
Ozlu and Allen (1961)	66 M.	Arteriosclerotic aneurysm	Third part	Died 26 hours after first haemorrhage
Aunon, Lopez, and Jimenez (1962)	60 M.	Arteriosclerotic aneurysm	Third part	Operation: Resection and graft. Well 6 months later
Dinapoli, Schirger, and Kirklin (1962)	59 M.	Arteriosclerotic aneurysm	Third part	Operation: Resection and graft. Renal arteries clamped for 50 minutes. Abscess behind aneurysm. Died in renal failure after 9 days
Kurai (1962)	61 M.	Arteriosclerotic aneurysm	Third part	Died rapidly
Law, Garrett, and DeBakey (1962)	63 M.	Arteriosclerotic aneurysm	Fourth part	Operation: Resection and graft. Well 4 months later
Macbeth (1962)	88 M.	Arteriosclerotic aneurysm	Duodeno-jejunal flexure	Died 36 hours after haemorrhage
Macbeth (1962)	63 M.	Arteriosclerotic aneurysm	Third part	Dead on arrival at hospital
Bela and Pavel (1963)	65 M.	Arteriosclerotic aneurysm	Third part	Died 24 hours after haemorrhage
Garrett, Beall, Jordan, and DeBakey (1963)	71 M.	Arteriosclerotic aneurysm	Third part	Operation: Resection and graft. Died 10 days later following further laparotomy and resection of gangrenous sigmoid colon
Payne (1964)	62 M.	Arteriosclerotic aneurysm	Third part	Died. Several previous laparotomies for gastro-intestinal bleeding, but aneurysm not found

Table I (*cont.*).—DETAILS OF THE CASES OF AORTODUODENAL FISTULA REPORTED IN THE LITERATURE SINCE 1951

AUTHOR	AGE AND SEX	AETIOLOGY	SITE	OUTCOME
Phillips and Jarrell (1964)	66 M.	Arteriosclerotic aneurysm	Third part	Operation: Resection and graft. Alive and well 18 months later
Minjer (1965)	55 M.	Arteriosclerotic aneurysm	Third part	Died following laparotomy. No procedure carried out
Schmich (1965)	66 M.	Arteriosclerotic aneurysm	Third part	Operation: Resection and closure of saccular aneurysm. Died from pulmonary embolus at 21 days
Diethrich, Campbell, and Brandt (1966)	63 M.	Arteriosclerotic aneurysm	Third part	Operation: Resection and graft. Alive and well 4 years later
Ferguson and Arden (1966)	50's M.	Arteriosclerotic ulceration	Duodenum	Died 7 hours after admission
Ferguson and Arden (1966)	52 F.	Arteriosclerotic aneurysm	Duodeno-jejunal flexure	Died 2 weeks after admission
Ferguson and Arden (1966)	59 F	Arteriosclerotic aneurysm	Third part	Died 6 weeks after admission
Ferguson and Arden (1966)	68 M	Arteriosclerotic aneurysm	Duodenum	Dead on arrival in hospital
Ghaphery, Gupta, and Currie (1966)	55 F.	Carcinoma of head of pancreas	Third part	Operation: Pancreaticoduodenectomy and oversewing of aorta. Died postoperatively
Schmauss and Perlin (1966)	72 F.	Arteriosclerotic aneurysm	Third part	Died 23 days after first haemorrhage
Schmauss and Perlin (1966)	76 M.	Arteriosclerotic aneurysm	Third part	Died 12 hours after first haemorrhage
Schmauss and Perlin (1966)	79 M.	Arteriosclerotic aneurysm	Third part	Died 12 days after first haemorrhage. Also found to have a carcinoma of the stomach at autopsy
Vlasak (1966)	73 M	Arteriosclerotic aneurysm	Duodenum	Died of haemorrhage
Chang and Liu (1967)	67 M.	Arteriosclerotic aneurysm	Third part	Operation: Resection and graft. Alive and well 10 months later
Bhagavan and Weinberg (1968)	55 M.	Arteriosclerotic aneurysm	Fourth part	Operation: Fistulous opening oversewn. Died postoperatively
Bhagavan and Weinberg (1968)	65 M.	Arteriosclerotic aneurysm	Third part	Died 86 hours after admission
Eadie and Pollock (1968)	80 M.	Arteriosclerotic aneurysm	Third part	Operation: Resection and graft. Secondary fistula occurred after 3 weeks. Died during second operation Possible old tuberculosis around aorta
Grimond, Enjalbert, Boulard, Gedeon, Saury, and Dambrin (1968)	60 M.	Arteriosclerotic aneurysm	Third part	Operation· Resection and graft Alive and well 3 months later
Sheldon, Lockie, and Mills (1968)	18 M.	Post-traumatic aneurysm	Third part	Operation: Excision of two saccular aneurysms (one above renal arteries) and Teflon patch under extracorporeal circulation and hypothermia. Survived
Gambill (1969)	64 M.	Arteriosclerotic aneurysm	Third part	Died 6 days after haemorrhage. Duodenal ulcer also found at autopsy
Seiferth and Castrup (1969)	74 M.	Arteriosclerotic aneurysm	Third part	Died 2 days after admission
Seiferth and Castrup (1969)	71 M.	Arteriosclerotic aneurysm	Third part	Died 3 weeks after admission
Seiferth and Castrup (1969)	63 M	Arteriosclerotic aneurysm	Second part	Died 12 days after admission
Seiferth and Castrup (1969)	55 M.	Arteriosclerotic aneurysm	Third part	Died 9 days after admission
Tornow (1969)	79 M.	Arteriosclerotic aneurysm	Duodeno-jejunal flexure	Died 6 days after admission
Evans and Webster (1972)	36 F.	Unknown	Third part	Operation: Resection and graft. Died of haemorrhage after 2 days
Evans and Webster (1972)	69 M.	Arteriosclerotic aneurysm	Third part	Operation: Resection and graft Alive and well 22 months later

Summary

Total No. of cases reported since 1951	56
No. of cases operated on	20
Survived 3 months or more	10
Died of postoperative complications	5
Died within 3 days of operation	5

Bhagavan and Weinberg (1968) emphasize the role of inflammatory changes between the duodenum and the aortic wall in the formation of the fistula, and this was very obvious in the first of our cases.

CLINICAL FEATURES

The clinical sequence in aortoduodenal fistula is usually typical of a secondary haemorrhage, in that after the initial bleeding there is a recovery period, often followed by several further episodes of haemorrhage before death. Whatever the cause the pathological process of local tissue damage is unlikely to produce any characteristic diagnostic features, except where an aortic aneurysm is detectable. Even then, however, a separate cause of gastroduodenal bleeding may coexist with an aortic aneurysm (Jones, Kirk, and Bloor, 1970).

In both of our cases we were impressed by the severe pain and collapse which accompanied the episodes of bleeding. These symptoms remitted as the bleeding stopped and were clearly not explained by hypovolaemia alone. The most likely differential diagnosis was combined bleeding and perforation of a peptic ulcer, which was disproved by a normal barium-meal examination in *Case* 1.

It is perhaps worth emphasizing that in the majority of reported cases there has been time after the initial presentation for arrangements for surgical treatment to be made (Roach, 1939; Voyles and Moretz, 1958).

TREATMENT

Treatment should be purely surgical, combined with energetic resuscitation. If the diagnosis is suspected, urgent laparotomy is mandatory, but probably in most cases the diagnosis will only be made at laparotomy for undiagnosed gastroduodenal bleeding.

An inflammatory mass is likely to be found in the region of the duodenojejunal flexure, and temporary proximal control of the aorta should be achieved, either in the hiatus or more simply through a small left thoracotomy. Until then care should be taken not to disturb the fistula, with the risk of external release of the full aortic flow, as happened in the present *Case* 1.

Three methods of dealing with the fistula have been attempted (*Table II*):—

1. **Transduodenal Repair.**—This was performed by Polk and others (1956), Garzon and others (1958), and Bhagavan and Weinberg (1968). The severe external haemorrhage prevents accuracy, and all the patients treated in this way have died during or within 3 days of operation.

2. **Separate Repair of Duodenum and Aorta.**—A few operative successes have been achieved by excising the aneurysm with its fistula, suturing the duodenum, and repairing the aorta by direct suture or a patch (Heberer, 1957; Schmich, 1965; Sheldon and others, 1968). However, the disease and associated damage to the aortic wall are likely to leave too great a defect for simple repair or patching, and this method is clearly unsuitable for the common fusiform aneurysm.

3. **Resection and Grafting of the Lower Aorta and Closure of the Duodenum.**—This is the procedure of choice and has given most of the long-term survivals. Eadie and Pollock (1968) recommend resection *en bloc* of the affected part of the duodenum—this may add considerably to the operation, and simple closure of the duodenal hole appeared to us to be adequate. It is, however, essential that the upper graft anastomosis is protected, preferably with a combination of a free cuff of the graft material, aneurysm wall, peritoneum, and, if necessary, a free omental graft. There is clearly an unusual risk of the not uncommon secondary aortoduodenal fistula that may follow prosthetic grafting of the aorta.

Table II.—COMPARISON OF OPERATIVE PROCEDURES

PROCEDURE	NO. OF CASES	SURVIVED 3 MONTHS OR MORE	DIED OF POST-OPERATIVE COMPLICATIONS	DIED WITHIN 3 DAYS OF OPERATION
Transduodenal repair	3	0	0	3
Separate repair of aorta and duodenum	4	2	1	1
Resection and grafting of lower aorta and closure of duodenum	13	8	4	1
Total	20	10	5	5

DISCUSSION

Spontaneous fistula formation between the aorta and the duodenum is a rare and highly dangerous cause of gastro-intestinal bleeding. The commonest cause is an arteriosclerotic aortic aneurysm, and the presence of such an aneurysm may suggest the diagnosis, particularly when the haemorrhage is associated with severe pain and circulatory collapse. When there is no aneurysm apparent clinically the diagnosis will probably only be made at laparotomy.

It is essential to attempt proximal control of the aorta before disturbing the fistula, and the most promising method of repair is to close the duodenum and to replace the affected segment of the aorta by a prosthetic graft.

It is clear from the published case reports that the majority of patients with this potentially lethal condition can be prepared for surgical treatment during a remission of the haemorrhage, and that a single massive fatal haemorrhage is unusual.

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PNEUMOPERITONEUM IN THE MANAGEMENT OF ABDOMINAL INCISIONAL HERNIA

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SUMMARY

From a group of 30 patients with incisional hernia, 10 were selected for preoperative treatment with an artificial tension pneumoperitoneum to expand the abdominal cavity sufficiently so that a repair could be completed without tension. There were no serious complications from the method and no recurrences of the incisional hernia. It is suggested that this simple and neglected adjuvant should be considered to ensure the successful repair of any large abdominal incisional hernia.

INCISIONAL herniae form 1·4–1·7 per cent of all abdominal herniae (Zimmerman and Anson, 1953; Obney, 1957; Iles, 1965), and most surgeons have encountered a situation in which the contents of the hernia are so large that it is not possible to return them to the general abdominal cavity without great tension on the repair of the abdominal wall. Numerous methods have been used to increase the potential size of the 'mother' cavity, including lateral relaxing incisions, phrenic nerve crush (Ross and Owen, 1954; Touroff, 1954), a transverse incision through all layers of the abdominal wall down to the peritoneum with a second-stage repair (Ziffren and Womack, 1950), and the creation of a subphrenic and peritoneal space by the use of a skeletomusculofascial flap (Handelsman, 1959).

The concept of using oxygen to induce an artificial pneumoperitoneum was introduced in 1940 at the Argentinian Surgical Congress with a case report of its successful use in the treatment of a supra-umbilical eventration. Subsequently Moreno (1947) amplified this report on the basis of about 50 cases. He advocated the use of the insufflation of air into the peritoneal cavity on four to five occasions during a period of 2–3 weeks in all cases when difficulty might be expected in closing defects of the abdominal wall in the treatment of eventration or massive hernia. In addition to making the operation technically simple, Moreno found that the use of pneumoperitoneum helped to avoid postoperative complications due to increased intra-abdominal pressure. Supporting evidence was reported by Berlemont (1952), who found that the preoperative use of pneumoperitoneum in 'enormous' abdominal hernia reduced the postoperative mortality from 5 out of 8 patients to 1 out of 17 patients. The development of respiratory embarrassment after the reduction of a large hernia in a patient who had not been prepared by pneumoperitoneum led Koontz and Graves (1954) to advocate the use of preoperative air insufflation.

This simple adjuvant has been used to assist the repair of other types of hernia: inguinal (Mensuy and Hager, 1958; Moore, Conn, and Guida, 1968; Pingree and Clark, 1968) and omphaloceles (Spratt, 1961; Whelan and Eaker, 1962; Ravitch, 1963; Nissan, 1965; Steichen, 1965). Using this method it is possible to enlarge the abdominal cavity sufficiently to permit a sound repair without resort to artificial implants, or attempts to reduce the normal abdominal contents by resection of bowel or omentum. Avoiding foreign material in the repair diminishes the risk of a persistent infection developing, which in itself increases the risk of a recurrence (Gibson and Stafford, 1964; Musca, 1967).

Table I.—DETAILS OF 10 PATIENTS WITH INCISIONAL HERNIA

CASE	AGE AND SEX	PREVIOUS OPERATION	QUANTITY OF AIR INTRODUCED (litres)	SIZE OF HERNIA (cm.)	STAY IN HOSPITAL (days)	
					Pre-operative	Post-operative
1	54 M.	Right paramedian incision; vagotomy/pyloroplasty	2·5 4·0 5·0 5·0	15 × 17·5	10	14
2	62 M.	Midline epigastric incision; partial gastrectomy	1·5 2·0 1·5	No record	10	11
3	38 F.	Right paramedian incision; cholecystectomy	4·0 1·0 1·4	14 × 15	9	13
4	58 M.	Midline epigastric incision; vagotomy/pyloroplasty	1·2 3·2	19 × 17	9	7
5	46 M.	Midline epigastric incision; vagotomy/pyloroplasty	1·26	15 × 12·5	10	12
6	48 M.	Right paramedian incision; vagotomy/pyloroplasty	1·6 3·0 6·0 6·0	12 × 10	10	10
7	75 F.	Right paramedian incision; cholecystectomy	No record	8 × 6	7	5
8	44 M.	Midline epigastric incision; vagotomy/pyloroplasty	3·0	12·5 × 10	7	7
9	53 M.	Midline epigastric incision; vagotomy/pyloroplasty	2·5 1·5 1·8 2·0	15 × 10	9	10
10	55 M.	Midline epigastric incision: *a.* Perforated duodenal ulcer *b.* Vagotomy/pyloroplasty	2·4 2·5 0·6 2·5	10 × 10	8	15

The use of pneumoperitoneum does not absolve the surgeon from preparing his patient in other ways. Since over 95 per cent of patients with incisional hernia are overweight (Trace, Kozell, and Mayer, 1950; Obney, 1957; Martin, 1966; Moore and others, 1968; Horton and Smith, 1969) an attempt at preoperative weight reduction is mandatory.

Despite the fact that pneumoperitoneum has been advocated for over a quarter of a century, no great support has been expressed for its use from North American clinics, where only 25 cases had been reported up to 1969 (Connolly and Perri, 1969), and no reports appear to have been published in the British literature.

CLINICAL EXPERIENCE

Ten patients with incisional hernia (*Table I*) were selected from 30 patients presenting at the University Department of Surgery, Sheffield, during a 5-year period. They all had defects which would have been difficult to close without considerable tension on the repair. A needle attached to a large syringe via a three-way tap was introduced into the peritoneal cavity under fully aseptic conditions. No difficulty was experienced in finding the peritoneal cavity. To obviate the risk of entering a viscus a site was chosen away from any previous scars to avoid possible associated adhesions. Aspiration was always undertaken before insufflation of room air was commenced, and the volume required varied from 0·6 to 6 litres (*Table I*). The insufflation was stopped when the patient complained of abdominal discomfort; after a short pause a further small quantity of air was introduced, but if pain returned the procedure was stopped. The manœuvre was repeated every 2–3 days over a period of 7–10 days (average 9 days).

Respiratory functions were performed on the first patient (forced expiratory volume, forced vital capacity, and arterial blood-gas estimations) and showed no alteration before, during, or after the induction of the artificial pneumoperitoneum in spite of the fact that a total of 16·5 litres of air was required (*Fig.* 1). In contrast, Moreno (1947) noted a fall in the vital capacity after the initial intraperitoneal injection which then returned to normal. The intra-abdominal pressure during the procedure in

Case 1 reached 25, 9, 12, and 15 cm. of water respectively after the introduction of 2·5, 4, 5, and 5 litres of air.

Pneumoperitoneum was beneficial in 7 out of the 10 patients. The 3 instances where it was not helpful are as follows:—

In *Case* 5 the single insufflation was inadequate. It is of interest, although perhaps coincidental, that postoperatively this man developed a chest infection.

Air was inadvertently introduced into the greater omentum and transverse mesocolon in *Case* 6, thus defeating the whole object of the procedure by increasing the volume of the abdominal contents. The repair was successful although difficult to perform.

One patient (*Case* 8), after a single insufflation of 3 litres, developed generalized surgical emphysema, which manifested itself as suprapubic pain and distension of the scrotum. This gradually spread into the neck, and a chest radiograph showed free air within the pericardial cavity extending alongside the aortic knuckle. The condition settled and 5 days later operation was undertaken successfully but with difficulty. The patient's postoperative course was uneventful.

In 2 patients Dacron mesh was used to reinforce the repair after the use of pneumoperitoneum. Wound infection developed in 3 patients. By using pneumoperitoneum the abdominal wall can be sufficiently stretched to allow the defect to be approximated without tension and does not need the reinforcement of an artificial medium, which led to a persistent sinus in 1 of our cases (*Case* 10).

There were no recurrences in the patients treated by pneumoperitoneum. In the 20 patients treated by standard means 3 herniae recurred; of these, 2 are controlled satisfactorily by surgical belts and 1 has had a further repair which has been successful.

DISCUSSION

The average preoperative stay in hospital for our patients who were treated by pneumoperitoneum was 9 days, in contrast to 2 days in those who were treated by conventional means. The time for operation was chosen arbitrarily in this series, but some objective criteria have been suggested. It has been claimed that the optimum time for surgery can be judged by plain abdominal radiographs to compare the amount of air between the loops of bowel and within the hernial cavity with the previous volume of the hernial contents (Spratt, 1961). In the majority of our cases air was introduced on alternate days. This allows abdominal expansion to take place before the next insufflation. If the procedure is carried out daily only small amounts of air can be introduced before discomfort is experienced (Connolly and Perri, 1969).

It has been suggested that care should be taken not to exceed an intra-abdominal pressure of 10 cm. of water (Spratt, 1961), but this has not been our experience or that of other investigators (Moreno, 1947). In fact, the majority of reports contain no record of pressure measurements, and Connolly and Perri (1969) considered it an unnecessary precaution.

A number of authors have proposed that pneumoperitoneum should continue for longer periods; in some cases even for months (Mason, 1956; Whelan and Eaker, 1962; Ravitch, 1963; Martin, 1966). A fine polythene catheter put into the abdominal cavity has been used for repeated insufflations of air over an extended time, so avoiding multiple paracenteses (Steichen, 1965). Its position can be verified by radiographs. The patient is then able to attend the out-patients' department for preoperative preparation.

In the present series there were two technical complications (*Cases* 6 and 8). The insufflation of omentum has not previously been described, and it is difficult to make sure that this is avoided in the future. The use of an indwelling catheter the location of which has been checked by the injection of a small amount of radio-opaque medium might be the answer.

Subcutaneous emphysema has been recorded (Ravitch, 1963; Pingree and Clark, 1968; Connolly and Perri, 1969), and it has been suggested that the air may be introduced extraperitoneally by the needle slipping outside the confines of the peritoneal cavity. This seems to have been unlikely in our patient (*Case* 6) as the emphysema was associated with scrotal swelling. It seems likely that leakage of air from the peritoneal cavity occurred through the diaphragm and into the mediastinum and subcutaneous tissues. A 10-month-old child has been described (Ravitch, 1963) who was being prepared for operation as an out-patient; he developed cyanosis and shortness of breath following insufflation which was treated by the withdrawal of air, the child quickly returning to his previous state. This complication should clearly be considered, but in adults the discomfort experienced by the patient is a sufficient indication that the procedure should be curtailed.

It has been suggested that the hernia should be bound up to prevent its distension at the expense of the 'mother' cavity (Moreno, 1947; Koontz and Graves, 1954; Mason, 1956). It has been our experience, however, that this is unnecessary. In fact, it has been noted that air tends to displace the bowels from the hernia rather than preferentially distending the hernia (Spratt, 1961; Ravitch, 1963; Connolly and Perri, 1969). Care must be taken with herniae having narrow necks, but this did not constitute a problem in any of our patients.

It is not easy to quantify the technical benefits of the use of pneumoperitoneum in the repair of incisional herniae. Clinical impressions are notoriously fallible. However, apart from our conviction that the operations were easier to perform after pneumoperitoneum, it can be seen that, to date, 1–6 years after repair, no hernia has recurred. This has not been a direct comparison because the herniae treated by pneumoperitoneum were the larger ones. None the less 3 patients have had a recurrence in the remaining 20 patients who were treated by standard methods, so that a distinct advantage would seem to accrue from the use of pneumoperitoneum, which is a simple procedure which we have found free from serious complications.

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SUBCUTANEOUS NODULAR LYMPHOHISTIOCYTIC HYPERPLASIA

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SUMMARY

Five cases of a subcutaneous lymphohistiocytic lesion arising in relation to the deltoid muscles are described. The histological appearances are described and the differential diagnosis is discussed.

SURGEONS and pathologists are justifiably worried by any lesion where the appearances suggest the possibility of neoplasia. During the past 7 years we have encountered five subcutaneous nodular lesions in young patients sharing a common histological picture and raising the possibility of a malignant lymphoma. As far as we are aware this precise lesion has not been described before, although subcutaneous nodules showing lymphoid hyperplasia are well known (Allen, 1948; Wells and Whimster, 1969).

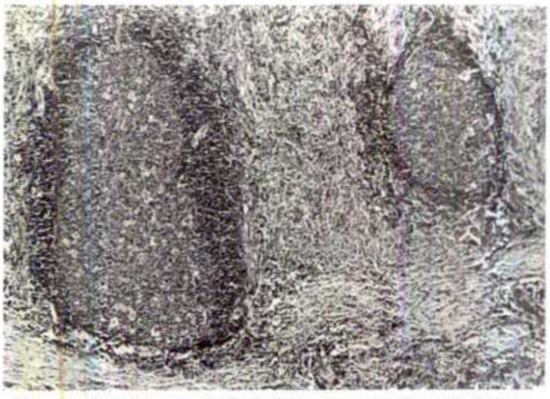

FIG. 1.—Reactive lymphoid follicles surrounded by histiocytes. H. and E. (× 70.)

CASE REPORTS

Case 1.—A 22-year-old male medical student presented in 1964 with two subcutaneous lumps over the deltoid muscle of the right arm. They had both been present for about 2 months. Occasional mild irritation was the only complaint. There was no history of trauma, insect bites, or injections, and the patient's general health was excellent. Laboratory investigations and chest radiographs were normal. The lesions were excised and the wounds healed satisfactorily. There has been no recurrence.

Case 2.—A 13-year-old schoolgirl presented with one symmetrical, hard, painful, subcutaneous nodule over each deltoid muscle which had been present for 18 months. The one on the left arm was about 1 cm. in diameter and that on the right somewhat smaller. A radiograph of the left arm revealed a very faint opacity in the position of the lesion. The patient gave a history of a previous lump on the left upper arm which had disappeared spontaneously. The nodule on the left arm was excised.

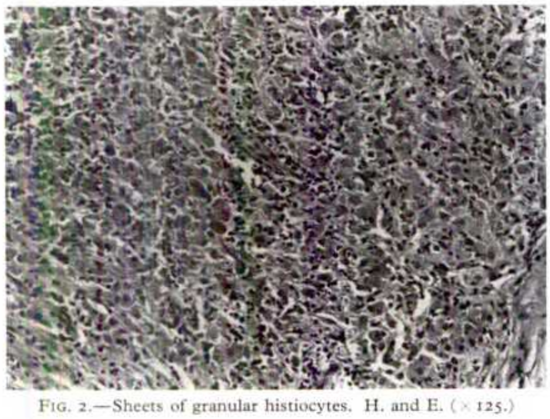

FIG. 2.—Sheets of granular histiocytes. H. and E. (× 125.)

The one on the right arm was left in situ and disappeared spontaneously after 6 months. Two years later there was no sign of a recurrence.

Case 3.—A 20-year-old female complained of a lump, 1 cm. in diameter, over the right deltoid muscle which was painful on pressure. Once again there was no relevant past history and all investigations were normal. The lesion was excised and 6 months later there was no sign of a recurrence.

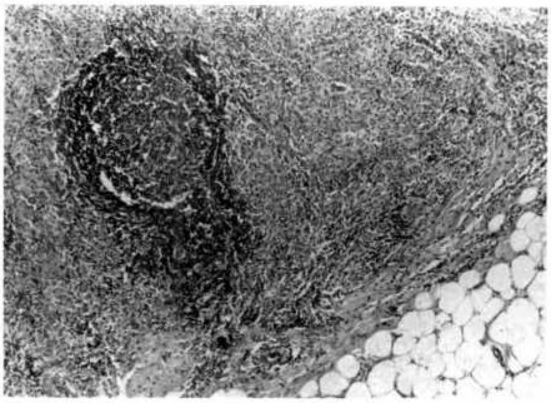

FIG. 3.—Involvement of fat by the lymphohistiocytic process. H. and E. (× 70.)

Case 4.—A 17-year-old female complained of a subcutaneous lump over the right deltoid muscle in relation to an old vaccination scar. There was no history of recent injections, trauma, or insect bites. The lump was excised recently.

Case 5.—A 6-year-old Jamaican girl presented recently with a painful subcutaneous lump over the left deltoid muscle which had been present for a year. The lesion was said to fluctuate in size. There was no history of trauma or insect bites, but the patient had received a poliomyelitis vaccination at the same site 6 months before the lump appeared. The lump was excised.

PATHOLOGY

Macroscopy.—All these lumps were firm in texture and yellowish-white in colour.

Microscopy.—All the lesions showed a similar histological picture. The lesion was characterized by the presence of well-defined lymphoid follicles with fully formed germinal centres. These were surrounded by aggregates of large pale histiocytes with somewhat granular cytoplasm. In addition, there was a round-cell infiltrate including lymphocytes, reticulum cells, and eosinophils. Although eosinophils were readily found, the degree of eosinophilia was not marked. The lesion was subcutaneous in position with no involvement of the skin and upper dermis. In some areas bands of collagen surrounded the lymphoid follicles. The process extended into fat. Characteristic appearances are shown in *Figs.* 1–3.

The nodule from *Case* 2 was subjected to histochemical examination and we are indebted to Professor I. M. P. Dawson for the following report:—

1. PAS positive, remaining so after diastase treatment.
2. Alcian-blue negative at *p*H 2.
3. High-iron diamine negative.
4. Fettrot negative.
5. Faintly positive with Sudan black B.
6. Nile blue: blue positive before and after acetone extraction. No red component.
7. OTAN: slight orange stain in unextracted material. Moderate blue stain after acid extraction.

These results point to the material being phospholipid in nature

DISCUSSION

We have been unable to match these appearances with any other entity in the literature. Lymphocytoma cutis may involve the subcutaneous tissues but is characteristically intradermal. There is, however, some similarity in the cell types observed. Careful questioning in all cases revealed no history of insect bites. Allen (1948) gave a detailed account of persistent insect bites (dermal eosinophilic granulomas), but these lesions showed pseudoepitheliomatous hyperplasia of the epidermis, dermal involvement, and pronounced eosinophilia. Wells and Whimster (1969) described a condition which they called 'subcutaneous angiolymphoid hyperplasia with eosinophilia' and discussed the differential diagnosis. Although there were some features in common with the lesions described here, the vascular component in our cases was minimal and the eosinophilia only moderate. The lymphoid follicles were clearly reactive and there was nothing in the histological picture or in the natural history to suggest a malignant lymphoma.

In 3 cases there was no history of trauma of any kind. In *Case* 4 there was a history of a smallpox vaccination in the distant past, and in *Case* 5 there had been a fairly recent vaccination. For the most part, therefore, the aetiology of these lesions and the strange constant relationship to the deltoid muscles remain unexplained.

Acknowledgements.—We thank Mr. R. Cox, Professor H. Ellis, and Mr. M. Naunton Morgan for allowing us to study their cases. We are indebted to Dr. N. Ferguson, Dr. N. Gowing, and Dr. N. Woolf for the pathological material, and Dr. E. Wilson Jones and Dr. I. Whimster for their comments.

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DEEP-VEIN THROMBOSIS IN PATIENTS WITH FRACTURES OF THE FEMORAL NECK*

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SUMMARY

Fifty patients with fractures of the femoral neck have been studied, using the ^{125}I-labelled fibrinogen test for diagnosing deep-vein thrombosis (D.V.T.). There was an overall incidence of D.V.T. of 54 per cent in fractured limbs. In pertrochanteric fractures there was an incidence of 75 per cent and in subcapital fractures the incidence was 34 per cent.

The radioactive fibrinogen test is a most useful method of screening for D.V.T. under the conditions presented by these patients.

PATIENTS with a fracture of the femoral neck run a high risk of developing deep-vein thrombosis (D.V.T.) This has been demonstrated by clinical studies (Sevitt and Gallagher, 1959), autopsy (Sevitt and Gallagher, 1959), and venographic studies (Culver, Crawford, Gardiner, and Wiley, 1970). None of these methods is suitable for day-to-day screening of large numbers of patients at risk.

The ^{125}I-fibrinogen test (Flanc, Kakkar, and Clarke, 1968) has been shown to be accurate and easy to use in surgical patients (Flanc and others, 1968; Negus, Pinto, LeQuesne, Brown, and Chapman, 1968), medical patients (Nicolaides, Kakkar, Renney, Kidner, Hutchison, and Clarke, 1971), orthopaedic patients (Pinto, 1970), and gynaecological and post-partum patients (Friend and Kakkar, 1970).

Table I.—DISTRIBUTION OF FRACTURES AND THE METHODS OF INTERNAL FIXATION

TYPE OF FRACTURE	NO.	METHOD OF FIXATION	NO.
Pertrochanteric fractures	24	'Pin and plate'	24
Subcapital fractures	26	Thornton nail	18
		Smith Peterson pin	6
		Moore prosthesis	2

The test is, however, unreliable in the region of the pelvis and over a wound or haematoma (Kakkar, 1969)—important factors in the femoral neck fracture situation. The present study was designed to determine whether the radioactive fibrinogen test is of value in diagnosing D.V.T. under these circumstances.

MATERIALS AND METHODS

Fifty patients sustaining subcapital or pertrochanteric fractures of the femur were studied. They were aged from 60 to 94 years (mean 74·2 years) and 46 were female and 4 male. All underwent internal fixation (*Table I*). Within 24 hours of admission each patient was given 100 μc. of ^{125}I-labelled fibrinogen and external scintillation counting with the Pitman 235 Monitor was begun. Details of the test are described elsewhere (Flanc and others, 1968; Kakkar, Nicolaides, Renney, Friend, and Clarke, 1970). Counting was performed on alternate days unless the counts suggested a developing D.V.T., in which case the counting was carried out daily. The usual method of counting at measured intervals over the femoral vein and the calf was employed. Counts over the femoral vein on the fractured side were invariably raised compared with those on the healthy side. In all the patients in this study a venogram was carried out on the fractured limb. In 40 patients this was performed 6–9 days after admission. In 10 patients venography was performed at 3–5 days. The techniques of venography have been described elsewhere (Kakkar and Flanc, 1968; Nicolaides, Kakkar, Field, and Renney, 1971). In 13 patients bilateral venography was performed. During the period of the study no patient developed clinical symptoms or signs of pulmonary embolism. Three patients died from causes other than thrombo-embolic phenomena. They are not included in this series as a full investigation by radioactive test and venography was not completed.

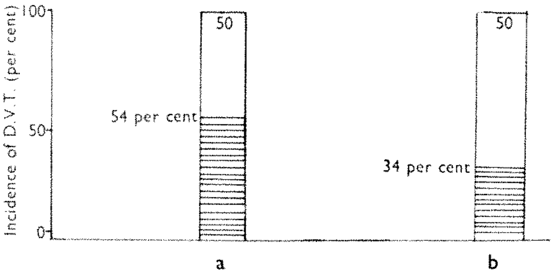

FIG. 1.—Incidence of D.V.T. (a) in fractured limbs and (b) in the opposite unfractured limbs ($\chi^2 = 3{\cdot}24$; $0{\cdot}05 < P < 0{\cdot}10$).

RESULTS

Fig. 1 shows the incidence of D.V.T. in the fractured limbs (54 per cent) and in the unfractured limbs (34 per cent) detected by the ^{125}I-fibrinogen test. In 28 per cent the thrombosis was detected in both limbs.

The results when analysed (*Fig.* 2) show a higher incidence of D.V.T. in limbs with a pertrochanteric fracture (18 limbs: 75 per cent) than in limbs with a subcapital fracture (8 limbs: 34 per cent).

A comparison was made between the incidence of D.V.T. determined by the ^{125}I-fibrinogen test and by venography in 63 limbs. There were 9 limbs in which the results of the tests disagreed. In only 2 was the ^{125}I-fibrinogen test negative when the venogram showed D.V.T. *Table II* gives a more detailed account of these 9 limbs.

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* Based on a communication to the Surgical Research Society of Great Britain and Ireland in July, 1971.

In *Fig.* 3 the distribution and extent of 31 thrombi found by venography are represented diagrammatically. In no case in this series was thrombosis *confined* to veins *above* the knee.

DISCUSSION

The results in this study indicate clearly that patients suffering from fractured necks of the femur form a 'high-risk' group for the development of D.V.T. (54 per cent). It is interesting to note that the pertrochanteric fracture has a considerably higher incidence of D.V.T. (75 per cent) than the subcapital fracture (34 per cent). This may be due to the greater severity of injury and the longer time required for operation (Flanc and others, 1968).

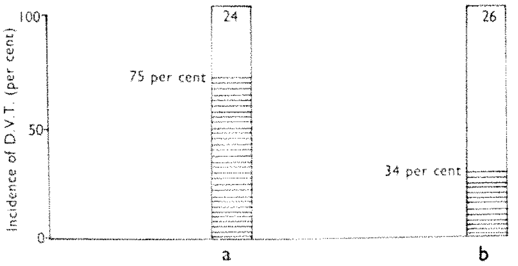

FIG. 2.—Differential incidence of D.V.T. in fractured limbs where the fracture was (a) pertrochanteric and (b) subcapital.

Table II.—REASONS FOR DISAGREEMENT BETWEEN FINDINGS OF VENOGRAPHY AND ^{125}I-FIBRINOGEN TEST IN 9 LIMBS

LIMB	^{125}I-FIBRINOGEN TEST	VENOGRAPHY	PROBABLE EXPLANATION
1	Normal	Small tibial vein thrombus, with collaterals	Old, non-extending thrombus
2	Normal	Soleal vein thrombus	Non-extending thrombus
3	Raised	N.A.D.	Superficial thrombophlebitis
4	Raised	Poor venogram	Ankle oedema—inadequate X-rays
5	Raised	N.A.D.	Superficial thrombophlebitis
6	Raised	N.A.D.	Unable to elevate legs for scanning
7	Raised	N.A.D.	Feeble patient—poor venogram
8	Raised	N.A.D.	No obvious reason
9	Raised	N.A.D.	No obvious reason

N.A.D. = No abnormality detected.

The acute problem is how to manage elderly patients with a fractured neck of the femur and this great tendency to D.V.T., with the risk to life from pulmonary embolism and the disability of the sequelae of the post-phlebitic syndrome.

With the clinical signs alone there will be a failure to diagnose the condition in 50 per cent of patients (Flanc and others, 1968; Negus and others, 1968; Kakkar and others, 1970). A pulmonary embolus may be the first indication of peripheral thrombosis (Sevitt and Gallagher, 1959; Culver and others, 1970). Venography, although a most accurate method of detecting thrombus in the deep veins, is not appropriate for screening large numbers of elderly patients. Ultrasonic techniques, though relatively simple and causing the patient little disturbance, may not detect thrombi in the early stages when they are small and not occluding the veins (Evans and Cockett, 1969).

The ^{125}I-fibrinogen test has been shown to be accurate (Flanc and others, 1968; Negus and others, 1968; Kakkar and others, 1970) and to detect thrombi at their earliest stages. Even in elderly people it can be used without too much discomfort (Kakkar and others, 1970). With the latest form, employing a ratemeter, a technician can scan both limbs in less than 10 minutes. The defect of the radioactive fibrinogen test is that it is inaccurate in the proximal femoral vein (Kakkar, 1969), the region of the pelvis, or in the presence of an operation wound with extravasation of blood and radioactive fibrinogen.

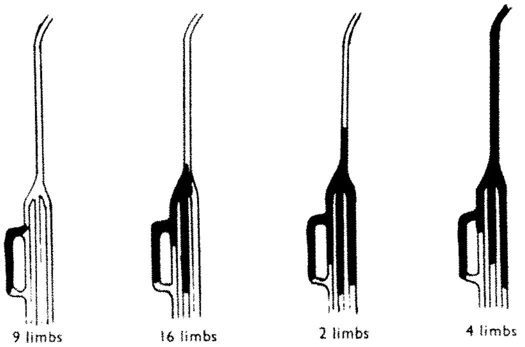

FIG. 3.—Pattern and extent of thrombi in 31 venograms in which thrombosis was detected, showing number of limbs with each pattern. In the left diagram only the soleal veins are thrombosed. On the far right soleal, tibial, popliteal, and ileofemoral thrombosis has occurred.

However, venography was performed in all our patients using techniques (Kakkar and Flanc, 1968; Nicolaides, Kakkar, Field, and Renney, 1971) which not only demonstrate the calf veins but also the length of the popliteal, femoral, and iliac veins and the lower inferior vena cava. By using both ^{125}I-fibrinogen and venography in 63 limbs we have shown quite clearly that the site of origin of most thrombi is in the calf, despite the fact that the injury and operation are in the pelvic region. We performed venography at 3–5 days after admission in 10 of our patients, chosen at random, to ensure that we were not missing transient thrombi in the large proximal veins. These findings confirm that the ^{125}I-fibrinogen test is a precise method of detecting developing thromboses in the leg at a very early stage.

The findings support those of many workers (Bauer, 1940; Gibbs, 1957). They are contrary to the view of other workers (Sevitt and Gallagher, 1959) that a significant number of thromboses, especially following trauma to the femoral neck or pelvis, arise within the large proximal veins. Some of these latter studies were based on autopsy findings. This involves a highly selected group of patients, many of whom die some weeks after the initial injury and after periods of prolonged hypotension with widespread venous stasis. The vast majority of patients with D.V.T. survive and it is only in these live patients that the dynamic process of venous thrombosis can be followed using the ^{125}I-fibrinogen test and repeated venography. Venography, however, is uncomfortable and does not lend itself to frequent repetition. A more extensive study (Kakkar, Howe, Flanc, and Clarke, 1969) in patients undergoing general surgical procedures indicated that the site of origin of thrombi was in the soleal veins but, as in the present study, a proportion of the thrombi propagated into larger proximal veins. The propagation was not always visibly continuous owing to lysis in some areas.

Finally, it is clear that the management of elderly patients with fractured femoral necks and D.V.T. presents a pressing problem. None of the available forms of anticoagulation, fibrinolysis, or defibrination is entirely successful or free from risk (Kakkar, Flanc, Howe, O'Shea, and Flute, 1969). There must therefore be specific indications for their use. There is little danger when the thrombotic process is confined to the calf. It is only when it extends into the popliteal or more proximal veins that there is a risk of pulmonary embolus (Kakkar, Howe, and others, 1969). In this particular group of patients, immobilized by age and injury, we gave heparin by intravenous infusion when the diagnosis was established. It was given at an early stage in an attempt to prevent propagation. It is still more important to carry out appropriate treatment with heparin or streptokinase if the thrombus does propagate and details of this treatment are given elsewhere (Kakkar, Flanc, and others, 1969).

CONCLUSIONS

In the absence of 100 per cent effective methods of prophylaxis against D.V.T. a reliable screening method is essential. Calf-vein thrombi are always present when D.V.T. occurs and screening the calf veins where the counts are reliable is the recommended method for patients with a fractured neck of the femur.

Acknowledgements.—We are grateful to Professor J. G. Murray for his encouragement and help; to Mr. R. C. F. Catterall and Mr. C. E. A. Holden for allowing us to study their patients; to Pfizer Ltd. (U.K.) for financing a Research Fellowship for A. N. Nicolaides; to the K.C.H. Research Fund for financial assistance to E. S. Field; to Mr. S. Serunkuma and Miss W. Bevis for technical assistance; to Mrs. J. Brazier and Mrs. A. Canning for nursing assistance; and to Mrs. M. G. Shelton and Miss S. Harte for secretarial help.

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NON-RECURRENT LARYNGEAL NERVE

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SUMMARY

During the performance of 2101 thyroid operations, 3496 recurrent laryngeal nerves were identified and exposed. Of the 1776 visualized nerves on the right side, 6 were found to be non-recurrent. A brief survey of the literature relevant to this anatomical abnormality is included, and its importance in the performance of thyroid surgery is emphasized.

A NON-RECURRENT laryngeal nerve is uncommon. Arising directly from the vagus nerve close to the thyroid gland, it lies in an exposed position far from its normal location. The risk of nerve injury is accentuated when a patient with this anomaly undergoes thyroid surgery. The recent finding of a non-recurrent nerve stimulated us to determine the frequency of this congenital abnormality.

RESULTS

Between the years 1959 to 1969 inclusive 2101 thyroid operations were performed at the Lahey Clinic Foundation for a variety of conditions. The recurrent laryngeal nerves were routinely exposed and identified whenever they were considered to be at risk, using the standard technique developed by Lahey (Lahey, 1918, 1923; Lahey and Clute, 1926). A total of 3496 recurrent laryngeal nerves (1776 on the right side and 1720 on the left side) was so visualized. Of the nerves dissected, 6 were found to be non-recurrent laryngeal nerves, and all occurred on the right side (*Table I*). It is interesting that a non-recurrent laryngeal nerve has never been reported on the left side. Despite attempted exposure on 41 occasions on the right side and 30 occasions on the left side, the recurrent nerve was not visualized. It was not possible to determine whether or not these nerves were non-recurrent.

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When the trachea and posterior surface of the right thyroid lobe are exposed a non-recurrent nerve (in either of these two positions), because of its unusual and unexpected situation, is obviously in jeopardy. The nerve could easily be injured before it is identified, thus producing a right vocal cord palsy. In the 6 instances reported the nerve was carefully preserved and no vocal cord changes occurred postoperatively.

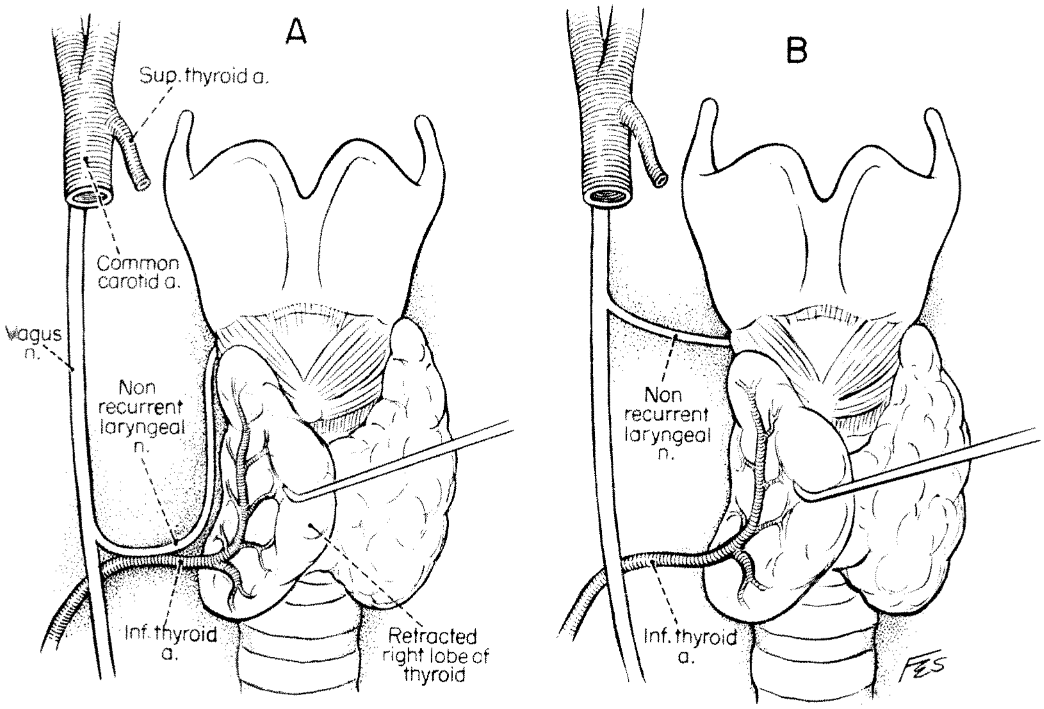
A
Sup. thyroid a.
Common carotid a.
Vagus n.
Non recurrent laryngeal n.
Inf. thyroid a.
Retracted right lobe of thyroid
B
Non recurrent laryngeal n.
Inf. thyroid a.
FES

FIG. 1.—The course of the non-recurrent laryngeal nerve: (A) accompanying the inferior thyroid artery in 2 patients, and (B) passing directly to the larynx at the level of the superior pole of the thyroid gland in 4 patients.

Table I.—INCIDENCE OF RECURRENT AND NON-RECURRENT LARYNGEAL NERVES FOUND IN 2101 THYROID OPERATIONS

	RIGHT	LEFT	TOTAL	PER CENT
Nerves at risk	1817	1750	3567	100
Recurrent laryngeal nerves found	1770	1720	3490	98
Non-recurrent laryngeal nerves found	6	—	6	
Nerves not found	41	30	71	2

In all 6 patients mentioned the non-recurrent laryngeal nerve arose from the cervical trunk of the vagus nerve. In 2 patients it arose at the level of the inferior thyroid artery, passing to the tracheo-oesophageal groove at the level of the inferior pole of the thyroid gland (*Fig.* 1 A). The nerve then followed the course of the normal recurrent laryngeal nerve, entering the larynx just below the inferior horn of the thyroid cartilage. In the 4 other patients, however, it arose at the level of the thyroid cartilage or superior pole of the thyroid gland and passed directly to the larynx (*Fig.* 1 B).

HISTORICAL REVIEW

As early as 1823 a non-recurrent laryngeal nerve was reported by Stedman. He located a nerve passing directly from the right vagus nerve to the larynx in a cadaver in which the right subclavian artery arose from the aortic arch and passed posteriorly to the oesophagus and trachea. Hart (1826), Hilton (1837), Hérard (1846), Demarquay (1848), and Hooper (1887) presented further reports in the literature. In all of these reported cases the anomaly occurred on the right side, and in all cases, except that of Hérard (1846), it was associated with an anomalous right subclavian artery. In 1924 Milianitch again drew attention to the associated anomalies, and in 1932 Pemberton and Beaver reported a right non-recurrent laryngeal nerve with suspected abnormal origin of the right subclavian artery. Work (1941) presented an additional case of a right non-recurrent laryngeal nerve associated with an anomalous right subclavian artery and reviewed the embryological basis as suggested by the previous literature. More recently Blackburn and Salmon (1961), Doyle, Watkins, and Halbert (1967), Hunt, Poole, and Reeve (1968), Reeve, Coupland, and Johnson (1969), and Nobles (1970) have reported cases and have further drawn attention to the abnormality and its importance to the thyroid surgeon.

EMBRYOLOGY

The recurrent laryngeal nerves arise embryologically from the vagus nerve in close proximity to the fourth branchial arch and the fourth primitive aortic arch vessels. On the right the fourth arch vessel persists as the right subclavian artery and on the left as the aortic arch itself. As the embryo elongates and the thoracic organs descend the nerves assume their recurrent course around the right subclavian artery on the right and the aortic arch on the left.

If the proximal part of the right fourth arch vessel fails to develop no vessel is present to draw the nerve down to its usual recurrent position. It therefore passes directly to the larynx as a non-recurrent or undescended right laryngeal nerve. Thus, the anomaly of the nerve is related to and dependent upon the presence of an abnormal right subclavian artery. The commonest associated vascular abnormality is a dorsal origin of the right subclavian artery from the aortic arch with or without a course posterior to the trachea and oesophagus (Stedman, 1823).

COMMENT

The non-recurrent anomaly of the right recurrent laryngeal nerve is uncommon, but its possible occurrence should be anticipated by all thyroid surgeons. It is particularly vulnerable to trauma during mobilization of the right thyroid lobe, which *precedes* exposure of the nerve in its normal location. Indeed, even if one has no intention of exposing the nerve, this lateral dissection must be performed to accomplish an adequate subtotal lobectomy.

Reeve and others (1969) reported 7 such nerves in approximately 1200 thyroid operations. Our series includes 6 such observations in 1776 visualized right recurrent laryngeal nerves and a total of 1817 nerves at risk (an incidence of just over 0·3 per cent on the right). It is interesting that four standard textbooks of surgery do not mention this abnormality.

We believe that a technique of thyroidectomy that includes routine direct visualization, identification, and subsequent protection of the recurrent laryngeal nerves enables the thyroid surgeon (if he is aware of this possible anomaly) to handle the nerve safely and easily. Precise identification and division of the middle thyroid veins permit exposure of the posterior surface of the right thyroid lobe, the trachea, and the oesophagus. If the recurrent laryngeal nerve is not found in its normal position the vagus is investigated to exclude the presence of an aberrant non-recurrent nerve. If the latter is found and visualized it can easily be protected from injury during subsequent dissection. No structure passing medially from the carotid sheath except the middle thyroid veins should be divided until after the nerve is identified.

Avoiding injury to the recurrent laryngeal nerves is a major consideration in every thyroidectomy. Advocates of routine exposure have been challenged by many surgeons who oppose exposure (Nobles, 1970). We agree with Riddell (1970), who stated that when these nerves are not identified the incidence of damage will be higher. All 6 non-recurrent nerves that we have reported would have been placed in greater jeopardy if we had employed a technique that depended upon 'staying away' from the normal position of the nerve to avoid injury. In our experience (Mountain, Stewart, and Colcock, 1971) the risk to the nerve from routine exposure has been shown to be negligible.

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SQUAMOUS CARCINOMA OF THE STOMACH FOLLOWING CORROSIVE ACID BURNS

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SUMMARY

Two cases of primary squamous-cell carcinoma arising in a stomach damaged by corrosive acid burns are reported. Thirty-three previously reported cases of pure squamous carcinoma of the stomach are tabulated and their pathogenesis is discussed. A plea is made for treating corrosive acid burns of the stomach by some form of resection of the entire area involved rather than by more conservative methods, such as gastrojejunostomy, which have been used in the past.

SQUAMOUS carcinoma of the stomach has rarely been reported in the literature. Dahlin (1956) failed to find a single case on reviewing 11,000 cases of carcinoma of the stomach seen at the Mayo Clinic between 1907 and 1955. Dreyer and Louw (1957) were able to collect only 9 cases from the world literature, to which they added 1 case of their own. Boswell and Helwig (1965) found reports in the literature of 43 cases of gastric carcinoma containing squamous tissue, but only 18 of these were pure squamous carcinomas, the rest being mixed squamous and mucin-secreting tumours (adeno-acanthomas). To the first group they added 12 cases of pure squamous carcinoma obtained from a study of 2634 cases of carcinoma of the stomach in the files of the Armed Forces Institute of Pathology. Only 3 further cases of pure squamous carcinoma of the stomach have subsequently been reported (Altshuler and Shaka, 1966; Urban, 1966; Sano, 1967—*Table I*). In all the reports there has been controversy about the possible origin of the tumours.

The cases reported here are unique in that in each instance the squamous carcinoma developed in a stomach which had been damaged by corrosive acid many years earlier.

CASE REPORTS

Case 1.—R. V., a Sinhalese male, aged 39 years, presented at the General Hospital, Kandy, complaining of vomiting after meals and loss of weight of 3 months' duration. Both symptoms had been progressive from their onset, and at the time of admission (23 March, 1970) the patient was vomiting soon after nearly every solid meal. He had begun to vomit even liquids during the past 2 weeks. The vomitus had neither been blood-stained nor appeared to contain bile at any time.

At about the age of 12 the patient had become involved in a drinking bout and whilst under the influence of alcohol had drunk about one cupful of a liquid which he had later realized was an acid (this was probably acetic acid as it was freely available in the part of the country where he lived because of its use in the manufacture of rubber). Soon afterwards he had begun to vomit rather severely and had been given a stomach wash. He had continued to vomit blood-stained material and had been treated with intravenous fluids as he had found difficulty in swallowing. He had made a slow recovery and had been discharged some 3 months later, at which time he had been able to take semisolid food. During the course of the following year he had returned to a normal diet of rice and curry but he had only been able to manage small quantities at a time, so that he had been forced to have meals every 2 hours in order to satisfy his hunger. Any attempt at ingesting a normal-sized meal had given rise to severe abdominal discomfort and vomiting.

Table I.—CASES OF PURE SQUAMOUS CARCINOMA OF THE STOMACH REPORTED IN THE LITERATURE

CASE	AUTHOR	AGE AND SEX	SITE
1	Rorig (1895)	— —	Lesser curvature
2	Eppinger (1895)	— M.	Fundus
3	Borst (1902)	— —	—
4	Calderara (1910)	54 F.	Pylorus
5	de Martel, Oberling, and Pernet (1930)	41 M.	Pylorus
6	Penna de Azevedo and Villela (1936)	57 M.	Lesser curvature
7	Weil (1936)	47 M.	Pylorus
8	Gauthier-Villars and Leger (1940)	68 M.	Pylorus
9	Scheffler and Falk (1940)	49 M.	Body
10	Reich (1944)	62 M.	Pylorus
11	Puccini and Stigliani (1950)	58 M.	—
12	Diaz (1951)	73 M.	Pylorus
13	Hicks (1953)	65 F.	—
14	Lange (1955)	78 M.	—
15	Lange (1955)	56 M.	—
16	Dreyer and Louw (1957)	44 F.	Pylorus
17	Cruze, Maas, Clarke, and El-Ferra (1960)	52 M.	Cardia
18	Johnston and Pitts (1962)	81 M.	—
19	Boswell and Helwig (1965)	36 M.	7 in the pylorus, 4 in the fundus, multiple tumours in 1 case
20	Boswell and Helwig (1965)	40 M.	
21	Boswell and Helwig (1965)	52 M.	
22	Boswell and Helwig (1965)	56 M.	
23	Boswell and Helwig (1965)	57 F.	
24	Boswell and Helwig (1965)	62 M.	
25	Boswell and Helwig (1965)	66 M.	
26	Boswell and Helwig (1965)	66 M.	
27	Boswell and Helwig (1965)	67 M.	
28	Boswell and Helwig (1965)	70 M.	
29	Boswell and Helwig (1965)	71 F.	
30	Boswell and Helwig (1965)	79 M.	
31	Altshuler and Shaka (1966)	75 M.	Body and cardia
32	Urban (1966)	— —	—
33	Sano (1967)	— —	—
34	Eaton and Tennekoon (1972)	39 M.	Body
35	Eaton and Tennekoon (1972)	26 F.	Body and cardia

The patient was found to be dehydrated and thin, weighing only 33·6 kg. The cardiovascular and respiratory systems were clinically normal, and physical examination revealed no abnormal findings in the abdomen or elsewhere.

On 4 April a barium-meal screening was carried out. The appearances were reported as those of 'a carcinoma of the body of the stomach, since a constant-filling defect was seen in this area. The stomach was greatly reduced in size and the pylorus lay well to the left of the midline' (*Fig.* 1).

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Gastric secretions collected overnight for 12 hours were found to contain no free hydrochloric acid, and gastric washings which were examined for malignant cells showed a large number of squames with the cells appearing uniform and the changes being of only Grade 1 intensity.

OPERATION.—On 18 April, following adequate preparation, the abdomen was opened through a midline epigastric incision. The first part of the duodenum was found lying across the midline with the pyloric part of the stomach well to the left. The antrum and the body of the stomach were markedly reduced in size and the peritoneal surface was smooth and shiny. This area was quite hard to the touch and the only area of the stomach which appeared normal was a 3·8-cm. segment of cardia, fundus, and lesser curvature just distal to the oesophagogastric junction. The diseased area of the stomach was mobile and metastases appeared to be confined to the few small and hard lymph-nodes along the right gastro-epiploic vessels.

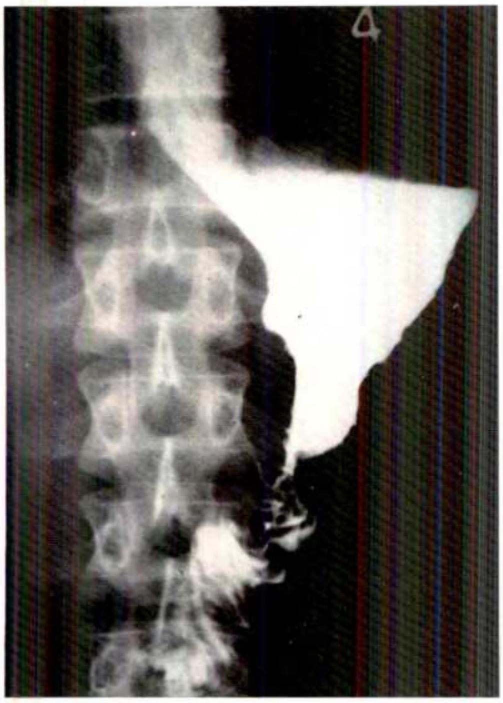

FIG. 1.—*Case* 1. Barium-meal film showing the deformity in the body of the stomach together with shortening of the stomach which has drawn the duodenum to the left.

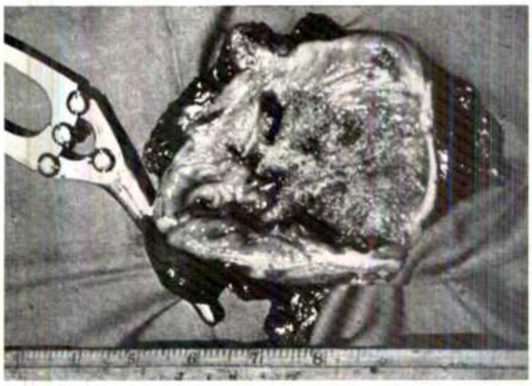

FIG. 3.—*Case* 1. The stomach has been opened along the lesser curvature to show normal mucosa towards the pylorus, a grossly ulcerated portion of the stomach in the middle, and smooth mucosa towards the oesophageal end in the upper right-hand portion.

A near-total radical gastrectomy was carried out, the tiny cuff of stomach at the cardiac end being anastomosed to the apex of a loop of proximal jejunum which was brought up behind the colon. The limbs of the jejunal loop were anastomosed side to side to each other to form a gastric pouch.

PATHOLOGY.—The resected specimen was 12·5 cm. in length and consisted of almost the entire stomach distal to the cardiac orifice (*Fig.* 2). When opened along the lesser curvature, normal-looking gastric mucosa was seen at the pyloric end of the stomach, the mid-portion of the stomach was granular and devoid of normal epithelium, and apparently normal mucosa was seen again at the cardiac end (*Fig.* 3).

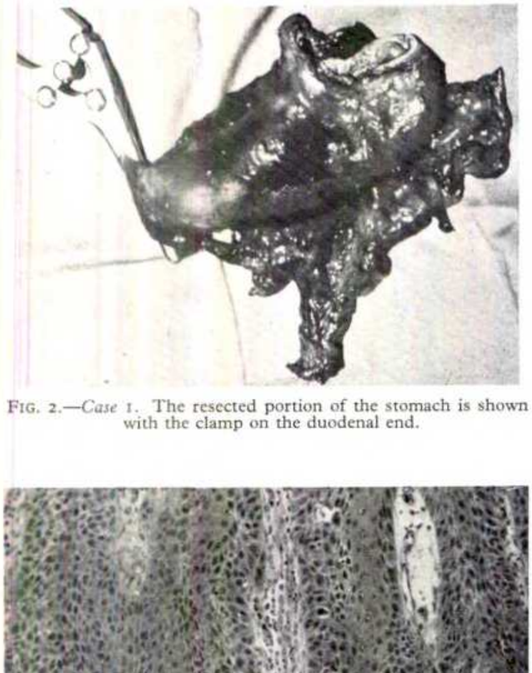

FIG. 2.—*Case* 1. The resected portion of the stomach is shown with the clamp on the duodenal end.

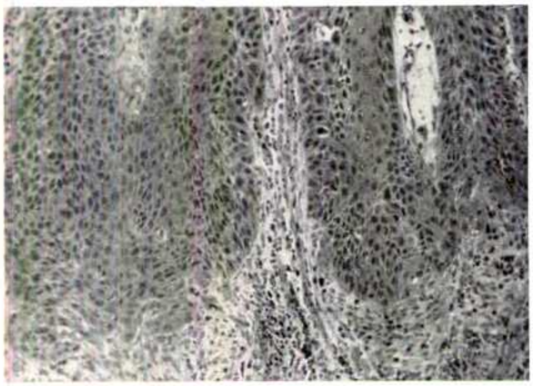

FIG. 4.—*Case* 1. Squamous carcinoma of the stomach from the ulcerated area. H. and E. (× 80.)

Histologically, the ulcerated area was a squamous carcinoma (*Fig.* 4), and sections taken from the edge of this area towards the cardia showed squamous epithelium all along it (*Fig.* 5). Sections from the distal part of the ulcerated area near the pylorus showed a transition to gastric mucosa (*Fig.* 6). Serial sections showed that the whole of the stomach proximal to this transitional area was covered with squamous epithelium with no intervening islets of gastric mucosa. The muscle coat of the stomach showed diffuse fibrosis with breaks of a complete nature with scarring in the floor of the ulcer (*Fig.* 7). No metastases were found in the lymph-nodes.

POSTOPERATION.—The patient's postoperative convalescence was complicated by a left subphrenic abscess which was drained on the seventeenth day after surgery. Following this there was rapid improvement and the patient was discharged home on 27 May, a little over 1 month after gastrectomy, having gained 4·5 kg. in weight and being able to eat a large plateful of rice without difficulty at a single meal.

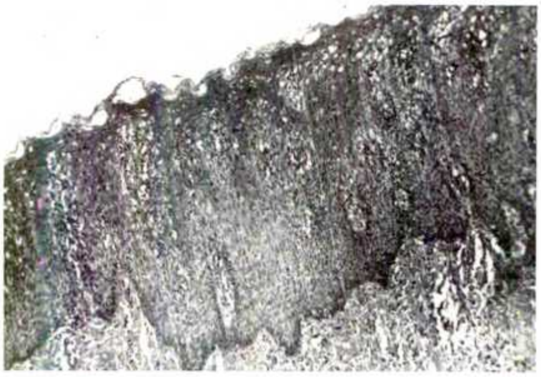

FIG. 5.—*Case* 1. Photomicrograph showing the proximal part of the stomach wall lined by hyperplastic squamous epithelium. H. and E. (× 50.)

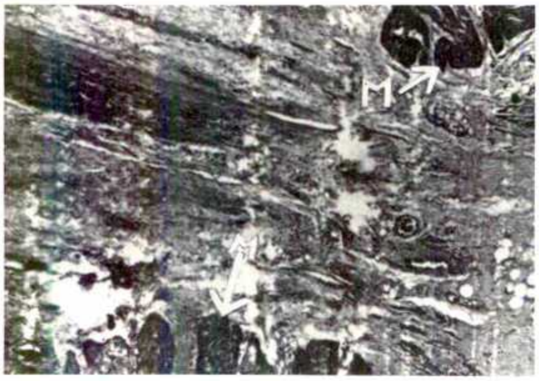

FIG. 7.—*Case* 1. Photomicrograph to show a break in the muscularis replaced by fibrous tissue. M, Muscle separated by fibrous tissue. H. and E. (× 70.)

The patient has been seen regularly at follow-up and has remained well. In April, 1971, his weight was stable at 44 kg. He has resumed work as a waiter, and has found that he can satisfy his hunger with about a cupful of rice (about half the quantity he was able to take soon after his operation), which is about the average quantity consumed at a single meal by a person not engaged in heavy manual work.

Case 2.—S. W. S., a Sinhalese housewife aged 26 years, was admitted to the Surgical Unit of the University at Kandy General Hospital on 7 Oct., 1970, complaining of progressive difficulty in swallowing of about 4 months' duration. During this period the patient had also experienced pain in the upper abdomen radiating to the back which had been worse when she had been hungry. There had been no vomiting but regurgitation of food mixed with blood had occurred occasionally. The patient was able to swallow solids only if they were accompanied by a drink. Symptoms were worse on lying down and were relieved on sitting up. Over the past 4 months loss of appetite had occurred and had become progressive, causing a significant loss of weight.

Twelve years earlier the patient had accidentally swallowed about a cupful of acid used for electroplating, after which she had vomited blood and subsequently had developed difficulty in swallowing. One month later she had undergone an operation in the General Hospital, Colombo, where a sleeve resection of the middle of the body of the stomach had been carried out for an acid stricture. She had been discharged 1 month later free of symptoms, and had remained well until the present illness. In the intervening period she had married and had had 1 child.

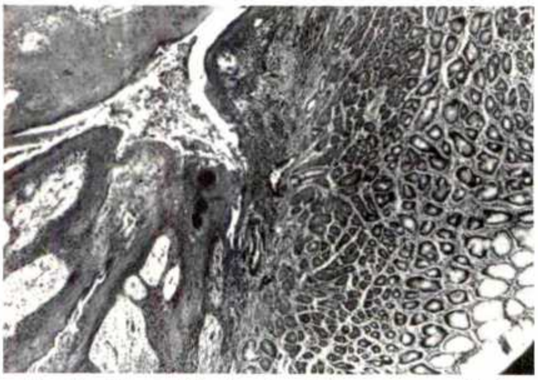

FIG. 6.—*Case* 1. The junction of the squamous epithelium with the gastric mucosa at the distal part of the ulcerated area. H. and E. (× 50.)

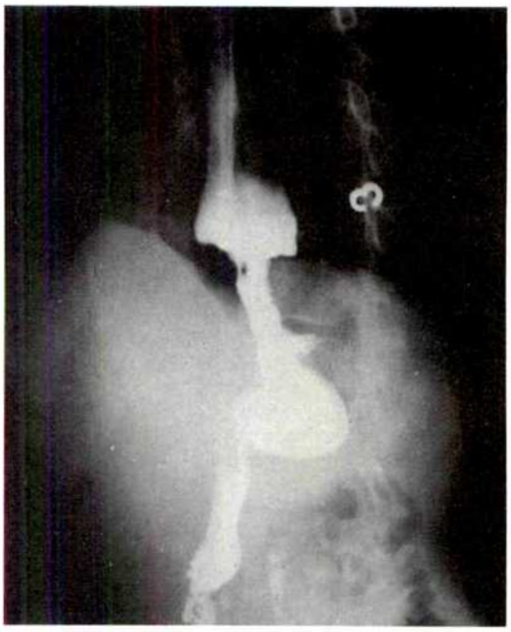

FIG. 8.—*Case* 2. Barium-meal film showing a normal oesophagus with a patulous oesophagogastric junction and a small part of the stomach in the thorax.

Examination showed an anaemic and wasted woman who was in obvious pain and weighed only 23 kg. The abdomen was scaphoid and showed an old midline epigastric scar. Except for vague tenderness in the epigastrium, physical examination showed no abnormality in the abdomen or elsewhere.

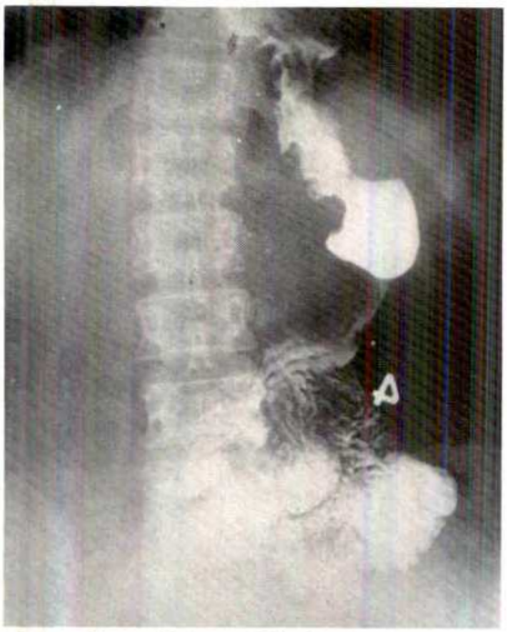

FIG. 9.—*Case* 2. Barium-meal film showing the gross irregularity in the mid-portion of the stomach with normal mucosal folds in the distal few centimetres.

Barium-meal screening carried out on 19 Oct. was reported as showing 'the proximal seven-eighths of the oesophagus to be normal. The rest of the oesophagus appeared to have been resected. A small part of the stomach was in the thorax and there was a patulous oesophagogastric junction (*Fig*. 8). There was gross irregularity of the mid-portion of the stomach with narrowing of the lumen (*Fig*. 9). There were two areas of severe stricture formation, as a result of which pockets had formed in the lesser curvature. The distal few centimetres of the stomach showed normal mucosal folds, and the gastroduodenal junction was normal though stretched to some extent. At 24 hours there was a small residue of barium in the stomach (*Fig*. 10). The appearances were strongly suggestive of malignancy of the stomach, very probably superimposed on corrosion by acid.'

On 17 Oct. the patient was oesophagoscoped and the oesophagus, though containing some fluid, was found to be clear up to 38 cm. Beyond this point the tip of the endoscope had to be deflected abruptly (? oesophagogastric junction) and thereupon the mucosa appeared whitish, protuberant, and hard. A biopsy was taken from this area with some difficulty as the jaws of the instrument tended to slip off the mass.

The biopsy was reported as showing a squamous carcinoma.

OPERATION.—After adequate preparation, exploration was carried out on 1 Nov. employing a left-sided thoraco-abdominal incision through the bed of the seventh rib. A tumour about the size of a cricket ball was found in the upper part of the stomach and was densely adherent anteriorly to the left lobe of the liver and posteriorly to the structures of the abdominal wall, making resection impracticable. A palliative Roux-en-Y end-to-side oesophagojejunostomy was constructed at the level of the hilum of the left lung.

Postoperatively, the patient's condition was unsatisfactory and she was managed in an intensive care unit; despite treatment she died on the morning of 3 Nov.

PATHOLOGY.—Only a partial post-mortem examination was allowed and the specimen removed showed the oesophagus to be normal down to the level of the diaphragm from where a growth was found extending down to within 5 cm. of the pylorus (*Fig*. 11). The growth was closely adherent to the liver, diaphragm, and posterior abdominal wall structures.

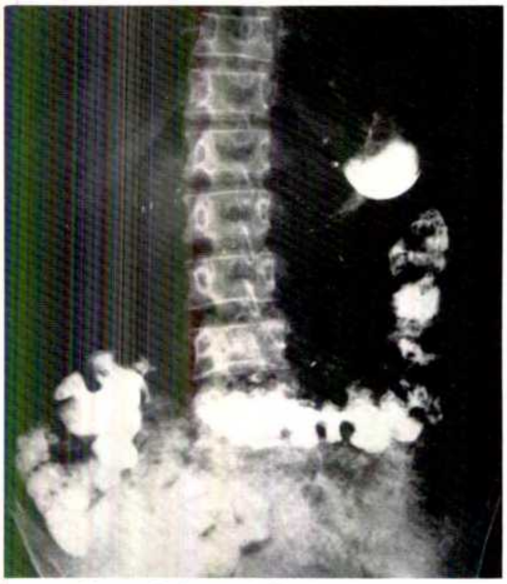

FIG. 10.—*Case* 2. Barium-meal film showing a residue in the stomach at 24 hours.

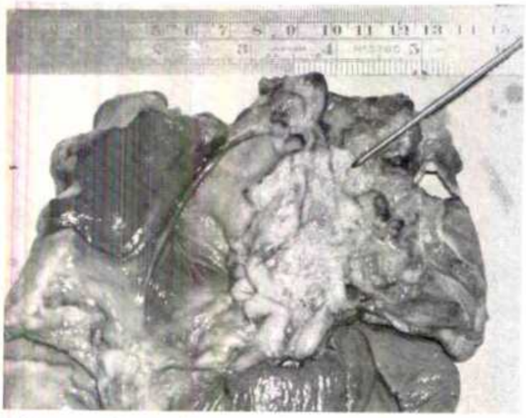

FIG. 11.—*Case* 2. The stomach opened at the post-mortem examination to show the tumour extending from the middle of the stomach to the oesophagogastric junction. The pointer is at the oesophagogastric junction.

Histology showed a squamous carcinoma infiltrating the stomach widely and deeply.

DISCUSSION

The pathological findings in *Case* 1 resemble those reported by Watson, Flint, and Stewart (1936) in a case where the upper loculus of an hour-glass stomach—caused by stricturing from hyperplastic tuberculosis—was found to be completely lined by squamous epithelium except for a narrow area along the lesser curve of the stomach. The oesophagogastric junction could not be identified from the mucosal aspect, suggesting that squamous epithelium had grown down from the oesophagus to cover the upper loculus.

In the present *Case* 1 the squamous epithelium found in the stomach was hyperplastic, was probably continuous with the epithelium of the oesophagus, and lined the whole of the stomach up to the distal margin of the ulcer. The fibrosis and discontinuity found in the muscularis subjacent to the squamous epithelium are evidence of the past damage to this area by the acid burns. In the cardiac portion of the stomach the gastric mucosa damaged by the acid had probably been completely replaced by epithelial downgrowth from the oesophageal mucosa, thus accounting for the achlorhydria found and the large number of squames seen in the gastric washings.

The malignant change that had subsequently occurred in the squamous epithelium had resulted in a pure primary squamous carcinoma.

In *Case* 2 there was also a past history of corrosive gastritis which had necessitated early surgery of an excisional nature. It is reasonable to assume that the resection of the strictured area had removed only the worst-affected area, leaving behind damaged epithelium which had been replaced by squamous epithelium. The tumour that had developed subsequently had involved the stomach extensively and the oesophagus minimally. Though the pathological picture was not as clear cut as in the first case, it is reasonable to suppose that the malignancy had supervened on squamous epithelium which had replaced gastric mucosa damaged by acid in this case as well.

Several explanations have been put forward with respect to the origin of squamous epithelium in the stomach. It has been considered to arise from (1) primitive undifferentiated basal cells in the mucosa, (2) heterotopic islets of squamous epithelium, (3) squamous metaplasia of gastric epithelium or a similar change occurring in an adenocarcinoma, and (4) a semisquamous epithelial layer covering the gastric mucosa (Duran-Jorda, 1945).

Squamous-cell metaplasia of the gastric mucosal epithelium though denied by Dreyer and Louw (1957) has been reported in 1 case by Hermann (1911), and a similar change has been produced experimentally in rats by Futterer (1904) and Saxen (1952). Boswell and Helwig (1965) have also reported squamous metaplasia—at the edge of a perforated gastric ulcer. The possibility must be accepted of subsequent development of squamous carcinoma in metaplastic gastric epithelium.

The explanation advanced by Duran-Jorda (1945) of a semisquamous epithelial layer covering the gastric mucosa was favoured by Diaz (1951) to explain the changes that he reported in his case, but Altshuler and Shaka (1966) discount this theory as they hold that electron microscopy has not shown the presence of this additional layer. On the contrary, they support the possibility of heterotopic squamous epithelium being the source of many such tumours, as islands of squamous epithelium are well known to occur, particularly near the cardia and along the lesser curve (McPeak and Warren, 1948).

In the cases reported here, in view of the past damage to the gastric mucosa, it is held that the squamous epithelial change was caused by regenerative downgrowth from the oesophagus. This conclusion is supported by the continuity of the squamous epithelium on the damaged area with that of the oesophagus.

Boswell and Helwig (1965), in analysing their 12 cases, found half of them suitable for only palliative procedures because of widespread intra-abdominal metastases. No case survived more than 1 year. These findings are in direct contrast to those of other authors who report absence of metastatic spread and forecast a reasonable prognosis. Our first case appears to fall into this category since there was no metastatic spread and the patient is in good health 1 year after surgery. He should have a better prognosis than if he had had an equivalent gastric adenocarcinoma.

The 2 cases reported here have a particular surgical significance in that malignant neoplasia followed on corrosive acid burns of the stomach. It has been the practice when dealing with acid burns of the stomach to consider them benign and to treat them by gastrojejunostomy or pyloroplasty, leaving the burnt area in situ. Paul (1951), in discussing the treatment of corrosive strictures of the stomach, stated that there appeared to be a place for partial gastrectomy rather than gastrojejunostomy as the latter may be followed by stomal or jejunal ulceration in later years and also because the possibility of malignant change cannot be discounted. Despite this he treated the patients reported by him by gastrojejunostomy only, and this appears to have been the practice followed by other surgeons too. A more radical form of surgery as suggested by us has only been performed in those cases where diffuse fibrosis has followed the corrosive burn (Strange, Finneran, Schumacher, and Bowman, 1951).

From the experience gained from these 2 cases it would appear that partial or subtotal gastrectomy rather than a conservative procedure should be adopted in patients presenting with corrosive strictures of the stomach, as they might otherwise develop a malignant lesion many years later in the deeply burnt area.

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CALCIFYING EPITHELIOMA OF MALHERBE

BY S. M. JONES AND K. H. CRUMPLIN
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SUMMARY

Experience with 34 cases of calcifying epithelioma of Malherbe is analysed, and the frequency of misdiagnosis is noted. The apparent dramatic rise in incidence over the past few years may be due to an increasing awareness of the existence of this benign tumour by both clinicians and pathologists. Evidence is cited to support the view that the lesion arises from the hair-forming cells of the dermis.

CALCIFYING epithelioma of Malherbe was first described in 1880 by Malherbe and Chenantais, who stated that it was an epithelioma arising from the sebaceous glands and that it frequently became calcified. Beck in 1933 first likened the appearance and differentiation of the 'tumour' cells to hair-matrix cells. This opinion has subsequently been confirmed by Forbis and Helwig (1961), who first coined the term 'pilomatrixoma', and by McGavron (1965), who further confirmed the hair-matrix-cell origin by electron microscopy and histochemistry.

CLINICAL MATERIAL

The earlier cases in the present series were found from the pathological diagnostic index of the Pathology Department of the Princess Margaret Hospital, Swindon. In recent months increasing awareness has led to cases being more frequently diagnosed clinically and subsequently confirmed by routine microscopy. Twelve cases were recorded between 1962 and 1967, while 22 presented between January, 1968, and January, 1970 (*Table I*).

INCIDENCE

The total number of all skin tumours excised and submitted for histological examination in the period from 1962 to 1970 at the Princess Margaret Hospital, Swindon, was 2151. Thus, the incidence of epithelioma of Malherbe was 1·4 per cent.

The lesion was found in all age-groups between 3 and 96 years, but half of the patients were less than 20 years of age. In 1 patient a lump had been noticed only 2 weeks before presentation, but the majority had had symptoms for some months, and a few for 'many years'. In this series more females than males were affected, the ratio being 1·4 : 1.

Anatomical Distribution.—There was a predilection for the head and neck as the commonest site, but the upper and lower limbs were also involved.

Table I.—PRESENTATION OF CASES

Year	*No. of Cases*
1962	3
1963	2
1964	1
1965	2
1966	2
1967	2
1968	6
1969	15
January, 1970	1
Total	34

Table II.—THE PREOPERATIVE DIAGNOSIS

Preoperative Diagnosis	*No. of Cases*
No diagnosis made	12
Calcifying epithelioma of Malherbe	9
Sebaceous cyst	7
Tuberculous node	2
Histiocytoma	2
Neurofibroma	1
Inclusion dermoid	1
Total	34

The frequent occurrence near the eye noted by other authors (Richardson, Pinzon, Fetterman, Musgrave, and Gaisford, 1965) was confirmed. Size variation in our series was between 0·3 and 5 cm. in diameter.

CLINICAL PRESENTATION

The lesion appears as a firm, rounded, lobulated, occasionally tender nodule attached to skin but not to deep structures (*Fig.* 1); occasionally it may be pigmented. Calcification, if present, may be demonstrated by a plain radiograph, but this can also occur in cysts and other skin tumours. The diagnosis was correctly made in a quarter of the present series, the frequency of other diagnoses being shown in *Table II*.

PATHOLOGICAL FEATURES

The lesion is a firm or hard, encapsulated tumour, with a chalky consistency when cut across. Microscopically, the appearance is characteristic (*Fig.* 2): sheets or clusters of basophilic and 'ghost' or 'shadow' cells are randomly placed in a scanty stroma. Various other cell types are seen, some of which are degenerate, which are presumed to be transitional forms between basophil and ghost cells. Foreign-body giant cells, analogous to those seen around parenchymal uric acid deposits in gout, are seen in the supporting stroma, and areas of calcification, even ossification, may be present.

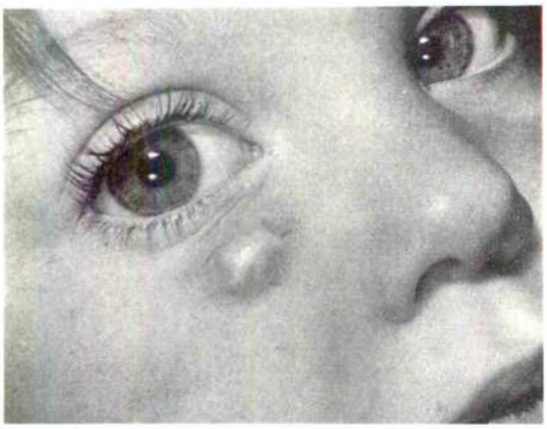

FIG. 1.—Typical lesion on the face of a 3-year-old girl. Note the prominent vessels in the overlying skin.

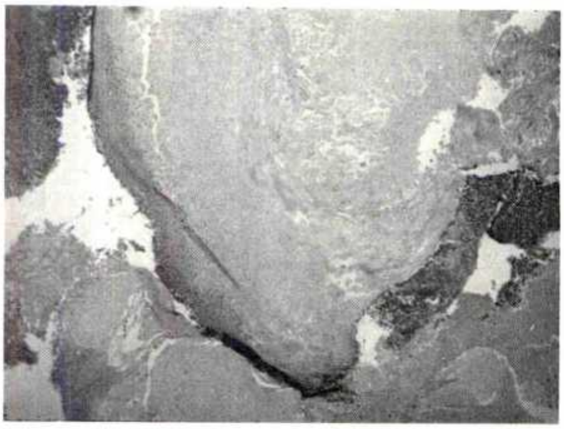

FIG. 2.—Part of a lesion showing darker-stained basal cells and ghost cells in the centre.

Differentiation from a calcified sebaceous cyst can be made by noting the presence of basophil cells, which are absent in calcified sebaceous cysts (Lever and Griesemer, 1949).

It is reasonable to term this unusual tumour a 'hamartoma of the pilogenetic structures'. McGavron (1965) has demonstrated with the electron microscope the cytological similarity between the matrix cells of this lesion and the normal hair-forming cells of the dermis. There is a transition of the matrix cells from basophilic to ghost-cell type. The nucleus : cytoplasm ratio of the basophilic cells decreases and the number of intracellular fibrils increases, forming bundles embedded in a matrix around the now redundant nucleus. The keratin that forms the cortex of normal hair shafts is also formed by aggregations of protofilaments embedded in a matrix. At the zone of keratinization the tumour-matrix cells have a high sulphydril content. This is also a feature of normal hair keratinization.

CONCLUSION

The size of previously reported personal series of epithelioma of Malherbe (Richardson and others, 1965, 55 cases; Henao and Martin, 1967, 38 cases) would seem to confirm its rarity. However, the fact that 22 of the cases in the present series (two-thirds) were seen in the past 2 years suggests that the lesion is more common than was previously supposed and that it is being recognized more frequently.

Although this lesion is most commonly seen in children and teenagers, all age-groups may be affected. There is no evidence that this tumour shows any malignant tendency, and its original name, although colourful, is inaccurate. When pigmentation is present the lesion may be mistaken for a malignant melanoma and widely excised, and if there is any doubt the lesion must be treated as a melanoma. In the absence of this diagnostic problem, simple excision is adequate and curative.

Acknowledgements.—We are indebted to Mr. P. H. Powley, Mr. E. J. C. Wynne, Mr. P. E. Huddy, and Dr. K. D. Crow for permission to include their patients in this series. We also wish to thank Dr. R. Martlew for his advice on the pathology and Mr. R. F. Gerrish of the Photographic Department.

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DAMAGE FROM THE FOGARTY BALLOON CATHETER

BY G. E. MAVOR, M. G. WALKER, D. P. DAHL, AND C. A. S. PEGG
ABERDEEN ROYAL INFIRMARY

SUMMARY

The Fogarty balloon catheter is an instrument which greatly facilitates arterial thrombo-embolectomy. However, it should be used with gentleness and care, particularly in relation to the lower leg vessels. The peroneal artery is particularly susceptible to damage, and arteriovenous fistula formation may result. Even though the incidence of damage is low, when it occurs the morbidity produced may compromise an otherwise satisfactory result.

BALLOON catheters, first introduced by Fogarty, Cranley, Krause, Strasser, and Hafner in 1963, are used routinely in the treatment of cases of acute arterial embolism and thrombosis. At least 3 cases of arterial damage caused by the catheter have been noted in the last 50 cases in which the instrument has been used by the present authors, an incidence of damage of about 6 per cent. Although rare, the nature of the possible damage should be realized as then its production can probably be avoided.

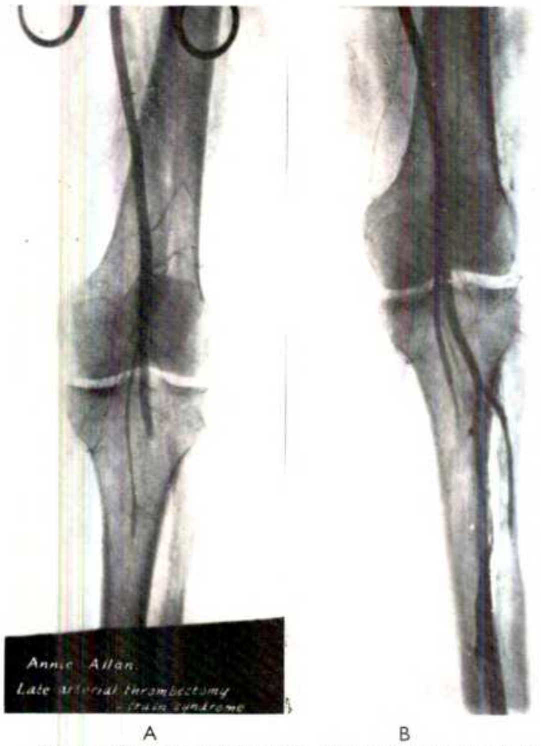

FIG. 1.—Operative arteriography shows (A) occlusion of the distal popliteal artery and (B), after clearance, contrast medium around the peroneal artery at mid-calf level and in the peroneal vein.

CASE REPORTS

Case 1.—A 62-year-old woman who had suffered serious injuries to the abdomen and pelvis in a traffic accident was seen with a 6-day-old ischaemic left foot. This was due to occlusion of the distal popliteal artery, and was presumably thrombotic in origin (*Fig.* 1 A). Clearance was satisfactorily obtained by the use of a balloon catheter. Operative arteriography confirmed this, but also showed that the peroneal artery had been damaged at mid-calf level and contrast medium was present in the peroneal vein (*Fig.* 1 B). The recovery of the leg was uneventful.

Case 2.—A 74-year-old woman who had previously been in good health apart from angina developed a right popliteal artery embolus 7 days after undergoing cholecystectomy (*Fig.* 2 A). Embolectomy was carried out and operative arteriograms showed good clearance of the popliteal artery. The anterior tibial artery was visualized, but it was stenosed at its origin (*Fig.* 2 C). The posterior tibial artery was not visualized, and the presence of contrast medium in the tissues at mid-calf level indicated damage to the peroneal artery (*Fig.* 2 B). Rapid clearance of the contrast medium from the tissues suggested that this was probably in part fistulous (*Fig.* 2 C). Distal limb ischaemia persisted, and had not the patient died 4 days later of a cerebrovascular accident, which was probably embolic in aetiology, amputation would have been necessary.

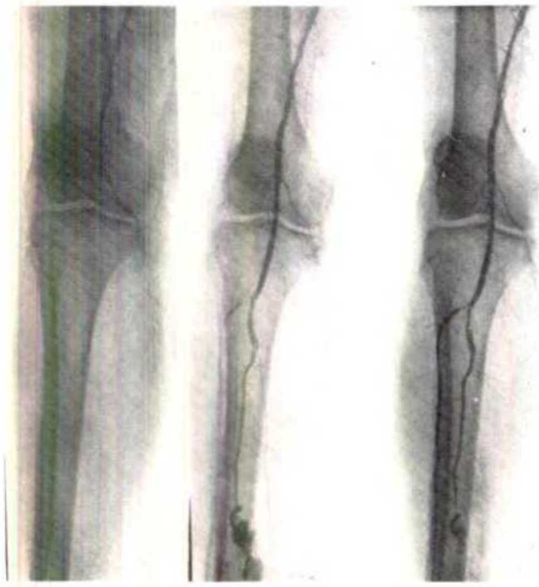

FIG. 2.—Operative arteriography shows occlusion of the popliteal artery from about joint line level (A). After clearance the posterior tibial artery is not visualized (B, C), and the anterior tibial artery is stenosed at its origin (C). The peroneal artery is perforated at mid-calf level (B), while clearance of the contrast medium is almost complete (C).

Case 3.—A 53-year-old man was admitted to hospital with a 3-week history of bilateral calf exercise pain of sudden onset, together with further complaints of coldness and discoloration of both feet. The patient was a beachcomber and the onset of pain had followed 4 miles of walking on the beaches. Three days before admission both feet had become numb and painful.

Arteriography revealed bilateral distal popliteal artery thrombosis, which was probably traumatic in aetiology (*Fig.* 3). Both popliteal arteries were exposed, opened, cleared using balloon catheters, and closed using autogenous vein-patch grafts. The right foot recovered quickly, the posterior tibial pulse being easily located. The left forefoot remained ischaemic, all the toes being anaesthetic and discoloured. No peripheral pulses were noted. Postoperative arteriography carried out 4 days after surgery showed patent arteries on the right side, but on the left side an arteriovenous fistula was present (*Fig.* 4). Serial films showed that this involved the peroneal artery and vein at about mid-calf level (*Fig.* 5). Subsequent auscultation revealed a loud bruit posteriorly at mid-calf level. Through a midline posterior calf approach the peroneal artery and vein were exposed. The fistula was located just at the origin of the nutrient artery to the fibula (*Fig.* 6). The vein was ligated and divided, and the peroneal artery was repaired. Subsequently, the forefoot recovered.

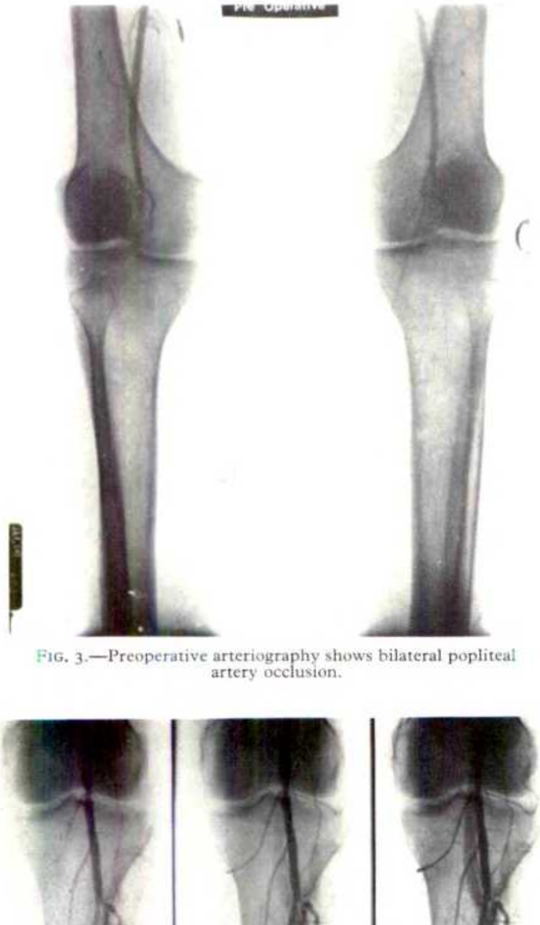

FIG. 3.—Preoperative arteriography shows bilateral popliteal artery occlusion.

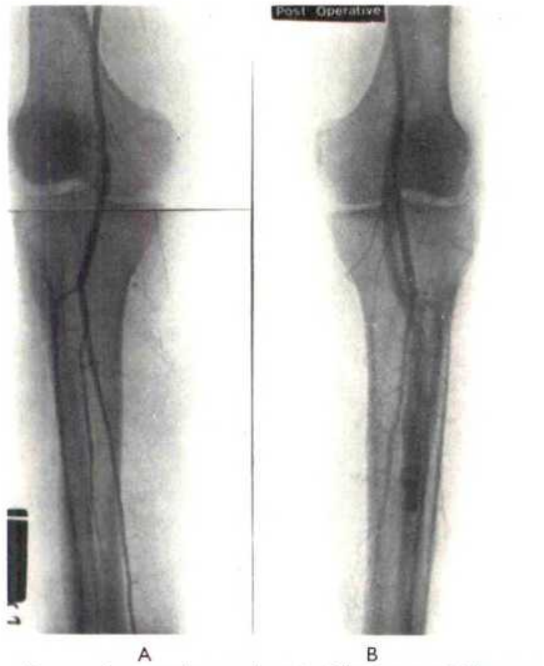

FIG. 4. —Postoperative arteriography following arterial thrombectomy and patch-graft repairs shows a satisfactory result on the right side (A). On the left side (B), there is an arteriovenous fistula situated at about mid-calf level.

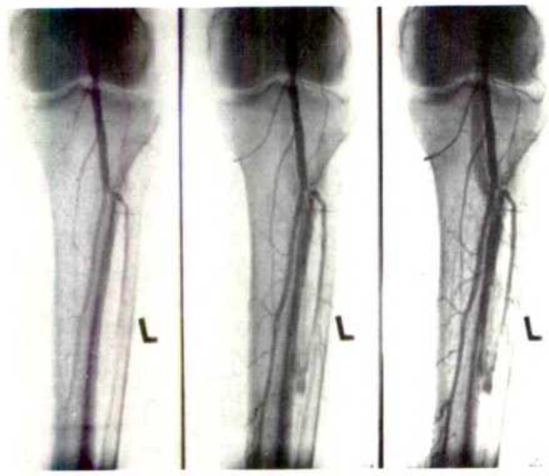

FIG. 5.—Serial arteriography shows a fistula involving the peroneal artery and vein.

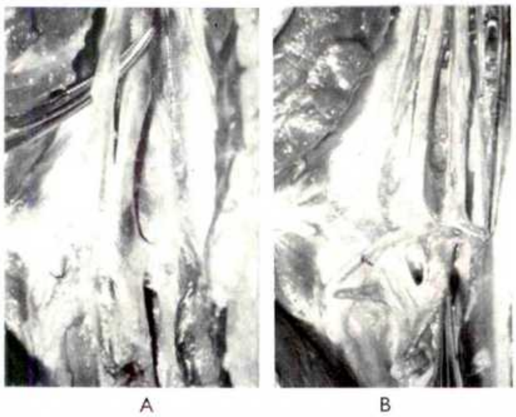

FIG. 6.—A, The peroneal artery lies over the artery forceps. The peroneal vein is considerably enlarged at the site of the fistula where it overlies and is adherent to the artery. B, Further dissection with the vein pulled medially shows the fistula opened. The nutrient artery to the fibula can be identified by the small linen stitch.

DISCUSSION

As far as can be ascertained there are only a few reports of complications arising from the use of intra-arterial balloon catheters (Krause, Cranley, Strasser, Hafner, and Fogarty, 1966; Hogg and MacDougall, 1967; Stoney, Ehrenfeld, and Wylie, 1968). Indeed it is not known what the incidence is of complications such as intimal damage or dissection with subsequent rethrombosis, or rupture of the posterior tibial or peroneal arteries. This may be because it is not routine practice to employ operative arteriography to ensure peripheral clearance during arterial embolectomy or thrombectomy. Without arteriography there is no way of judging whether in some cases damage has occurred, and clinical failures are generally, though perhaps not accurately, ascribed to failure to remove all thrombus. Where arteriography is in routine use in arterial embolectomy and thrombectomy, as in this clinic (Mavor, Walker, and Dhall, 1972), evidence has been obtained that damage as reported in the present 3 cases is possible.

It may be argued that damage is often clinically without significance, but this is uncertain. Much depends on the nature of the damage and, in the case of the lower leg, on the state of the other arteries. The type of damage which has been described includes a small false aneurysm of the profunda femoris (Stoney and others, 1968) and the avulsion of small intimal plaques (Krause and others, 1966), presumably without clinical effect. However, it would seem more certain that where the peroneal and posterior tibial arteries are ruptured or perforated there may be significant morbidity. If both are damaged the end-result of embolectomy will probably be amputation as rethrombosis is very likely (Hogg and MacDougall, 1967), while if one is damaged and both the other lower leg arteries are thrombosed or compromised by disease the same result is likely (*Case* 2).

The peroneal artery is apparently most susceptible to damage by balloon catheters, as in the 5 cases of damage to the lower leg arteries which have been reported (including the present 3), all involved the peroneal artery, although in 1 case the posterior tibial artery was also ruptured (Hogg and MacDougall, 1967). Peroneal arteriovenous fistula formation has not previously been reported, but this appears to be the nature of the damage in 2 of the present cases, and probably also in the third and in 1 of the cases reported by Hogg and MacDougall (1967). In 3 of the 4 cases serious morbidity resulted, although in 1 case (*Case* 3) repair of the fistula brought about a satisfactory result.

The position of possible peroneal damage and fistula formation is where the large nutrient artery to the fibula arises from the peroneal artery at about mid-calf level (*Fig*. 6). Undue pushing with the catheter if it sticks about mid-calf level may easily perforate the artery and simultaneously damage the neighbouring vein. It would appear prudent, therefore, to resist any tendency to attempt to push the balloon catheter if it feels obstructed and is at mid-calf level on the understanding that it may well be half-way down the peroneal artery.

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ORBITAL HYDATID DISEASE IN IRAQ

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SUMMARY

Twenty-one patients with orbital hydatid disease are presented, constituting 19·8 per cent of the cases with unilateral exophthalmos seen from 1959 to 1971. The presenting features, investigations, and type of treatment are discussed.

THE literature contains a number of specialist studies on orbital tumours, but very little is recorded about orbital hydatid cysts, and it is of interest to examine the problem as seen by the general surgeon.

Echinococcosis can involve almost every organ or tissue in the body via the portal and the systemic circulations, but among the uncommon sites of infestation, even in the densely endemic areas, is the orbit. Lidgett (1956) reported 2 cases, making the total number of cases of orbital hydatid recorded in Australia 12. McClatchie and Manku (1967) treated 3 patients with orbital hydatid cysts in Kenya, and Jain and Rangbulla (1967) reported 1 case in India. From 1959 to 1971 the author has treated 21 patients with hydatid cyst of the orbit, of whom 13 have already been reported (Talib, 1968).

INCIDENCE

Orbital hydatid is uncommon and the frequency with which it occurs is difficult to estimate.

During the past 12 years 106 patients with unilateral exophthalmos have been admitted to the Republican Teaching Hospital, Baghdad (*Table I*). Of these, 21 patients (19·8 per cent) were proved to have hydatid cysts. This percentage makes hydatid cyst the commonest 'tumour' that involves the orbit in this series. By contrast, orbital hydatid cyst is rare in Western countries.

The age of the patients ranged between 6 and 55 years, both sexes being equally affected. There was a preponderance of infection in the left orbit over the right in the ratio of 2 : 1. This variation may be explained anatomically by the fact that the left common carotid artery arises directly from the 'summit' of the arch of the aorta.

CLINICAL FEATURES

Hydatid cyst is a slowly growing lesion and unless there are sudden changes in its morphological behaviour it may remain dormant for a long time; this is not so in the case of orbital involvement, as the orbit is conical in shape with fixed dimensions and constant capacity. Therefore, any space-occupying lesion may displace the eyeball, hinder ocular movements, and, if the cyst is located near the apex of the muscular cone, interfere with the neurovascular mechanism, thus giving rise to visual disturbances, chemosis, and oedema.

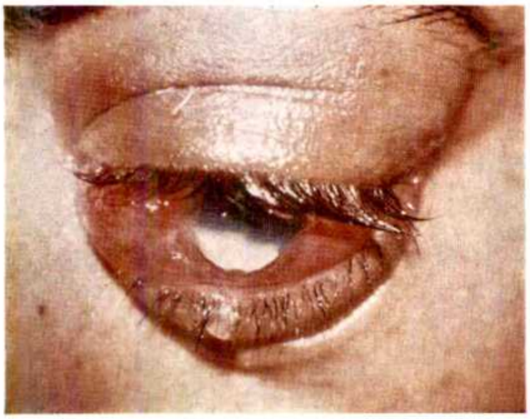


FIG. 1.—Orbital hydatid presenting with chemosis, lid oedema, and hypopyon.

Table I.—THE CAUSE OF UNILATERAL EXOPHTHALMOS IN 106 CASES ADMITTED TO THE REPUBLICAN TEACHING HOSPITAL, BAGHDAD, BETWEEN 1959 AND 1971

Cause of Exophthalmos	*No. of Cases*	*Percentage*
Conal Lesions		
Hydatid cyst	21	19·81
Vascular	4	3·77
Nerve	7	6·60
Lacrimal gland	5	4·72
Non-specific granuloma	4	3·77
Meningeal	2	1·89
Malignant	24	22·64
Encroaching Lesions		
Antral	6	5·66
Bony	3	2·83
Skin	14	13·21
Distant Metastasis		
Bronchogenic carcinoma	1	0·94
Undetermined	15	14·15
Total	106	

Unilateral proptosis was the main presenting feature in 18 patients. The average duration of the protrusion of the eye was between 5 months and 2 years. In 17 patients it was static for some time before the patient sought advice because of asymmetry or exophthalmos; only in 1 case was the proptosis variable.

One patient presented with chemosis, lid oedema, hypopyon, and rapid visual deterioration (*Fig.* 1). The remaining 2 patients presented with progressive exophthalmos and severe conjunctivitis (*Fig.* 2).

Diplopia was not a feature in spite of some degree of limitation of ocular movements.

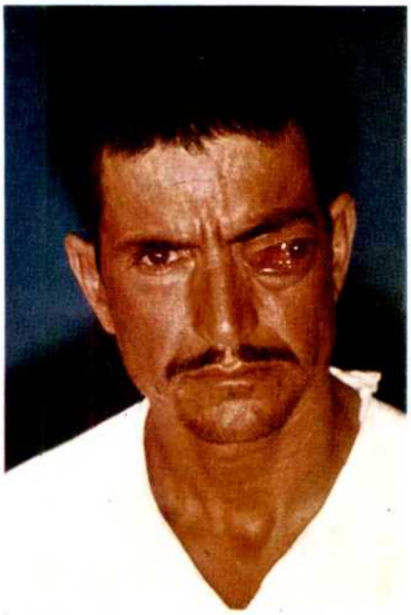


FIG. 2.—Patient with an orbital hydatid cyst showing severe conjunctivitis.

Patients with uncomplicated lesions had an almost normal visual acuity (*Fig.* 3), whereas those with complications such as infection and recurrence showed diminution or complete loss of vision (*Fig.* 4).

Local pain and headache occurred only in cases of progressive protrusion and infection.

DIAGNOSIS

It is extremely difficult to diagnose that the cause of the unilateral exophthalmos is a hydatid cyst of the orbit in the absence of other cysts elsewhere in the body. However, local physical examination may shed some light on the diagnosis if the cyst is palpable behind the medial or lateral canthus as a tense, well-defined swelling or when it is subconjunctival. An ear, nose, and throat examination should routinely be carried out in these patients to exclude antral lesions.

Radiographs of the orbit and optic foramina rarely show a soft-tissue shadow or a fine rim of calcification. Carotid angiography should be restricted to lesions which are suspected to be intracranial. Retro-orbital oxygen insufflation or lipiodol injection have not been used, as we think that any injudicious needling in the area may harbour the risk of rupture and dissemination. A chest radiograph is important to exclude the possibility of pulmonary hydatid disease or other thoracic lesions.

The Casoni intradermal test is unreliable, and a high eosinophil count may be due to helminthiasis which is endemic in Iraq.

In spite of elaborate laboratory and radiological investigations, none of the patients showed evidence of hydatid disease elsewhere in the body on admission. However, 1 patient returned later with a pulmonary hydatid cyst, and another came back after undergoing two laparotomies elsewhere for an hepatic hydatid cyst; a third patient developed paraplegia, presumably due to cord compression, diagnosed as a case of acute transverse myelitis although no investigations were carried out.

From these facts one reluctantly but inevitably admits that no diagnosis can be made with certainty before surgical exploration.

Bilateral exophthalmos can be seen as a manifesta- of metabolic, systemic, and neoplastic diseases, but it has not been noted in cases of hydatid disease either in this or in other series; this is interesting and needs more explanation.

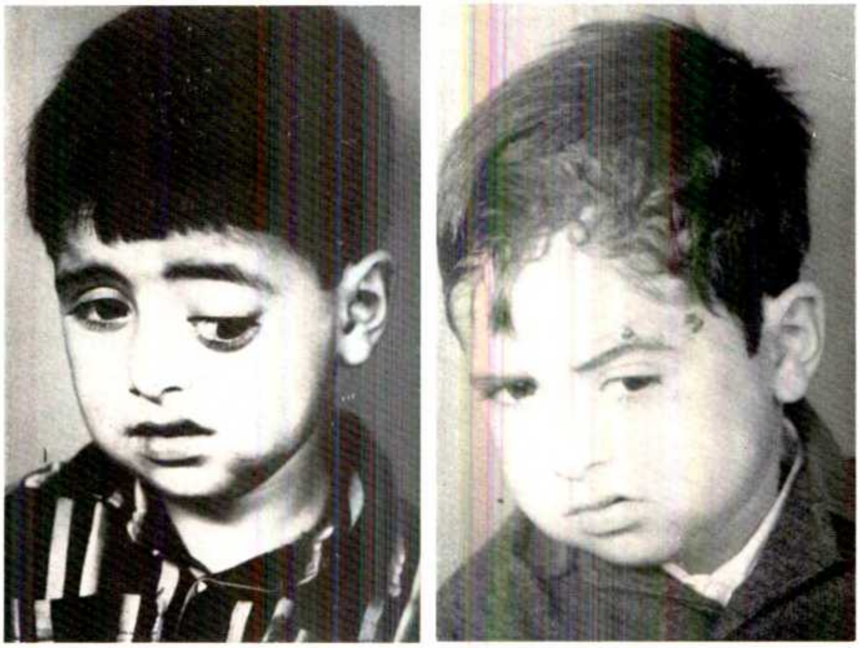
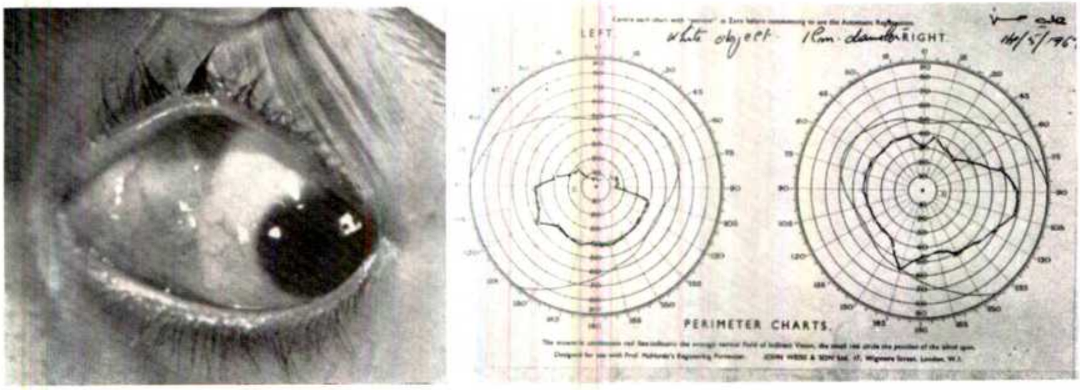

A B

FIG. 3.—A, Child with an uncomplicated hydatid cyst of the orbit. B, Same patient 1 month after surgery



A B

FIG. 4.—A, Recurrence with a subconjunctival hydatid cyst. B, Perimetric study of the same patient showing marked restriction of the visual field on the left side.

The commonest sites of orbital hydatid are the superolateral and superomedial angles of the orbit; no hydatid cyst has been seen in the floor of the orbit, although Handousa (1947) reported 1 such case.

TREATMENT

If left for some time an orbital hydatid sooner or later will exert untoward effects on the eyeball. Provided the lesion is within the orbit it is our policy to subject every patient with unilateral exophthalmos to surgical decompression. Earlier in this series 2 patients underwent the Naffziger technique (Naffziger, 1954); the remaining patients have all been treated by a modified Dickson Wright anterolateral decompression. The latter approach gives an adequate exposure and can be extended medially should the need arise.

Partial tarsorrhaphy was used routinely either immediately after admission as an emergency measure against severe conjunctivitis or impending corneal ulceration, or during operation prior to decompression.

On 3 occasions an attempt was made to excise the ectocyst, which is a fairly thin fibrous capsule; this was not found to improve the results, and, furthermore, it is a time-consuming procedure and may endanger various delicate structures adherent to the ectocyst. Following evacuation, the cavity is wiped with 5 per cent formaldehyde solution.

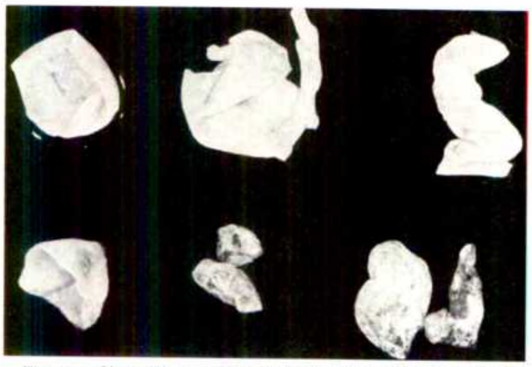


FIG. 5.—Six solitary orbital hydatid cysts. The two on the lower right represent very thin endocysts with their ectocysts; the rest are endocysts of variable thickness.

In cases of short duration the endocyst is very thin and difficult to separate from the ectocyst, while in those of long duration it is thick and can be extruded easily. In 19 cases solitary cysts were found (*Fig.* 5), and in both of the other 2 cases there were two daughter cysts.

On no occasion in this series was enucleation of the eyeball performed, even when it was severely inflamed, as the inflammation, surprisingly, subsided eventually.

Regarding postoperative complications, 6 patients developed ptosis; this corrected itself in due course, only 1 patient requiring a fascial sling. Temporary partial trismus occurred in 1 case, probably caused by fibrosis of the temporalis muscle as a result of its stripping from the temporal bone. Another patient developed a persistent discharging sinus due to erosion of the bone, necessitating curettage.

Following operation the eye remains swollen for some time owing to operative trauma and oedema, but the swelling gradually subsides.

DISCUSSION

Iraq is an endemic area for hydatid disease; unlike other such areas the incidence of orbital involvement is much higher in Iraq.

All patients present with unilateral exophthalmos varying from 6 months to 2 years in duration. The exophthalmos in most of the cases is static, but rarely it is progressive when the cyst is infected. Other clinical features include chemosis, severe conjunctivitis, deterioration of vision, and limitation of ocular movements.

In spite of all the clinical, laboratory, and radiological investigations it is extremely difficult to diagnose the condition, which can only be confirmed during surgery.

Patients with unilateral exophthalmos should be given the chance of decompression before the occurrence of serious complications which may carry the risk of damaging the eyeball.

Acknowledgements.—I wish to thank my colleagues in the Department of Ophthalmology, the Republican Teaching Hospital, Baghdad, and the Ophthalmological Staff at the Hospital for Eye Diseases for referring these patients to me.

I am also deeply grateful to Professor Harding Rains for his valuable comments and criticism.

Finally, I offer my gratitude to my senior house-surgeon, Dr. Garabet Awanes, for looking after my patients and collecting the necessary data for this work.

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PROXIMAL JEJUNAL AND DISTAL ILEAL EXTRINSIC INNERVATION IN THE RABBIT AND DOG

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SUMMARY

The varying patterns of motor behaviour of isolated and interposed jejunal and ileal segments in the rabbit and the dog previously reported (Jenkins and Macleod, 1970) were examined by selective denervation techniques. One hundred and twenty-three paired experiments were conducted on rabbits and 55 similar experiments were performed on dogs.

Length-matched paired segments of proximal jejunum and distal ileum were isolated and filled with saline at a constant rate. Segmental resistance to filling was regarded as an index of tone. The influence of vagotomy and of sympathectomy on the tone of the segments was studied in segments supplied by one or by two vessels.

Vagotomy caused a decrease in tone in the proximal jejunal segments, while sympathectomy had little effect. In segments of distal ileum sympathectomy

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resulted in segments behaving in a similar fashion, while vagotomy had an unpredictable effect on tone.

The results suggest a uniform distribution of the vagus to the whole length of the small bowel in the rabbit and the dog, serving to maintain the tone of the bowel. It is deduced that sympathetic supply to the proximal jejunum is absent in these animals and is distributed to the distal ileum only in an irregular fashion.

The relevance of these observations to the clinical use of interposed small-bowel segments is considered.

ISOLATED, interposed, antiperistaltic segments were initially used in the treatment of the dumping syndrome by Henley (1952), and others since then have utilized the technique to include the management of intestinal hurry (Rutledge, 1964; Poth, 1969). Surgical experience indicates that jejunal segments are more predictable in behaviour and safer in use than segments of distal ileum, but there has been no satisfactory explanation of this phenomenon, nor has any simple rule emerged to relate the length of the segment to its proposed therapeutic function.

Earlier work by the present authors (Jenkins and Macleod, 1970) indicated that the behaviour of an isolated and interposed segment of the small intestine in the rabbit is influenced both by the site of the segment and by the number of vessels supplying it. Interposed segments of ileum supplied by a single vessel behaved in an unpredictable manner irrespective of their polarity, and some caused obstruction out of all proportion to their short lengths. Similar findings have been reported by Youmans (1949) and Torbey (1960) in the dog and by Poth (1969) in man.

Motility and tone of the small intestine have been shown to be influenced by intestinal hormones (Fishlock, 1966; Misiewicz, Waller, and Durrell, 1966; Bennett, Misiewicz, and Waller, 1967; Murrell and Deller, 1967; Bennett, 1968), anoxia (Kosterlitz and Lees, 1964; Nylander and Wikstrom, 1968), autonomic nerve distribution (Puestow, 1932; Celender, 1959; Kerwenter, 1965; Bennett and Whitney, 1966; Burnstock, Campbell, and Rand, 1966; Smith, 1970), and the intrinsic activity of the smooth muscle (Prosser and Rafferty, 1956; Baker, 1969).

Of those mechanisms which modify intestinal tone and motility, that which is most affected by segment isolation and interposition and by changes in the vascular supply is the extrinsic innervation. It was felt that a closer study of this aspect might lead to a rational selection of segments for use in surgical procedures.

The present experiments were designed to demonstrate in the proximal jejunum and distal ileum of the rabbit and the dog the relationships between tone and extrinsic segmental innervation and blood-supply.

MATERIALS AND METHODS

In each experiment on a rabbit or a dog anaesthesia was induced with intravenous Nembutal, 24 mg. per kg., and was maintained with nitrous oxide, 1·5 litres per minute, halothane, 0·5 per cent, and oxygen, 0·75 litre per minute open circuit.

Rabbits.—

Segmental Intraluminal Pressures.—Seventy-one paired experiments were conducted on the distal ileum and 52 similar experiments were conducted on the proximal jejunum in 76 rabbits. In each experiment two adjacent intestinal segments of the same length (±0·5 cm.) supplied by one or by two vessels were selected and isolated. Segments were measured in the relaxed state, the minimum length each of a pair being 5 cm. and the maximum 10 cm. Owing to individual variations in vasculature, it was not possible for all the segments to be of the same length.

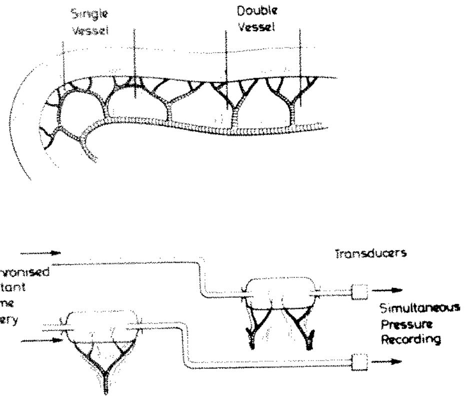
Single Vessel
Double Vessel
Synchronised Constant Volume Delivery
Transducers
Simultaneous Pressure Recording

FIG. 1.—The experimental model. Length-matched segments supplied by one and two vessels were selected and pressures recorded as filling progressed.

Portex plastic cannulas, 4·7 mm. in diameter, were inserted into each end of the isolated segments and tied in place. The margins of the longitudinal abdominal incision were supported and the open abdominal cavity was filled with 0·9 per cent saline at 37° C. to maintain a constant environment. The segments were filled with isotonic saline at 37° C. until a mean intraluminal pressure of atmospheric +5 mm. Hg was obtained, and basal recordings of segmental activity were made.

Saline was then pumped into the length-matched paired segments simultaneously at a rate of 7·5 ml. per minute by a double-barrelled constant-delivery infusion pump, and the pressures within the segments were continuously monitored via 0·9 per cent saline-filled 4·7-mm. Portex tubing connected to a Sanborn transducer No. 267BC and recorded on moving paper (*Fig.* 1). Pressure recordings were stopped and final pressures noted when the pressure in one segment had reached a value close to 20 mm. Hg. The filling time taken to reach the minimum pressure in each of the comparable groups was also noted.

The same procedure was repeated in neurologically intact, in vagotomized, and in sympathectomized length-matched paired segments from proximal jejunum and distal ileum.

Experimental Groups.—

A. Distal ileum:—

1. Normally innervated: 32 paired experiments. Length-matched adjacent segments supplied by one and by two vessels.

2. Vagotomy: 31 paired experiments. Complete vagotomy was achieved by division of the oesophagus and accompanying vagi 1 cm. above the cardio-oesophageal junction.
3. Sympathectomy: 18 paired experiments. Complete sympathectomy was achieved by division of the spinal cord above the level of the first thoracic vertebra.

B. Proximal jejunum:—
1. Normally innervated: 14 paired experiments.
2. Vagotomy: 19 paired experiments.
3. Sympathectomy: 19 paired experiments.

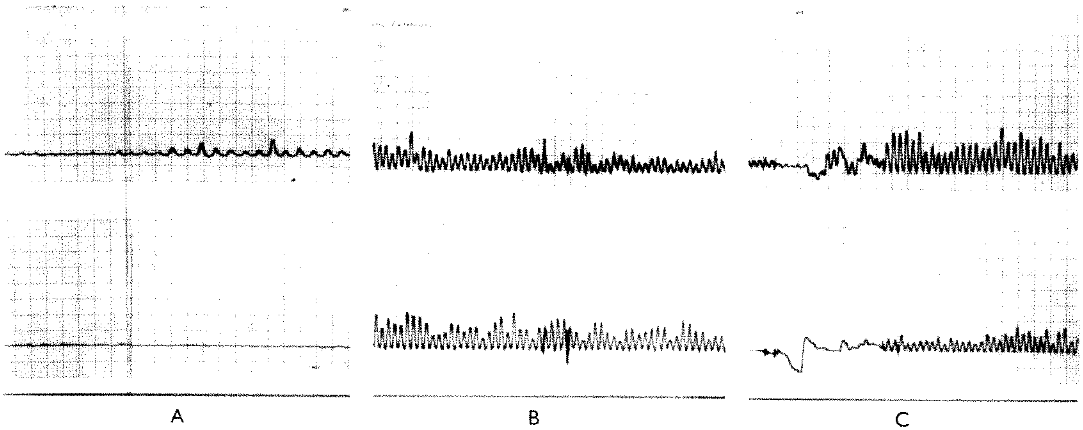

FIG. 2.—A, Pressure recordings from double-vessel (upper) and single-vessel segments (lower) of rabbit jejunum at atmospheric pressure after vagotomy showing segmental activity. B, Recordings from double-vessel (upper) and single-vessel (lower) segments of rabbit jejunum at atmospheric pressure after sympathectomy. C, Recordings of normally innervated double-vessel (upper) and single-vessel (lower) segments of rabbit proximal jejunum.

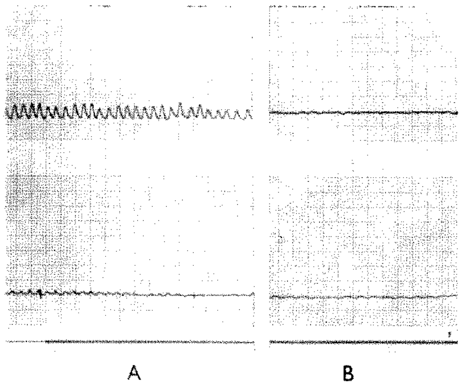

FIG. 3.—A, Recordings of double-vessel (upper) and single-vessel (lower) segment contractions in the normally innervated distal ileum of a rabbit. B, Recordings of double-vessel (upper) and single-vessel (lower) segment contractions in the distal ileum of a rabbit after vagotomy.

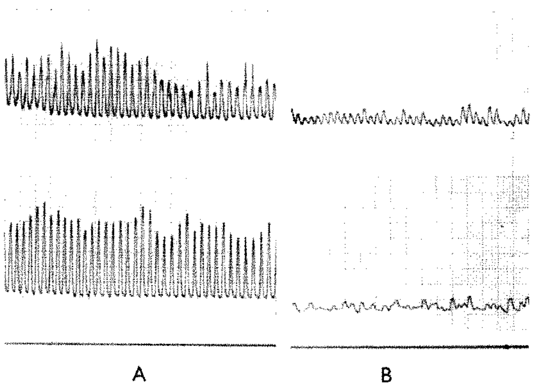

FIG. 4.—Recordings of double-vessel (upper) and single-vessel (lower) segment contractions in the distal ileum of a rabbit after sympathectomy, showing the variation in response. All segments were of the same length (8 cm.).

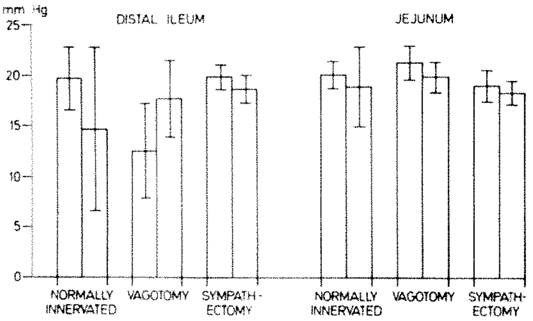

FIG. 5.—Mean values of pressure reached in the distal ileum and jejunum of the rabbit. Standard deviations are also shown Single-vessel segment values are on the left in each pair.

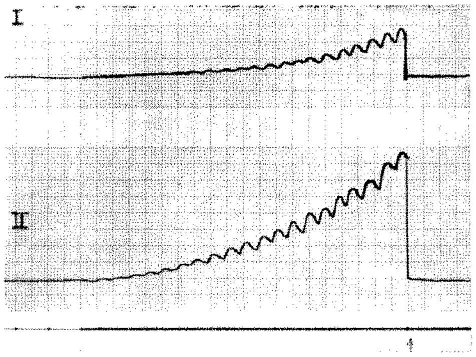

FIG. 6.—Typical pressure recordings made during simultaneous length-matched single-vessel (upper) and double-vessel (lower) segment filling in the distal ileum of the rabbit, demonstrating the difference in response which is frequently seen.

Dogs.—Fifty-five paired acute experiments were conducted on 7 dogs. The same experimental methods were adopted as in the rabbits, but in view of the greater musculature of the small intestine of the dog the rate of filling was increased to 50 ml. per minute and filling was continued until the pressure in one segment was approximately 40 mm. Hg.

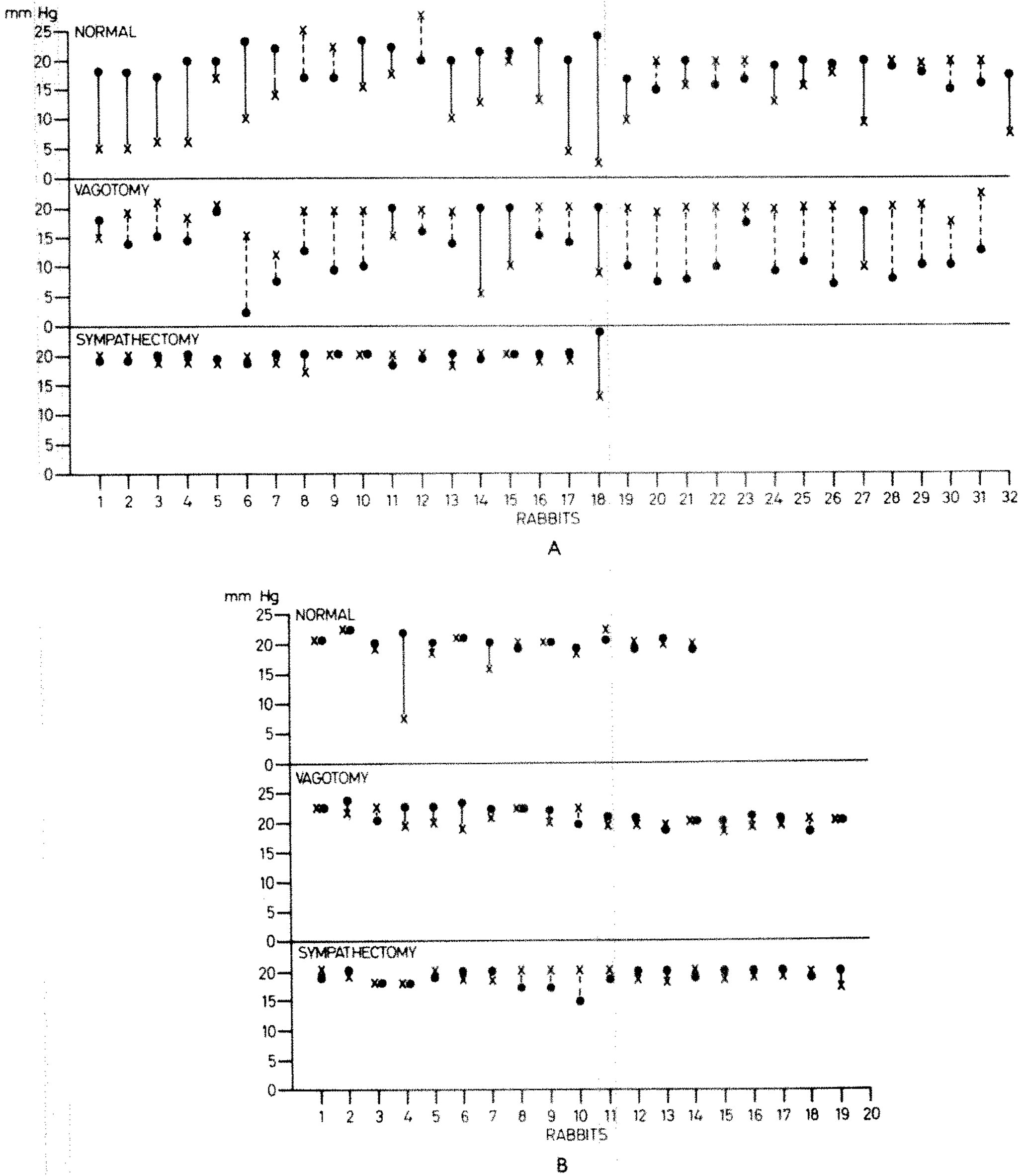

Fig. 7.—Paired pressure recordings in normally innervated and selectively denervated distal ileum (A) and jejunum (B) in the rabbit. The points recorded are those at the same point on the x-axis when one or both pressures had reached a value close to 20 mm. Hg (*see* arrow on *Fig.* 6). ×, Double-vessel segment; ●, Single-vessel segment.

Experimental Groups.—

1. Distal ileum: 30 paired experiments.
2. Jejunum: 25 paired experiments.

Selective denervation experiments were not made on dogs.

RESULTS

1. **Unstimulated Motility.**—Nineteen of the 32 single-vessel segments of normally innervated rabbit distal ileum visibly contracted in varying degrees of isolation. High tone in these segments was always demonstrated by the resistance to filling technique, but high tone was also seen in 2 segments which did not visibly contract on isolation. Single-vessel segment contraction was observed in 24 of the 30 segments of dog distal ileum. All single-vessel segments of the dog which contracted on isolation exhibited high tone of varying degrees. Only 6 of the 30 single-vessel segments of dog distal ileum did

not contract and none of these exhibited high tone. Contraction following isolation was not observed in any of the double-vessel segments of distal ileum or in any of the segments of proximal jejunum in either animal.

Recordings taken with rabbit segments filled with 0·9 per cent saline at atmospheric pressure +5 mm. Hg indicated that extrinsic innervation modifies the activity of the gut. In the proximal jejunum vagotomy decreased the amplitude of type II segmental contraction, while sympathectomy had no effect on amplitude or wave-form (*Fig.* 2). In the distal ileum vagotomy similarly decreased segmental contraction (*Fig.* 3), but sympathectomy caused considerable variation in amplitude and markedly increased it in 4 of the 18 double-vessel segments (*Fig.* 4).

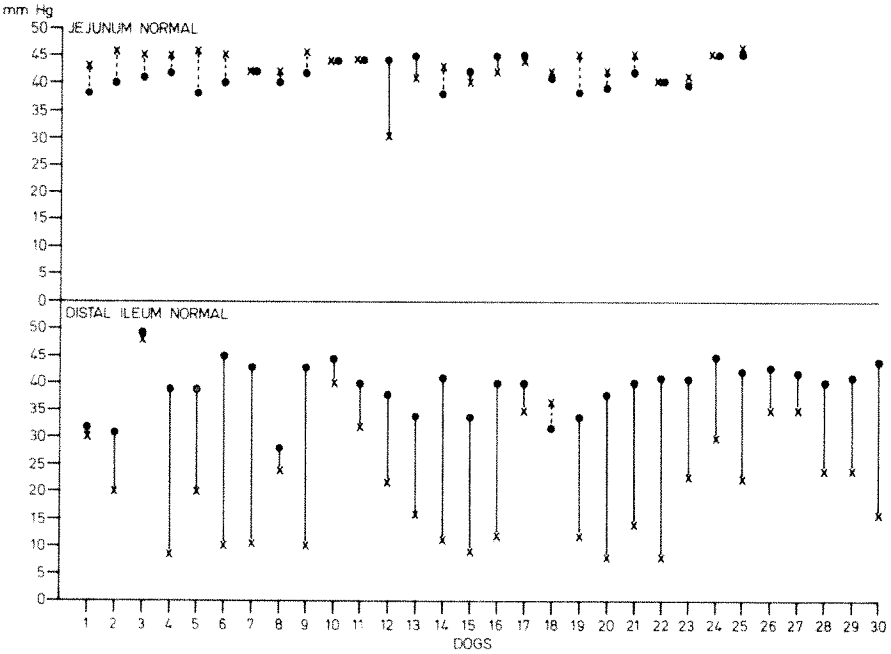

FIG. 8.—Representation of individual pressure values in single-vessel and double-vessel segments in the jejunum and distal ileum of the dog, demonstrating the comparatively high tone in most single-vessel segments of distal ileum. The points recorded are those at the same point on the x-axis when one or both pressures had reached a value close to 50 mm. Hg. ×, Double-vessel segment; ●, Single-vessel segment.

2. **Response to Filling.**—

a. Pressure Relationships.—In the normally innervated distal ileum of the rabbit the pressures reached during simultaneous filling were significantly greater in single-vessel segments than those reached in double-vessel segments ($P < 0·001$) (*Fig.* 5).

In the vagotomized group pressures were significantly greater in double-vessel segments ($P < 0·01$). Sympathectomy had no effect on comparative pressures in single- and double-vessel segments of the distal ileum.

The wide variations in tone in normal and vagotomized single- and double-vessel segments of distal ileum are shown by the high standard deviations in these groups.

In the proximal jejunal groups comparative pressures were similar and there was a low variation in response to filling. *Fig.* 6 shows typical recordings in the normally innervated distal ileum of the rabbit during segmental filling.

Variations in behaviour in terms of tone which are shown collectively in *Fig.* 6 are individually demonstrated in *Fig.* 7, and the differences between the normally innervated and the vagotomized single- and double-vessel segments of distal ileum and the other four groups are clearly seen.

In the dog, as in the rabbit, the pressures reached in the normally innervated distal ileum during simultaneous filling were significantly greater in single-vessel segments than those reached in double-vessel segments ($P < 0·001$), but in the normally innervated proximal jejunum the values were not significantly different (*Fig.* 8).

b. Filling Times.—Filling time varies with segment length as well as with segment tone.

The time necessary to reach a standard pressure (5 mm. Hg in the rabbit and 8 mm. Hg in the dog) was measured and the effect of the length of the segment (L) was removed by considering this time (T) per unit length of segment (T/L). In the rabbit there was no significant difference in filling times between all normally innervated single- and double-vessel segments. Filling time following vagotomy in single-vessel segments of proximal jejunum is significantly greater than that in normally innervated single-vessel segments ($P < 0·01$), but there is no difference in times between sympathectomized and normally innervated single-vessel segments. The same significance values are found comparing double-vessel segments of proximal jejunum. Following vagotomy in the distal ileum, both single- and double-vessel segments relaxed and in both groups filling times were significantly greater than in the normally innervated groups ($P < 0·02$ for single-vessel segments; $P < 0·1$ for double-vessel segments).

Sympathectomy caused an increase in tone, shown by a decrease in filling time, in both distal ileum groups. The filling time was significantly less than that of the normally innervated groups ($P<0{\cdot}02$ in both groups compared with normal) (*Fig.* 9).

In the dog, contrary to the findings in the rabbit, there was a significantly increased filling time in single-vessel segments of distal ileum when compared with single-vessel segments of jejunum ($P<0{\cdot}005$). This difference was also seen between double-vessel segments of jejunum and ileum ($P<0{\cdot}01$) (*Fig.* 10).

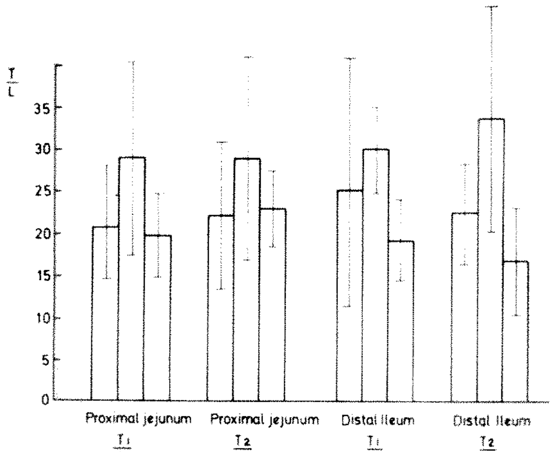

FIG. 9.—Filling times for the proximal jejunum and distal ileum of the rabbit to reach a pressure of 5 mm. Hg in single-vessel (T_1/L) and double-vessel (T_2/L) segments adjusted for length. The values for normally innervated segments are shown on the left, those after vagotomy in the centre, and those after sympathectomy on the right of each group of columns.

DISCUSSION

We believe our results can be fully explained by variations in the distribution of the autonomic system: if the parasympathetic and sympathetic systems were equally distributed to all parts of the gut, division of one or the other would be likely to have a similar effect in all regions.

Vagotomy decreased tone in both single- and double-vessel segments of proximal jejunum and also reduced motility. This might have been due either to the effect of the hypothetical extrinsic sympathetic system or to the intrinsic autonomic system. Since the intrinsic parasympathetic system is known to predominate over the intrinsic sympathetic system of the jejunum and a fall in tone was recorded following vagotomy, the vagus clearly exerted a considerable influence on tone. If extrinsic sympathetic innervation exists a reduction in filling time following sympathectomy owing to the unimpeded action of the vagus might be expected. This was not recorded. One can conclude therefore that there is no extrinsic sympathetic supply to the jejunum in the rabbit. This finding corroborates that of Kerwenter (1965) in the cat.

Our results in the distal ileum are markedly different. Unlike the proximal jejunum in which segmental behaviour was independent of differences in vascular supply, distal ileal segments exhibited marked variations in tone dependent on the number of vessels supplying them. The effect of sympathectomy was to decrease filling time in all distal ileal segments, indicating an increase in tone, and also to abolish the random behaviour, shown by variations in final pressures, of the single-vessel segments, indicating that the unimpeded vagal supply stabilized segmental tone. The greater tone in the vagotomized double-vessel segments of distal ileum shown by significantly greater group pressures over the single-vessel segments is unexplained.

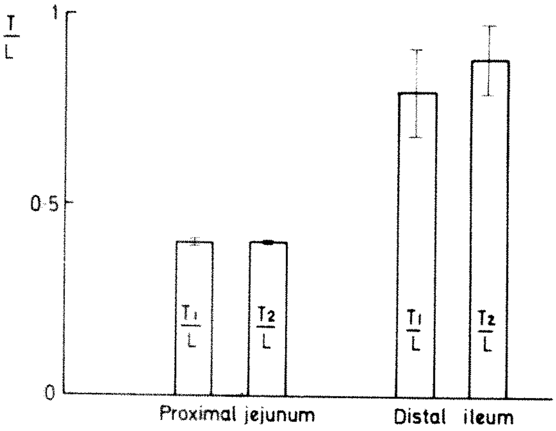

FIG. 10.—Filling times for the proximal jejunum and distal ileum of the dog to reach a pressure of 8 mm. Hg in single-vessel (T_1/L) and double-vessel (T_2/L) segments adjusted for length.

Segments of distal ileum of the dog appear to be dependent on the vascular supply in a manner similar to that of the rabbit. Unlike the rabbit, however, where tone, in terms of filling time, is the same in both parts of the small bowel, the tone in the distal ileum is greater than that in the proximal jejunum.

It is suggested that the vagus is regularly distributed to all parts of the distal ileum with the major branches of the superior mesenteric artery, but that the sympathetic supply is haphazardly distributed with some vessels. If by selecting a segment supplied by a single vessel one is isolating that segment from the sympathetic supply, a vagal effect, i.e., high tone, is to be expected, and is seen in our experiments. If, however, one selects segments supplied by two vessels, one or both of which are accompanied by a branch of the extrinsic sympathetic system, the tone is expected to be low. Some single-vessel segments will obviously be those to which the parent vessel brings sympathetic innervation.

From the results we conclude that while the vagus is supplied to all parts of the small intestine in a regular and orderly manner with each main branch of the superior mesenteric artery, the sympathetic supply is only distributed to the distal ileum, and there in a rather haphazard manner.

APPLICATION

From this and our earlier work we suggest that segments of the proximal jejunum will behave similarly and predictably according to length irrespective of the number of vessels supplying them. Segments of the distal ileum in the dog and the rabbit if selected solely by length will behave in an unpredictable manner, owing to the irregular extrinsic sympathetic distribution, and many of the short segments will exhibit an exceptionally high tone making them unsuitable for use where antiperistaltic segments causing low degrees of obstruction are required. The contraction of some short single-vessel segments of distal ileum observed on being isolated in the rabbit and the dog indicates that such segments will exhibit obstructive qualities out of all proportion to their short lengths. They will not be suitable for use as antiperistaltic segments in the treatment of short-bowel syndrome, but their use may be considered in operations of sphincter substitution.

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SHORT NOTES OF RARE OR OBSCURE CASES

POST-IRRADIATION FEMORAL ANEURYSM TREATED BY ILIOPOPLITEAL BY-PASS VIA THE OBTURATOR FORAMEN

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SUMMARY

This unusual case is presented for two reasons. First, it illustrates the value of a long by-pass graft from the common iliac artery to the popliteal artery passing through the obturator foramen when there are complications which forbid operation through the femoral triangle. Secondly, it provides clinical and histological evidence of the late effects upon neighbouring large arteries of radiotherapy—given in this instance for a fibrosarcoma in a thigh muscle.

THE bifurcation of the common femoral artery is a convenient site for anastomosis in by-pass procedures and for arteriotomy in disobliteration. It may happen, however, as in the case reported here, that direct arterial surgery is necessary but some complication forbids the usual approach through the femoral triangle (*Table I*). If this is so, a by-pass may be established from the iliac vessels to the popliteal artery via the obturator foramen. The technique was first described by Shaw and Baue (1963), and since that date further reports of the successful use of the method have been made, and these, together with the original 3 cases, are summarized in *Table II*.

Table I—INDICATIONS for OBTURATOR BY-PASS

1. Infections of aortofemoral and femoropopliteal prostheses.
2. Large aneurysms of the iliac and femoral arteries.
3. Ulceration in the femoral triangle owing to carcinoma (primary or secondary), ischaemia of skin-flaps, and radiation necrosis.
4. Trauma with loss of soft tissue suitable for covering the femoral vessels.
5. Mycotic aneurysm of the femoral vessels (increasingly common in heroin addicts).

The case reported here is of additional interest because an aneurysm of the femoral artery is believed to have developed as an after effect of radiotherapy.

CASE REPORT

B. S., a woman aged 79 years, was admitted on 6 March, 1969, complaining of swelling in her right thigh, which was increasing in size.

In 1920 an undifferentiated fibrosarcoma had developed in her right adductor longus. The tumour had been

Table II.—SUMMARY OF 22 CASES TREATED BY THE OBTURATOR BY-PASS TECHNIQUE

AUTHOR	CASE NO.	AGE AND SEX	INDICATION FOR BY-PASS	PROSTHESIS USED	LENGTH OF FOLLOW-UP (months)	WHETHER PATENT
Shaw and Baue (1963)	1	58 M.	Infected Dacron iliopopliteal by-pass	Dacron	12	Yes
	2	65 M.	Infected autologous femoro-popliteal by-pass	Dacron	7	Yes
	3	43 M.	Infected Dacron aortofemoral by-pass	Dacron	12	Yes
Mentha, Launois, and Delaere (1965)	4	43 M.	Spontaneous rupture of femoral artery following radionecrosis in femoral triangle	Dacron	Died 1 month after operation	
	5	62 F.	Radionecrosis of femoral triangle following treatment of carcinoma of vulva	Dacron	Died 3 months after operation	
Mahoney and Whelan (1966)	6	42 M.	Infected autologous vein femoropopliteal by-pass	Autologous vein-graft	36	Yes
	7	47 M.	Mycotic aneurysm of femoral artery (right)	Autologous vein-graft	3	Yes
Donahoe, Froio, and Nabseth (1967)	8	40 M.	Squamous-cell carcinoma of femoral triangle excised plus femoral vessels	Dacron	10	Yes
Macpherson 1967	9	38 M.	Haematoma in the femoral triangle following excision of femoral artery aneurysm and insertion of Terylene prosthesis	Terylene	2	Yes
De Palma and Hubay (1968)	10	49 M.	Infected Dacron aortofemoral by-pass	Dacron	36	Yes
	11	75 M.	Infected Dacron aortofemoral by-pass	Dacron	15	Yes
	12	68 F.	Infected Dacron femoro-popliteal by-pass	Dacron	15	Yes
	13	65 M.	Aortic bilateral iliac and femoral and (left) popliteal aneurysms (left)	Dacron (right aorta to superficial femoral)	0	No
Guida and Moore (1969)	14	40 F.	Infected femoral arteriotomy. Second haemorrhage	Teflon	6	Yes
Hegarty, Linton, and McSweeney (1969)	15	59 M.	Radionecrosis in femoral triangle with spontaneous rupture of femoral artery	Dacron		
Fromm and Lucas (1970)	16	45 M.	Ruptured mycotic aneurysm aneurysm	Dacron	18	Yes
	17	46 M.	Elective treatment of mycotic aneurysm of femoral vessels	Dacron	17	Yes
	18	36 F.	Elective treatment of mycotic aneurysm of femoral vessels	Dacron	12	Yes
	19	45 F.	Elective treatment of mycotic aneurysm of femoral vessels	Dacron	6	Yes
Spiro and Cotton (1970)	20	61 F.	Femoral artery aneurysm	Dacron	18	Yes
	21	57 F.	Mycotic aneurysm of femoral artery	Dacron	3	Yes
	22	70 M.	Aneurysmal dilatation of femoropopliteal arterial homograft	Dacron	3	Yes

excised, together with the proximal two-thirds of the muscle. The following year a local recurrence had been excised and the area had been irradiated. In 1954 the scar tissue had broken down, and in 1955 the ulcerated area in the femoral triangle had been excised down to the femoral vessels. Troublesome infection had occurred, but healing had ultimately been achieved. Histological examination of the ulcer and underlying tissue showed post-irradiation changes, but no recurrence of the tumour.

Two months before the present admission the patient had slipped and fallen, and shortly after this she had noticed a swelling in the lower part of her right femoral triangle. The swelling had been asymptomatic, but she had also observed some swelling of the right ankle at this time.

On examination the patient's general health was good for her age. There were some crepitations at both bases. The blood-pressure was 210/130 mm. Hg and the pulse-rate was 84 with regular rhythm. There was an early systolic murmur in the aortic area, conducted to the neck. Examination of the local condition revealed a saccular aneurysm of the superficial femoral artery at the apex of the femoral triangle, measuring 5 cm. in diameter. The skin and scar tissue overlying the femoral triangle showed irradiation telangiectasia; all pulses were present in both lower limbs and there was minimal oedema of the right ankle.

The haemoglobin was 12·6 g. and the white blood count was 6000 per c.mm. The blood-urea was 39 mg. per cent and the serum cholesterol was 310 mg. per cent. Electrocardiograms showed ischaemic changes and a radiograph of the chest showed left ventricular enlargement. A plain film of the right thigh revealed extensive calcification in the femoral artery.

A right femoral arteriogram (*Fig.* 1) showed moderate diffuse dilatation of the common and superficial femoral vessels, with a somewhat crimped appearance. The aneurysm containing thrombus was also demonstrated, as well as the grossly abnormal femoral artery which terminated at the level of the adductor opening—this corresponded to the lower limit of irradiation. The collateral circulation was very poor.

On 18 March resection of the aneurysm and the establishment of a conventional iliopopliteal Dacron by-pass were carried out. A longitudinal incision was made from 5 cm. above the inguinal ligament down to the level of the proximal popliteal artery. The external iliac and the popliteal artery showed minimal arteriosclerosis, but the common, superficial, and profunda femoral vessels were dilated and very thin walled. There was a large amount of perivascular scar tissue resulting from the previous surgery and radiotherapy, and the arteries and veins were separated mainly by sharp dissection.

The lower half of the superficial femoral artery, including the aneurysm, was resected. The vessel was ligated above this level, but the upper half of the superficial femoral artery was not resected. This was because the profunda vessel was involved in the aneurysmal process and the benefits of resection did not justify the technical hazards and the additional time involved in this procedure. In order to isolate the common femoral bifurcation a ligature was tied around the common femoral artery just below the inguinal ligament. A Dacron prosthesis, 10 mm. in diameter, was then anastomosed end to side to the external iliac artery and end to end obliquely to the proximal part of the popliteal artery.

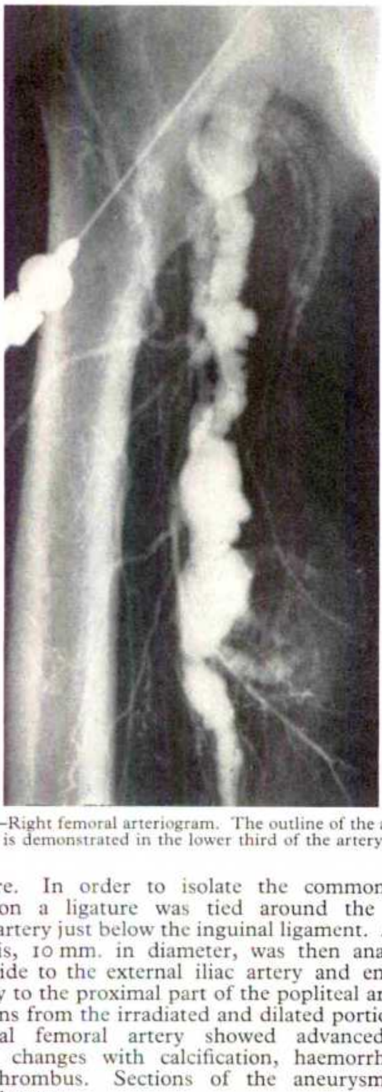

FIG. 1.—Right femoral arteriogram. The outline of the aneurysm is demonstrated in the lower third of the artery.

Sections from the irradiated and dilated portions of the superficial femoral artery showed advanced atherosclerotic changes with calcification, haemorrhage, and mural thrombus. Sections of the aneurysm showed similar changes.

Postoperatively the patient's initial progress was satisfactory, and both ankle pulses were palpable. However, on the seventh postoperative day the femoral wound broke down in the irradiated area and became infected. Culture revealed coliform bacilli and *Pseudomonas aeruginosa*. The patient was treated with systemic antibiotics and local irrigations, but the wound did not heal and the prosthesis became exposed. On 20 April she developed left-sided chest pain; radiographs of the chest showed elevation of the left dome of the diaphragm and a small left-sided pleural effusion. A pulmonary embolus was diagnosed, and she was treated with intravenous heparin, 5000 U. 6-hourly. On 26 April she developed a temperature of 40·1° C., and blood culture produced a growth of coliform bacilli, probably a result of infection from the exposed graft.

In view of the failure of the wound to heal and the continued exposure of the prosthesis a tube pedicle was raised from the anterior abdominal wall and swung down to cover the defect in the thigh. Initially the graft was satisfactory but by 7 Aug. the pedicle flap had become necrotic over the prosthesis, and the wound was discharging watery pus. The infection proved resistant to treatment. A left retrograde femoral arteriogram showed patency of the prosthesis with poor run-off to the anterior and posterior tibial arteries. The iliac vessels on both sides showed minimal atherosclerosis, as did the left femoral artery. It was therefore decided to insert another prosthesis using the obturator by-pass technique.

On 19 Aug. a femoral by-pass through the obturator foramen was performed. The operative technique has been described in detail by Guida and Moore (1969) and the procedure in this case differed only in detail. The patient was supine, with the right hip flexed 10° and externally rotated. Steridrape was used to seal off the infected area in the femoral triangle. The abdomen was opened through a right paramedian incision. While exploring the area of the iliac vessels and obturator foramen it became apparent, first, that an extraperitoneal approach was difficult and unsatisfactory, and, secondly, that in order to avoid angulation of the graft the upper end should be anastomosed to the common iliac artery and not to the external iliac artery (*Fig.* 2 A). The peritoneal cavity was therefore opened and, having identified the ureter at the iliac bifurcation, the posterior parietal peritoneum was incised to expose the common artery.

Synchronously with the abdominal operation a second operator exposed the popliteal fossa through the lower end of the recent by-pass incision, and the site of the previous anastomosis was identified. The popliteal artery was secured 4 cm. below this level for the new anastomosis.

In establishing the pathway through the obturator foramen and traversing the adductor compartment it has been advised that a third incision should be made on the posteromedial aspect of the thigh. We decided not to make this incision because of the after effects of the previous operation and radiotherapy, and because of the risk of infection from the femoral triangle.

The obturator membrane was incised by sharp dissection just below the obturator artery and nerve, and this incision was enlarged by digital dissection, thus making sure that there was no sharp fascial edge which might compress the graft. The tunnelling was then carried out using the graft passer employed in conventional by-pass procedures; this instrument has a long malleable shaft. Preliminary trials in a cadaver showed that the instrument tends to pass anteriorly and thus to enter the subsartorial canal. This tendency is corrected by defining the adductor magnus in the lower dissection, and the second operator was thus able to guide the instrument down along the posterior aspect of this muscle, using sponge-holding forceps. A 10-mm. Dacron prosthesis was attached to the end of the graft passer and was pulled up through the tunnel (*Fig.* 2B). End-to-side anastomosis was established to the common iliac artery above and to the popliteal artery below, using 00000 Dacron sutures; the anastomoses were made obliquely in order to minimize turbulence. When flow had been established through the new by-pass the peritoneum was closed over its upper end.

The ends of the previous graft were then defined and the external iliac artery was ligated just proximal and the popliteal artery just distal to the attachments of this graft. There was no evidence that the graft had become adherent to the surrounding tissues. The old anastomotic sutures were cut and unpicked. The abdominal and thigh incisions were closed without drainage. Finally the old Dacron by-pass was grasped with artery forceps through the defect in the pedicle skin-graft in the femoral triangle and was pulled out without difficulty. Five pints of blood were transfused during the operation, and 8000 U. of heparin were given to cover the period of insertion of the by-pass.

The patient's postoperative recovery was very good, both ankle pulses being present within 24 hours. She started to walk on the twelfth day, and developed some oedema of the foot and ankle but this did not interfere with her mobilization. The oedema was probably lymphatic and was partially controlled by an elastic stocking. She was discharged on the eighteenth postoperative day and was last seen exactly 6 months after leaving hospital when she was fully mobile. In view of the danger of late occlusion of the Dacron by-pass, long-term anticoagulant therapy was started 3 months after the operation and has been continued until the date of this report.

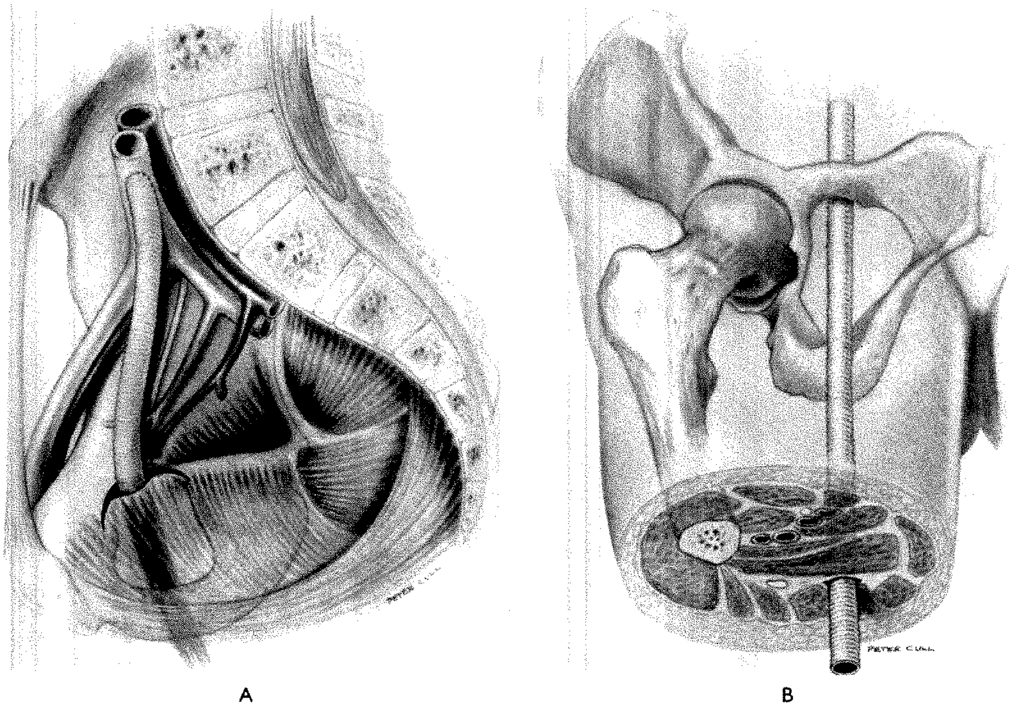

FIG. 2.—The pathway of the graft.

DISCUSSION

Clinical Management.—In view of the tissue damage in the thigh resulting from the previous operative treatment and radiotherapy, it was perhaps optimistic to hope for satisfactory healing in this area. In retrospect the obturator route for the by-pass should have been chosen at the outset. We also consider that we should have abandoned the first by-pass at an earlier date. The likelihood of salvaging an infected Dacron graft is very small, and although the pedicle skin-graft healed very well initially, as in *Case* 3 in *Table I*, it failed to maintain skin cover of the infected foreign material. Meanwhile, the infection gave rise to the danger of secondary haemorrhage from the anastomoses and was detrimental to general health, as shown by intermittent high fever, rigors, and a positive blood-culture. The failure of antibiotics and skin-grafting to combat the infection was partly due to the involvement of the entire length of the graft in the infection. Evidence of this fact was provided by the lack of adhesion of the Dacron to the surrounding tissues which facilitated its extraction through the skin defect at the end of the final operation.

The use of Dacron in both operations is open to question. In this case there was no right long saphenous vein, and the left long saphenous and the upper limb veins were of poor calibre. The extra length of the by-pass from the iliac segment instead of from the common femoral bifurcation would result in a very narrow channel if a vein were used, and it is likely that the advantages of a 10-mm. lumen more than offset the increased chance of late failure due to using Dacron. It is probable that a suitable autogenous vein would be the material of choice, but the fact that a vein was used only twice out of 22 cases in *Table II* suggests that a suitable vein is not usually available.

The Clinical Effect of Radiation on Large Arteries.—Radiation may damage an artery in two ways. First, by direct action on the elements of its wall and, secondly, by the indirect effect due to scarring and damage in the surrounding tissues (Sams, 1965). The pathological changes in the vessel are limited to the field of irradiation.

The acute and long-term effects of radiation on arterioles and capillaries have been well described (Woolbach, 1909; Warren 1942). As for larger vessels, Lindsay, Kohn, Dakin, and Jew (1962) have studied the short-term effects of radiation on segments of dogs' aortic walls. They showed that atherosclerosis appeared in the irradiated segments and was indistinguishable from natural atherosclerosis. They felt that this was due to selective injury of the internal elastic lamina leading to intimal fibrosis and plaque formation. Smith (1961) has suggested that this occurs as a result of damage to the vasa vasorum. From these experiments and others (Berdjis, 1960; Sams, 1965) it would appear that the effect of irradiation is to accelerate the natural degenerative process in the arterial wall. The mechanism of this process is not fully understood.

Clinically, large arteries can tolerate normal megavoltage radiotherapeutic schedules of 5000–6000 rad in 28–42 days without obvious immediate damage. However, Cade (1940) described a case of perforation of the aorta following radium therapy of a carcinoma of the oesophagus. Jones (1948) described a similar case after 1 MeV. X-ray therapy in which failure to repair the deficit caused by tumour invasion was the basic factor. Marcial-Rojas and Castro (1962) reported 11 cases undergoing irradiation of the neck in combination with surgery, and irradiation of inoperable neoplasms of the oesophagus in which the carotid artery or aorta ruptured during or shortly after treatment. There was associated mediastinitis from perforation of the neoplasm in all the cases with aortic rupture, and salivary fistulae with necrosis of the skin-flaps in all the cases with rupture of the carotid artery. It is probable that infection and salivary fistulae were the principal causes of the vessel ruptures and that irradiation potentiated their effect.

There are only scattered reports of the late effects of radiation on large arteries. In most instances major vessel occlusion has occurred. Thomas and Forbus (1959) described the case of a young man who developed localized necrosis of the aortic wall with associated thrombosis 2½ years after irradiation of a mediastinal lymphoma. Rubin and Casarett (1968) reported the case of a 38-year-old woman who thrombosed her aorta and common iliac arteries 4 years after internal and external irradiation for carcinoma of the cervix. Obliteration of the subclavian and narrowing of the common carotid and innominate arteries has been described by Heidenberg, Lupowitch, and Tan (1966). This occurred in a 21-year-old woman 11 years after irradiation for Hodgkin's disease. The artery was obliterated by a combination of vessel-wall damage and dense fibrosis in the surrounding tissues. Superficial femoral artery thrombosis was described by Gross (1969) after irradiation of nasopharyngeal carcinoma metastases in the groin.

Narrowing only of the major vessels following irradiation has also been reported. Selective constriction of the profunda femoris artery in a 23-year-old woman following irradiation of a labial haemangioma was found to be due to adventitial scarring (Pouliaf, Giannopoulos, and Frangagis, 1967). Johnson, Lane, Harding Rains, O'Connell, and Ramsay (1969) reported the case of a 61-year-old woman who had presented with intermittent claudication due to bilateral iliac artery stenosis 6 years after external irradiation for carcinoma of the uterus. The stenosis was caused principally by perivascular fibrosis. Why some arteries should occasionally be more susceptible to damage by normal therapeutic schedules is not known. Asscher, Wilson, and Anderson (1961) have shown experimentally that irradiation increases the susceptibility of blood-vessels to damage by hypertension and this may be a factor in some cases.

The case reported here had had irradiation of the right thigh for a recurrent sarcoma in 1921. We do not have a record of the dose that she received, but we do know that it was of low-quality irradiation and sufficient to produce severe skin and subcutaneous changes after 6 years, and a small area of frank skin necrosis after 24 years. Arteriograms showed that the left femoral artery was within normal limits for the age of the patient, whereas the right femoral artery showed gross irregularity of the arterial wall and a saccular aneurysm. The vessel wall was distorted by areas of dilatation and constriction, but an adequate lumen was maintained. The reason for these changes is that the effect of irradiation on the cells of the wall of a large artery is not uniform and therefore the subsequent degenerative processes are irregular within the field of irradiation.

Irradiation produces characteristic changes in small blood-vessels: namely, sausage-shaped segmentation of the arterioles and looping of the capillaries (Lindop, 1970). Some such changes could be seen in the present case, but the majority of the small vessels in the field of irradiation did not show advanced changes. This was probably due to the increased endothelial turnover and new vessel formation stimulated by the surgery to the thigh in 1954.

Histology of the arterial wall showed gross irregular thickening due principally to changes in the intima. This was thickened and composed mainly of hyalinized collagen focally calcified and showing atheromatous changes at intervals along its inner aspect. The media was thinned and in places completely absent. It showed almost complete disappearance of the muscle cells and marked loss and fragmentation of the internal elastic lamina with collagen replacement. There were thinning and patchy deficiency of the external elastic lamina. The aneurysm was filled with old and partially organized thrombus, and its wall was composed of attenuated layers of fibrous tissue. The vasa vasorum in the adventitia showed only slight hyalinization. These changes were considered to be consistent with chronic irradiation damage, the prominent features being the fragmentation of the elastic tissue and the replacement of the arterial wall by collagen.

There are several reasons why clinically the long-term effects of radiation on large arteries are rarely seen. First, the changes take years to develop owing to the very slow turnover of cells in the arterial wall. Secondly, damage to the artery may not become manifest unless it is subjected to some form of stress, such as further irradiation, infection, or physical trauma. These may precipitate thrombosis, embolism, or the development of an aneurysm, as occurred in this case after a fall.

Johnson and others (1969) have shown that such effects on arteries can be produced by normal therapeutic dosages. It therefore seems likely that as this damage is related to dose the clinical effects of post-irradiation arterial pathology will be seen more frequently in the future. One reason is that dosage used to be limited by skin tolerance but with modern techniques large doses can now be given to deep structures without damaging the skin.

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RECTAL STONES

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SUMMARY

A case is reported of a rare complication of total cystectomy and ureterocolic anastomosis for carcinoma of the bladder. The patient suffered not only from some of the more common complications of this procedure but also developed bleeding per rectum, the cause of which was impaction of two calculi in the rectum. Analysis of these stones showed an inner core of mixed gall-stone and an outer shell of urinary struvite.

CASE REPORT

A 68-year-old blind ex-serviceman presented with a 4-month history of painless haematuria and was found on cystoscopy to have a papilliferous carcinoma of the bladder, which was treated initially with cystodiathermy. The patient was otherwise fit and had undergone retropubic prostatectomy for benign hypertrophy 18 months previously. Subsequent recurrences on routine-check cystoscopy over a 3-year period necessitated a course of radiotherapy with a good result and no evidence of recurrence of the tumour. Unfortunately the patient developed a severe post-irradiation cystitis, reduced bladder capacity, and persistent haematuria, these symptoms being so severe that total cystectomy and ureterosigmoid implantation were performed. At operation he was noted to have gall-stones but till then these had been quite asymptomatic.

The patient made a good postoperative recovery, but his subsequent follow-up was complicated by several admissions during the following 12 months for electrolyte imbalance and periodic episodes of ascending urinary infection. He was treated with long-term sulphonamides and potassium bicarbonate therapy with a reduction in the clinical attacks of pyelitis and better stabilization of his hyperchloraemic acidosis. On two admissions he also complained of mild upper colicky abdominal pain and vomiting, but he was never jaundiced. Cholecystitis was not diagnosed clinically, even with the knowledge of gall-stones being present at the time of his total cystectomy.

Five years following the cystectomy he presented in the out-patients' department with bright red bleeding per rectum, and on examination was found to have two calculi in the rectum that required an anaesthetic for their removal. They measured $3\cdot5 \times 2\cdot5$ cm. and 3×3 cm. (*Figs.* 1, 2). These stones were analysed and revealed a central core of mixed gall-stone (cholesterol and bile pigment) and an outer shell of struvite ($MgNH_4PO_4.6H_2O$) approximately 1·75 cm. thick.

The patient had no further bleeding per rectum, but his renal function deteriorated and he died at home some weeks later in uraemia, 5 years following his cystectomy. A post-mortem examination was not performed.

DISCUSSION

This case is reported as a rare complication of ureterocolic anastomosis with total cystectomy for carcinoma of the bladder. On reviewing the literature it would appear to be a unique case. The patient also demonstrates the more common complications of this operative procedure, the treatment of which may have had a bearing on the occurrence of this unusual complication.

At the time of total cystectomy it had been noted that gall-stones were present and under the circumstances they were not removed. The attacks of upper abdominal pain and vomiting would in retrospect be compatible with cholecystitis and subsequent ulceration of the stones into the intestine. They probably entered the large intestine as, owing to their size (approximately 1·75 cm. in diameter), gall-stone ileus might well have developed if they had entered the small bowel. The gall-stones therefore reached the large bowel and were bathed in urine and coated in struvite ($MgNH_4PO_4.6H_2O$) during their passage to the rectum. It is well documented that following ureterosigmoid implantation, urine passes backwards in the colon as far as the caecum, so that the stones would have close contact with urine during their passage. Struvite is only deposited in alkaline urine and is an uncommon cause of urinary calculi alone, usually being combined with calcium phosphate and carbonate. The urine excreted by this patient was presumably heavily alkaline as he was taking regular daily doses of potassium bicarbonate and there was an abundance of urea-splitting organisms in the bowel. Renal calculi are a known complication of ureterocolic anastomosis for the same reasons. The dual nature of these calculi can therefore be explained, and their size, in conjunction with a degree of anal stenosis due to the long-term passage of fluid faeces, prevented natural voiding per rectum.

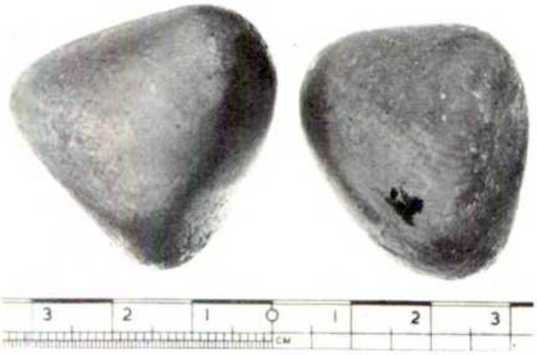

FIG. 1.—Rectal calculi.

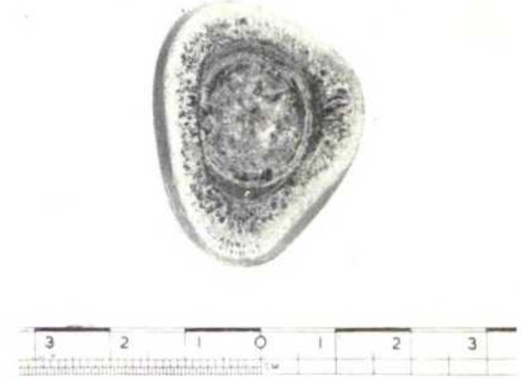

FIG. 2.—Cross-section of a rectal calculus, showing an inner core of mixed gall-stone and an outer shell of struvite.

Acknowledgements.—I wish to express my thanks to Mr. Robert Cox for permission to publish this case. I am grateful to the Department of Medical Photography, Westminster Medical School, for assistance with the photographic reproductions.

HAEMANGIOSARCOMA OF THE SPLEEN

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PRIMARY splenic tumours are extremely rare and because of this are not usually considered in the differential diagnosis of splenomegaly. We report here a patient with a primary haemangiosarcoma who presented with splenomegaly and unusual haematological findings and in whom spontaneous rupture of the spleen occurred.

CASE REPORT

A 72-year-old joiner was admitted to hospital with left upper abdominal pain of 10 days' duration. Apart from some shortness of breath in previous weeks he had otherwise been in good health. The patient had not had serious illnesses in the past and he had never had radiological examinations involving the use of Thorotrast. On examination his general condition was satisfactory but he was clinically anaemic. The spleen was tender and enlarged, being easily palpable 6 cm. below the left costal margin. The liver was not enlarged and there was no ascites. There was no significant lymphadenopathy.

The following investigations were performed: haemoglobin, 8·1 g. per 100 ml.; white cell-count, 5500 mm.^{3}, with neutrophils, 59 per cent, lymphocytes, 32 per cent, monocytes, 7 per cent, eosinophils, 1 per cent, basophils, 0 per cent, myelocytes, 1 per cent; reticulocyte count, 6·5 per cent; platelet count, 50,000 mm.^{3}; the red cells showed anisocytosis and mild anisochromia, and there were fairly frequent schistocytes and burr cells with occasional microspherocytes; Howell Jolly bodies were frequent; normoblasts formed 5 per cent of the total nucleated cell count; direct anti-human globulin (Coombs) test was negative; red-cell osmotic fragility showed small 'tails' of cells of both increased and decreased fragility. The blood-urea was 22 mg. per 100 ml.; serum sodium, 138 mEq./l.; chloride, 102 mEq./l.; potassium, 4·4 mEq./l.; CO_2 content, 27 mEq./l. Serum alkaline phosphatase was 84 I.U.; total serum bilirubin, 0·1 mg. per 100 ml.; S.G.P.T., 10 I.U.; flocculation tests, negative; total serum proteins, 6·2 g. per 100 ml.; albumin, 3·6 g. per 100 ml. A chest radiograph showed emphysematous changes in the lung fields with marked unfolding of the aorta. A straight radiograph of the abdomen showed the spleen to be grossly enlarged, extending downwards as far as the iliac crest.

Six days after admission the patient collapsed with generalized abdominal pain. He was shocked, there was generalized distension of the abdomen, and paracentesis from the right flank revealed fresh blood. A diagnosis of spontaneous rupture of the spleen was made. At laparotomy 4–5 litres of blood were found in the peritoneal cavity. The spleen was grossly enlarged, being approximately six times normal size, with a deep 8-cm. tear on the convex surface. The liver was normal. The spleen was extremely friable and was removed piecemeal after ligation of the splenic pedicle.

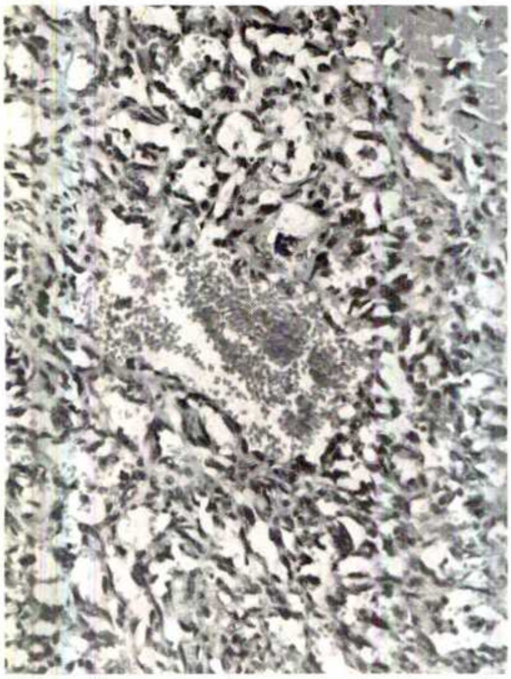

FIG. 1.—The normal splenic structure is replaced by a capillary network with a cavernous channel in the centre of the picture. H. and E. (× 198.)

Pathological examination of the excised spleen showed it to consist of two ragged masses, together weighing 1125 g. The tissue was firm with innumerable black haemorrhagic areas up to 1 cm. in diameter. In an intact subcapsular area there was a yellowish infarct, 2 × 1·5 × 1 cm., and several tiny infarcts were present elsewhere; there was no evidence of infarction in the area of the laceration. Sections showed the spleen to be the site of a diffuse haemangiosarcoma. Only traces of normal splenic structure could be identified. The tissue was composed of a capillary network with multiple large cavernous spaces, most of which were thrombosed (*Fig.* 1). The capillary network lay in a stroma of hyperchromatic oval and spindle cells of endothelial type with quite frequent mitoses and occasional more bizarre cells including tumour giant cells, some being multinucleate. Several of the cavernous spaces were partially lined by several layers of these malignant cells.

Postoperatively the patient made an immediate satisfactory recovery. However, after 2 months he became ill again with anaemia, jaundice, and enormous hepatomegaly. He died at home 5 months after his admission to hospital. A post-mortem examination was not performed.

DISCUSSION

Haemangiosarcomas of the spleen are extremely rare tumours and few have previously been recorded (Bauer and Stanford, 1946; Wright, 1949; Wilkinson, Lucas, and Foote, 1968). There is some doubt about their histogenesis, but it is thought by some authors (Hastings-James, 1949) that they arise from malignant change in pre-existing haemangiomas. Wright (1928) considered that they were primary malignant splenic tumours which metastasized secondaries to the liver. In the present case it is of interest that at laparotomy the liver was macroscopically normal, but that within a few weeks it had enlarged enormously and was obviously the site of secondary malignant deposits. This rapidly fatal course with widespread metastases to the liver, peritoneum, lymph-nodes, and bones has been stressed by other authors (Wright, 1949; Blix and Jacobsen, 1963; Wilkinson and others, 1968). Haemangiosarcomas of the liver have been described following the use of contrast media containing thorium dioxide (Thorotrast) (MacMahon, Murphy, and Bates, 1947; Silva Horta, Abbatt, Da Motta, and Roriz, 1965), but there was no evidence of this patient having had previous radiological examinations.

The haematological findings in the present case share many features of similarity with the syndrome of micro-angiopathic haemolytic anaemia delineated originally by Brain, Dacie, and Hourihane (1962). They regarded the basic disorder of this syndrome, seen in such diseases as malignant hypertension and disseminated carcinoma, as being direct erythrocyte damage by irregular vascular endothelium and fibrin strands. As a result, features of haemolysis with large numbers of damaged red cells presenting as burr cells and schistocytes may be seen. Certainly the racemose structure of a large splenic haemangiosarcoma could provide the appropriate mechanism for such a micro-angiopathic haemolytic anaemia, and other authors have commented on this type of haematological change (Baker, Paget, and Davson, 1956; Alpert and Benisch, 1970). A consumptive coagulopathy has also been described in patients with giant haemangiomas (Zervos, Vlachos, Karpathios, and Mantas, 1967; Thatcher, Clatanoff, and Stiehm, 1968) and in a haemangiosarcoma of the spleen (Blix and Jacobsen, 1963). In these cases the thrombocytopenia and fibrinogen deficiency resulted in widespread bleeding presumably due to consumption of platelets and fibrinogen during haemostasis within the tumour.

Apparent spontaneous rupture of the diseased spleen is now a well-recognized entity, having been described in arteriosclerosis of the splenic vessels (Jones, 1944), splenic abscess (Gelfand, 1947), infective mononucleosis (Rawsthorne, Cole, and Kyle, 1970), sarcoidosis (Roberts and Rang, 1958), leukaemia (Cooray, 1952), and actinomycosis (Sperling, Heredia, and Gillesby, 1967). Primary splenic tumours are not usually considered in the diagnosis of spontaneous splenic rupture, but this complication may occur in a splenic haemangioma (Ingham and Thompson, 1960) and in haemangiosarcoma as in the present case.

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LEIOMYOSARCOMA OF THE SPERMATIC CORD

A CASE REPORT

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Summary

A case of leiomyosarcoma of the spermatic cord is presented, the twenty-sixth case in the world literature. The tumour metastasized to the skin and to the lungs, and had to be differentiated from a neurofibromatous lesion. There was histological evidence to suggest that the lesion had originated as a benign leiomyoma and then had undergone malignant change. The primary tumour was excised. The secondary deposits were radioresistant but showed some response to chemotherapy. It is suggested that the most suitable form of treatment is wide excision of the primary tumour with close follow-up and chemotherapy when recurrence or metastasis occurs.

Tumours of the spermatic cord are of infrequent occurrence. We have been able to find only 25 cases of leiomyosarcoma of the spermatic cord in the literature. We have recently come across a case which had metastasized to the skin and thereby presented a peculiar problem in histological diagnosis.

CASE REPORT

A 55-year-old white male attended a surgical clinic in May, 1966, complaining of a swelling in the right groin which had been present for 3 months.

Physical examination revealed a hard, round, non-tender, irreducible mass in the right groin below the internal inguinal ring.

Laboratory investigations revealed nothing of consequence. A chest radiograph showed no lesion.

A diagnosis of encysted hydrocele was made. However, at operation 1 month later the lesion was found to be a solid tumour lying beside the spermatic cord within the external spermatic fascia. The entire spermatic cord with the tumour and the right testis was excised below the internal inguinal ring.

In January, 1969, the patient developed a small brown nodule in the middle of the chin. The lesion was about 1 cm. in diameter and was raised above the skin surface. He also had a small nodule behind the left ear. The nodule on the chin was excised and was found to be histologically similar to the spermatic cord tumour.

In June, 1969, the patient developed pain in the right side of the chest, breathlessness, and loss of weight. A chest radiograph showed extensive patches of increased density throughout the right lung, and a diagnosis of metastases to the lung was made.

The patient was given a course of actinomycin D, a total dose of 5 g. being administered in 10 days. While there was no change in the skin nodule or chest radiograph, there was considerable subjective improvement and the patient remained reasonably fit for about 6 months.

In January, 1970, the patient developed more skin nodules (on his scalp) and some deeply placed nodules in the soft tissues of the right thigh. He was given a course of X-ray therapy to his leg to relieve the pain from the latter lesions and a course of Oncovin, 1·5 mg., intravenously at weekly intervals for 4 weeks. Little response was obtained by X-ray therapy despite a total dose of 5000 rad in 50 days by Tele caesium unit.

In May, 1970, the patient had developed more skin nodules and had pains over his sacrum. He was also becoming emaciated. His condition deteriorated rapidly and he died in August. No autopsy was performed.

Pathology.—The mass from the spermatic cord consisted of a hard, multilobular, rounded tumour, 8 × 6 cm. Histologically, it appeared well encapsulated and was composed of interlacing strands and sheets of spindle-shaped cells with elongated nuclei (*Fig.* 1). The cells were arranged compactly and appeared to be benign over the greater part of the tumour. However, a sharply defined focus of obviously malignant change was seen involving about one-fifth of the tumour (*Fig.* 2). The cells in this region were much larger than in the rest of the mass, and were arranged in an irregular manner, though in places a pattern of interlacing strands was seen. The nuclei too were larger, with marked variation in size and chromatin distribution. A large number of mitotic figures was seen. A few small areas of necrosis were present in this zone. The tumour showed no attachment to the vas deferens.

The nodule from the chin was made up of tissue very similar to that in the spermatic cord (*Fig.* 3). The tumour lay in the deeper dermis, being separated from the epidermis by a layer of collagenous tissue.

Both tumours showed similar staining characteristics. Very little collagen or reticulin could be demonstrated. The tumour cells did not stain with the Glees and Marsland technique, but stained red with Masson's trichrome stain and the Lissamine fast-red technique.

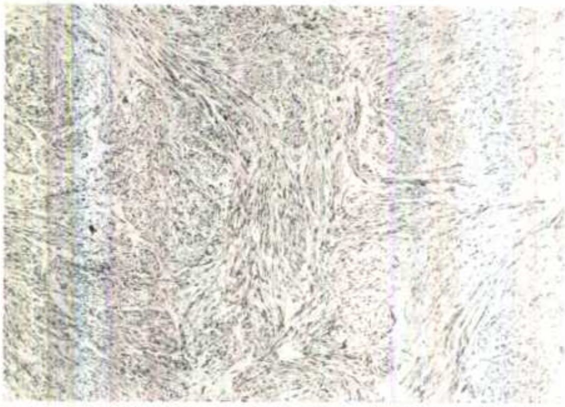

FIG. 1.—Section from the benign part of the tumour, showing interlacing bundles of smooth-muscle fibres. H. and E. (× 32.)

DISCUSSION

As Stout (1953) has pointed out, the criteria for recognizing some of the varieties of sarcoma are not sufficiently well established to make the published diagnoses reliable. We would, therefore, like to make clear the factors that led to the diagnosis of leiomyosarcoma in the present case.

When the spermatic cord tumour was first seen, the histology of the benign-looking areas was considered typical of a smooth-muscle tumour; no dianosis other than that of a leiomyoma with malignant change was entertained. However, the occurrence of skin nodules later suggested three possibilities: (1) the tumour in the spermatic cord was a leiomyosarcoma and the skin nodules were secondaries; (2) the skin and spermatic cord lesions were both manifestations of neurofibromatosis with malignant change in the spermatic cord tumour; (3) the skin and the spermatic cord lesions were independent of each other, the former being a neurofibroma.

The occurrence of the nodules in the chin and behind the ear 2 years after removal of the spermatic cord tumour, followed some months later by nodules on the scalp, suggested that the skin lesions were secondaries rather than neurofibromas.

Histologically the lesions in the chin and the spermatic cord appeared identical and showed identical staining characteristics. The positive reaction with the Lissamine fast-red technique and the negative reaction with the Glees and Marsland technique were in favour of a diagnosis of leiomyosarcoma. There was no evidence of palisading to support a diagnosis of neurilemmoma. The stroma was compact and did not have the loose oedematous appearances commonly seen in neurofibromas. Myofibrils could be seen in the better differentiated areas. Thus, the diagnosis of leiomyosarcoma with metastasis appears to be well established.

Patel and Chalier (1907) reported the first case of leiomyosarcoma of the spermatic cord. Kyle (1966) reviewed the literature, which then included 21 cases, and added 1 of his own. We have found 3 more cases in the subsequent literature (Lundblad, Mellinger, and Gleason, 1967; Weitzner, 1967; Arlen, Grabstald, and Whitmore, 1969). Our case is therefore the twenty-sixth reported in the literature.

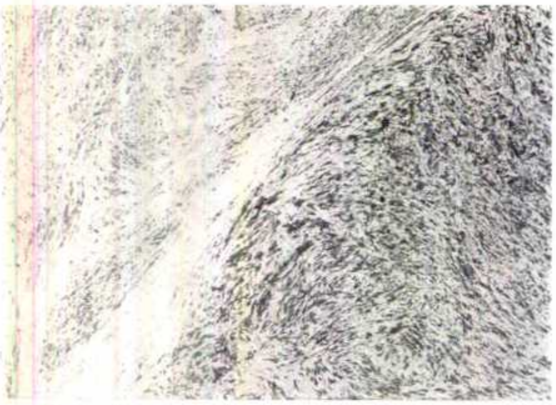

FIG. 2.—Junction of the benign and malignant parts of the tumour, showing an abrupt transition to large cells with hyperchromatic nuclei. H. and E. (× 32.)

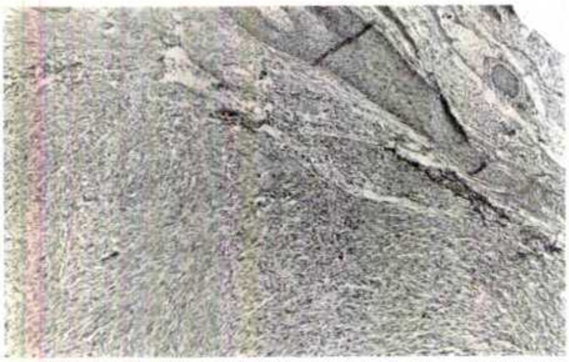

FIG. 3.—Section of a skin nodule, showing compactly arranged interlacing strands of spindle-shaped cells, some of the nuclei being large and hyperchromatic. Masson's trichrome stain. (× 32.)

The exact site of origin of leiomyosarcomas of the spermatic cord is unknown. Undifferentiated mesenchymal cells, smooth-muscle cells in the cremaster, walls of blood-vessels, and the vas deferens have all been suggested as possible sites of origin (Weitzner, 1967). In the present case the tumour was quite free of the vas deferens. The ubiquity of leiomyomas and leiomyosarcomas suggests that primitive mesenchymal cells or walls of blood-vessels are the likely sites of origin.

As Kyle (1966) has pointed out, distant metastasis, when it occurs, is much more likely to be haematogenous than lymphatic. The presence of skin and pulmonary involvement in this case is in favour of haematogenous spread. This is the first case of leiomyosarcoma of the spermatic cord in which skin metastasis has been recorded. The presence of the skin metastases presented a peculiar problem in diagnosis, both clinically and histologically.

The age of the patients with leiomyosarcoma of the spermatic cord reported in the literature ranges from 15 to 78 years, with the majority being over the age of 50 years. As Gowing and Morgan (1964) have pointed out, paratesticular tumours of connective tissue can be divided into two groups based on the age of onset. The first group consists of the embryonic sarcoma and the rhabdomyosarcoma which occur almost exclusively in children and adolescents. The second group, into which the leiomyosarcomas fall, occurs in older subjects. The present case occurred at the age of 55 years, thereby being consistent with the other cases in the literature.

One of the features of the present case was that malignancy was confined to a small part of the tumour, which was sharply distinct from the remaining benign-looking tissue, suggesting that the lesion had started as a benign leiomyoma with subsequent malignant change. This has been a feature in 6 of the cases in the literature (Dreyfuss and Goodsitt, 1940; Wessel, 1953; Bevan, 1954; Meinardi, 1961; Kyle, 1966; Weitzner, 1967).

The treatment of leiomyosarcomas in general is by wide surgical excision, which produces a 25–30 per cent 5-year survival rate. In the case of leiomyosarcoma of the spermatic cord, metastases often seem to arise after a long period of apparent freedom from disease. Since spread is mainly haematogenous as distinct from other sarcomas of the spermatic cord (Banowsky and Shultz, 1970) there is no place for retroperitoneal node dissection or postoperative irradiation. In the present case the secondary deposits appeared to be radioresistant, no response being obtained to a large dose of radiotherapy.

The effect of chemotherapy with antimetabolites on this disease has not so far been reported. In the present case a course of treatment with actinomycin D led to subjective improvement and arrest of progression of the disease for 6 months. Thus it would appear that the most suitable form of treatment is wide local surgery and a close follow-up with the use of chemotherapy when metastasis or recurrence occurs.

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DOES SQUAMOUS CARCINOMA OF THE COLON EXIST?

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SUMMARY

A patient with a histologically unusual carcinoma of the colon had a successful surgical resection and primary anastomosis. The tumour showed certain squamous features. It is doubtful if any of the previously reported cases of 'squamous carcinoma' represents more than squamous metaplasia with variable degrees of differentiation in existing adenocarcinomas.

To find 'squamous' malignant tissue in the colon is not necessarily to imply that the tumour is metastatic or inoperable.

Four cases of 'squamous carcinoma' of the colon have previously been reported. Of these, only 1 involved the left half of the colon. The rarity of this type of tumour may be of critical importance when, as in the case described here, the preliminary colonic biopsy might be incorrectly interpreted as indicating spread of tumour into the colon from a more typical 'squamous' territory.

CASE REPORT

A 63-year-old unmarried assistant school matron was admitted to the Gastro-intestinal Unit of the Western General Hospital, Edinburgh, in June, 1969, for investigation of an episode of rectal bleeding 1 month previously. The bleeding had been dark red, had lasted for 2 weeks, and had been associated with bowel movements and an occasional 'twinge' of pain in the left iliac fossa. Her bowel action was regular and the stools were well formed. She took no drugs apart from oral supplements of iron. Her general health was good and she had not lost weight.

Thirty years previously the patient's anaemia had been investigated and found to be of an iron-deficiency type. In 1945 a routine appendicectomy had been done for acute appendicitis, and in 1957 a barium meal and cholecystogram carried out after several episodes of vomiting were reported as normal.

Examination on Admission.—The patient looked well and showed no signs of weight-loss. The abdominal examination was normal and her previous scar had healed well. There were no abnormal lymph-nodes and no palpable abnormality on rectal examination.

Investigations.—The haemoglobin was 83 per cent (red cells 'normocytic and normochromic'), and the erythrocyte sedimentation rate was 23 mm. in the first hour (Westergren). Liver-function tests and plasma proteins were normal. Faecal occult blood was slightly positive on repeated examinations.

At sigmoidoscopy an ulcerated mass was biopsied at 16 cm. The histology report indicated that the tumour was 'unlike a primary growth of colon, but had the appearance of a poorly differentiated squamous carcinoma'. The pathologist further suggested that metastasis from a primary source in the uterus or the urinary tract would be most likely to produce such an appearance.

A chest radiograph was normal, but a barium enema showed a 'small area of narrowing in the sigmoid colon' (arrowed in *Fig.* 1).

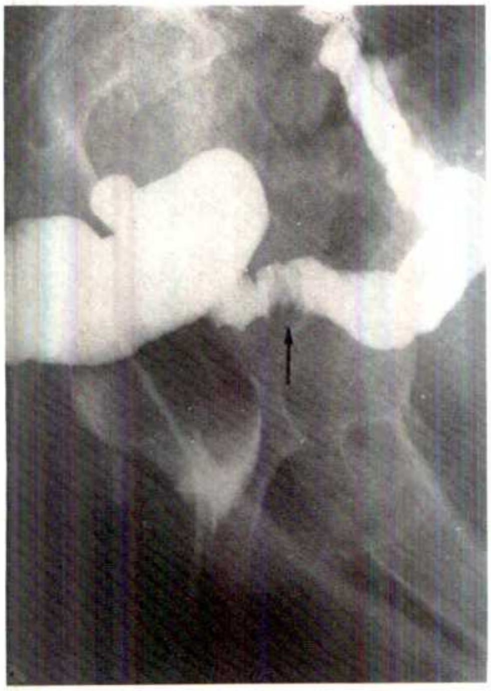

FIG. 1.—Barium-enema photograph showing localized narrowing in the low pelvic colon.

Examination of the urine was normal; the blood-urea was 33 mg. per cent and an intravenous pyelogram detected no abnormality in the kidneys, ureters, or bladder.

Examination under anaesthesia and endometrial curettage showed no abnormality in the genital tract.

OPERATION.—On 10 July, 1969, laparotomy (Mr. W. P. Small) confirmed the presence of a discrete tumour in the pelvic colon (*Fig.* 2). The colon was fully mobile and the tumour was palpated as an irregular nodule entirely within the lumen of the bowel. There was no evidence of hepatic metastases. The bladder, kidneys, and uterus appeared normal. A primary resection and anastomosis were completed.

PROGRESS.—The patient recovered well apart from a localized wound infection, and was discharged home on the eighteenth day. Six weeks after the operation she was enjoying a normal day's activity, her wound was healed, and her bowel action was normal. Eighteen months after her operation she remains well with no abnormal bowel symptoms. There is no clinical evidence of 'squamous carcinoma' elsewhere.

PATHOLOGY.—The macroscopic appearance (*Fig.* 2) was of a rounded, sharply demarcated, nodular plaque of yellowish tumour tissue. The serosa was not involved but one pericolic lymph-node was enlarged, firm, and whitish.

Microscopically the tumour (*Fig.* 3) was quite unlike a colonic adenocarcinoma. It was composed mainly of masses of closely packed cells with, in places, peripheral palisading. Some of the cells contained eosinophilic material which could have represented developing keratin. However, there is no specific stain for keratin and the same appearance could have been caused by colonic mucin.

There were no obvious prickle cells nor any classic epithelial 'pearls'. Therefore a diagnosis of pure squamous carcinoma could not be made. The most

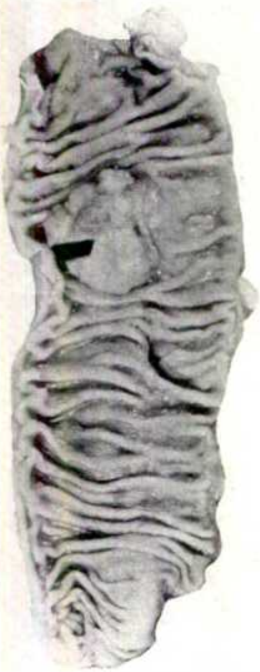

FIG. 2.—Resected specimen of pelvic colon showing localized tumour.

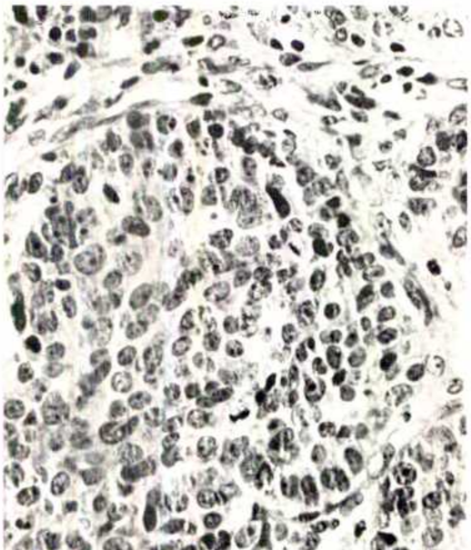

FIG. 3.—Photomicrograph of a section of the tumour showing a discrete mass of typical cells with early peripheral palisading. H. and E. (× 375.)

likely diagnosis was 'squamoid' degeneration in poorly differentiated adenocarcinoma. The possibility of an atypical carcinoid tumour was also considered, but specific staining did not support this.

The enlarged pericolic lymph-node showed infiltration with tumour cells of a similar type.

DISCUSSION

The only previous case of squamous carcinoma of the left colon was described by Thompson (1940). A 32-year-old woman with 'ulcerating squamous carcinoma' of the sigmoid flexure and no evident metastases underwent colonic resection and died 21 months later of local recurrence. However, his case fails as an example of pure squamous carcinoma since the author also reported adenocarcinoma in the neighbouring mucosa. It therefore represents 'squamous metaplasia', though of a mature form with keratinization and epithelial pearls.

Schmidtmann (1919) reported a 65-year-old man with an advanced 'keratinised squamous cell cancer' of the ascending colon with necrotic metastases in the inguinal lymph-nodes. No surgical treatment was attempted and accurate histological details are not available for this case. It may again represent squamous metaplasia, or, in view of the unusual spread to the inguinal lymph-nodes, it may be a rare example of squamous-cell carcinoma at another undiagnosed site which had metastasized both to the colon and to the superficial lymph-nodes.

A squamous tumour of the ascending colon was found by Hicks and Dowling (1955) in a 90-year-old woman. Again no surgical treatment was attempted and the tumour was later shown to have metastasized widely to the liver and intra-abdominal lymph-nodes. The histological features of this tumour were very similar to those of our patient. It too most likely represents squamoid degeneration in a poorly differentiated adenocarcinoma.

No squamous carcinoma of the transverse colon has ever been recorded, although Sanerkin (1968) described a poorly differentiated adenocarcinoma with prominent squamous metaplasia and also stromal ossification.

The longest surviving patient with a squamous carcinoma of the colon was described by Gaston (1967). A 65-year old man had a right hemicolectomy for a tumour of his caecum. No metastases were detected and the patient was in good health 2 years after the operation. Here again typically squamous features coexist with poorly differentiated adenocarcinoma.

The aetiology of such 'squamous' tumours in 'columnar' territory is unknown. The concept of an origin in embryonic cell rests seems to have been largely discredited. The theory of developmental error carries some weight in the region of the transitional epithelium (derived from the cloacogenic membrane) lying between the squamous epithelium of the anal canal and the columnar epithelium of the rectum. Certain 'squamous' cells might extend cephalad beneath the rectal mucosa, and even into the distal colon, but it is difficult to visualize them reaching the ascending colon or caecum. The remaining possibility is that of squamous metaplasia, which occurs frequently in the rectum, usually in response to chronic infection or trauma. Drennan and Falconer (1959) described a patient whose entire rectal mucosa had undergone squamous metaplasia with malignant change in places. However, such metaplasia has never been reported in the colon except in association with a poorly differentiated adenocarcinoma.

Although Hicks and Dowling (1955) did not attribute their case to squamous metaplasia, they did admit that it lacked the features of a well-differentiated mature squamous carcinoma. There was no clear gradation from basal cells to prickle cells with intercellular bridges to keratinous cell nests. They described birefringent areas which were suggestive of keratin and which could be accentuated by fluorochromes. Our case shows a similar cellular pattern. Histological uncertainty will always be found in such tumours until fresh tissue from them can be examined for squamous cells by the electron microscope, or until a stain is found which is entirely specific for keratin.

In 3 of the 4 cases described in the literature the tumour seems to have been advanced. By contrast, our patient had a very localized plaque of tissue in the bowel wall. She had a short history of 1 month and can be classified as 'early' despite the one involved lymph-node.

Surgical treatment was attempted in only 2 previous patients. One patient died of recurrence after 21 months and the other was well after 2 years. Our patient remains alive and well after 18 months with no indication of recurrence and no evidence of primary squamous carcinoma at any other site as far as can be determined.

CONCLUSION

Primary squamous carcinoma of the colon probably does not exist in a form which would satisfy modern histological criteria. The few cases reported to date in the literature probably represent squamous metaplasia or cellular degeneration in atypical adenocarcinomas.

Whether or not squamous carcinoma can affect the colon is to some extent academic. The practical importance is that when a patient is found on sigmoidoscopy to have a tumour of the distal colon with the appearance of squamous carcinoma the diagnosis becomes uncertain. There is a danger of unnecessary delay while searching for a primary site, which in a woman is often suspected to be the cervix. There is even the chance that operation may be denied on the grounds of presumed inoperability.

Acknowledgements.—I thank Mr. W. P. Small for his advice and encouragement, Dr. J. M. Drennan for his histological expertise, and Dr. J. McManus for permission to study a patient under his care.

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REVIEWS AND NOTICES OF BOOKS

Hirschsprung's Disease. By THEODOR EHRENPREIS, M.D., F.A.A.P., Stockholm. 8¾ × 5¾ in. Pp. 175, with 44 illustrations. 1971. Chicago: Year Book Medical Publishers. £6·30.

IT is 85 years since Harald Hirschsprung, Professor of Paediatrics at Copenhagen, reported the clinical features of 2 infants who died of the disease which now bears his name, and which has become the most important and possibly the commonest cause of acute intestinal obstruction in the newborn. The control which paediatric physicians have established over gastro-enteritis has allowed other causes of diarrhoea and vomiting to be recognized more often in the small baby, and of these, Hirschsprung's disease is the most important. This book comes at an opportune time and there is no doubt that it will become the most important and comprehensive source of information about this disease. The whole subject is treated in the well-balanced manner which one would expect from Dr. Ehrenpreis, who for so long has been the foremost European authority on Hirschsprung's disease. He has reviewed the huge mass of published material on the historical aspects, morphology, aetiology, and clinical features, and has appraised calmly the various types of operative treatment on which so much controversy has been lavished since before Swenson and Bill introduced the first effective definitive method of treatment in 1948. There is still much to learn about this disease and its management. In this book what is known so far is collected, arranged, and judged, and no surgeon or physician who has to deal with the newborn infant can afford not to read it again and again.

A Short Textbook. Ear, Nose and Throat. By R. PRACY, F.R.C.S.; J. SIEGLER, F.R.C.S., D.L.O.; and P. M. STELL, F.R.C.S. 8½ × 5¼ in. Pp. 155 + iv. Illustrated. 1971. London: The English Universities Press Ltd. 95p.

THIS is a useful and cheap pocket-book on the surgery of the ear, nose, and throat. It is written in a clear and concise style and is illustrated by some interesting line drawings, many of which are original.

The authors have concentrated throughout the book on those diseases with which the doctor will often have to deal during general practice. Students can carry this book in their coat pocket for ready reference while attending the out-patient clinic on diseases of the ear, nose, and throat.

Die gynäkologischen Operationen. Ninth edition. By HEINRICH MARTIUS, Göttingen, and HUGO HUSSLEIN, Wien. 10¼ × 7 in. Pp. 274 + xi. Illustrated. 1971. Stuttgart: Georg Thieme Verlag. DM.98.

THE first edition of this book by Martius appeared in 1942, and the ninth edition, revised by Husslein, was printed in 1971, which proves that this book is popular among gynaecologists in German-speaking countries. A complete survey of gynaecological operations, abdominal and vaginal, repair of fistulae, etc., is presented, accompanied by many instructive illustrations.

Though urinary incontinence may belong to the working area of the urologist, the descriptions of plastic operations in cases of sphincteral incompetence are of a striking comprehensibility. The technique of resection of the small intestine, colostomy, herniotomy, and appendicectomy can be found in this book; these operations should, if possible, be delegated to the general surgeon. The author rightly does not recommend systematic appendicectomy following abdominal gynaecological operations.

Laparoscopy is regarded as a very valuable diagnostic technique, which is more trustworthy than culdoscopy.

This book is without doubt an excellent technical handbook for everybody interested in operative gynaecology.

Trauma to the Liver. Second edition. By GORDON F. MADDING, M.D., M.S., F.A.C.S., Stanford, and PAUL A. KENNEDY, M.D., F.A.C.S., Stanford. 9½ × 6 in. Pp. 186 + xiv. Illustrated. 1971. London: W. B. Saunders Co. Ltd. £4·05.

THE experience gained during the Second World War and the multiple injuries caused by motor accidents have caused a spate of articles on trauma to the liver both in this country and in America. Added to this, American surgeons have also had extended experience over the years in Korea and Vietnam.

The authors of this monograph had practical experience of cases of liver trauma in the Second World War and this experience was well reported in the first edition of this book. This second edition is a most useful book, for it gives all the facts on liver trauma and the treatment that is required.

The problems of liver haemostasis, lobectomy and liver resection, the use of Gelfoam, and bile peritonitis are all covered in a very practical way.

The line drawings are clear and they enhance the value of the book. There is an excellent bibliography at the end of each chapter.

This book will be of real value to all abdominal surgeons, and as a reference volume on trauma of the liver it could not be bettered. It is Volume III in the series 'Major Problems in Clinical Surgery'.

Die einfachen Kreislaufgrössen beim chirurgischen Patienten. By C. BURRI. 9 × 6 in. Pp. 130 + viii. Illustrated. 1971. Berlin: Springer-Verlag. DM.48.

THIS book offers a survey of the average standards of the blood circulation in normal and pathological conditions. These standards include: the pulse-rate, the systolic blood-pressure, the shock index, which is the quotient of pulse-rate/systolic blood-pressure, the central venous pressure, the blood-volume, and the haematocrit.

Combination of these standards enables the surgeon to regulate the intravenous substitution therapy. Experience proves that overdosing is needed in cases of severe blood-loss to compensate for the lowered central venous pressure. This central venous pressure is measured by intravenous PVC catheters connected with the infusion system in order to regulate the infusion speed in coordination with the central venous pressure.

Thoracic injuries are more quickly accompanied by a lowered arterial tension (and here the venous pressure is an unreliable standard) than abdominal injuries and crushed extremities.

The author demonstrates convincingly that the standards as described are indispensable in the fight against shock, in cases of blood-loss, burns, and septicaemia, and are a great help in the prevention of overdosing.

Bailey and Love's Short Practice of Surgery. Fifteenth edition. Revised by A. J. Harding Rains, M.S. (Lond.), F.R.C.S. (Eng.), Professor of Surgery, University of London; and W. Melville Capper, F.R.C.S. (Eng.), Consulting Surgeon, Bristol Royal Hospital. 9¾ × 6¼ in. Pp. 1296 + xii, with 1592 illustrations. 1971. London: H. K. Lewis & Co. Ltd. £6·50.

This most popular book on surgery has enjoyed a wonderful reputation for over 30 years and more than 259,000 copies have been published. This new fifteenth edition has been most thoroughly revised and new illustrations have made their appearance. There are 1592 illustrations, of which 241 are in colour. This is the ideal surgical book for the student, and we have nothing but praise for it. It is also popular abroad and there are Italian, Spanish, and Turkish editions.

A great credit to British medical literature.

Total Hip Replacement. Edited by Malcolm Joyson, Department of Medicine, University of Bristol, Royal National Hospital for Rheumatic Diseases, Bath, and Winford Orthopaedic Hospital. 9¾ × 6 in. Pp. 152. Illustrated. 1971. London: Sector Publishing Limited. £3·60.

This book contains a series of original papers by experts dealing with total hip replacement.

These authors discuss at some length the design, clinical results, complications, and follow-up of the various forms of hip replacement. Separate chapters deal with Ring, McKee-Farrar, Charnley, and total hip arthroplasty.

Each operation is explained, discussed, and illustrated with radiographs taken before and after the operative procedure.

John Charnley has written a foreword to the book.

The layout of the book is quite original, the main subject being tabulated in bold print at the side of each page; this makes for easy reading.

A useful book for all those who are interested in the reconstruction of the osteo-arthritic hip-joint.

Kurzer Leitfaden der praktischen Infusionstherapie. By W. Seifart. 7½ × 4¾ in. Pp. 179, with 5 illustrations. 1971. Berlin: VEB Verlag Valk und Gesundheit. DM.12.60.

One is pleased to find a good description of fluid and electrolyte disturbances and the measures to be taken to cure them. The tables giving normal values and the standard solutions that ought to be available in a hospital are extremely useful.

The dangers and implications of transfusions of whole blood get the attention that they need; counter-measures are briefly described.

The price is very moderate. The book with its pliable cover is apparently meant—and rightly so—to be carried in the pocket of hospital dresses.

Manuel de l'Aide en Chirurgie. By P. Orsoni. 8⅝ × 6⅝ in. Pp. 126, with 89 illustrations. 1971. Paris: Masson et Cie. 38F.

A most attractive little book that gives us a thorough survey of the surgical assistant's craft. The technique of the various ligatures and sutures is described in considerable detail, simple line drawings illustrating and reinforcing the text. The author also expounds ways of manipulating instruments, such as dressing forceps, scissors, artery forceps, and retractors. Anyone who can master all the variations described will have the legerdemain of a conjuror. The greatest merit of this book is that it gives the beginner a theoretical background, from which he can make a personal selection. It is to be hoped that an English translation will appear before long.

Idiopathic Ischemic Necrosis of the Femoral Head in Adults. Edited by W. M. Zinn, F.M.H., Ragaz. 9½ × 6½ in. Pp. 220 + xii. Illustrated. 1971. Stuttgart: Georg Thieme Verlag. DM.78.

This important paperback is the most comprehensive study of idiopathic ischaemic necrosis of the femoral head in adults that has so far been published. It is the outcome of an international meeting in Switzerland in June, 1968, and the contributors to this book come from far and wide. The book is superbly illustrated throughout; the photomicrographs are excellent.

Every facet of ischaemic necrosis is discussed in detail. Biopsy drilling as a means of early diagnosis of idiopathic ischaemic necrosis of the femoral head is set out in an interesting and practical way.

Legg-Perthes' disease in dogs is debated. Cases of avascular necrosis of the femoral head in rheumatoid arthritis, lupus erythematosis, athrombocytosis, ankylosing spondylitis, gout, cirrhosis of the liver, and kidney transplantation are discussed.

This study of osteonecrosis seems to provide an exciting bridge between clinical orthopaedics, general metabolic abnormalities, and basic science.

Here is an intriguing book full of interesting facts and figures which should prove of interest to all practitioners and clinicians.

Gynaecological Cancer. Edited by T. J. Deeley, M.B., Ch.B., F.F.R., D.M.R.T., Cardiff. 8½ × 5½ in. Pp. 324 + xi. Illustrated. 1971. London: The Butterworth Group. £5.

This book is one of a series of volumes under the general title of 'Modern Radiotherapy'. Since the Second World War the use of radiotherapy in the treatment of various forms of cancer has greatly increased, and this is especially so in the treatment of cancer of the female genital tract.

This volume, with its nineteen chapters contributed by radiotherapists and pathologists from well-known centres in Britain, Sweden, Germany, and America, contains a wealth of information regarding the most modern methods of radiotherapy used in the treatment of gynaecological cancer. The use of hyperbaric oxygen and radiotherapy in advanced carcinoma of the cervix is discussed in detail. A chapter on the value of computers in pelvic dosimetry makes interesting reading.

All who are interested in the treatment of malignant disease of the genital tract in the female will find much of value in this book. The book is a most useful reference volume.

Nouvelle Practique Chirurgicale illustrée. Vol. 4. Edited by Jean Quénu. 10½ × 7 in. Pp. 251. Illustrated. 1971. Paris: Dion Editeurs. 50F.

The present volume is the fourth to appear in the second series of Jean Quénu's illustrated operative surgery. In it we find successively: excision of a cervical rib, Blalock's operation for Fallot's tetralogy, surgical treatment of an arteriovenous fistula, portacaval anastomosis in portal hypertension, correction of a colpocele, and Bricker's transileal cutaneous ureterostomy.

The series is probably familiar to the majority of the surgical readers: pictorial handbooks in which the consecutive stages of an operation are illustrated by serial drawings. The steps taken are small, so that the operation can be followed very easily. The drawings are perfect gems and if operating could be learned from any book this one would have to be compulsory. It can be thoroughly recommended to those preparing an unfamiliar operation, or incidentally to those preparing a demonstration. In the latter case the short introductory remarks preceding each chapter will also be of great help. The value of these books could be definitively improved by giving short bibliographies justifying the particular technique favoured.

Carcinoma of the Bronchus. Edited by T. J. DEELEY, M.B., Ch.B., F.F.R., D.M.R.T., Cardiff. 8½ × 5½ in. Pp. 358 + xi. Illustrated. 1971. London: The Butterworth Group. £7.

CARCINOMA of the bronchus is a very common condition today and the majority of cases are far advanced when they are diagnosed. This being so most cases are treated by some form of radiotherapy. This multiple-author book covers the subject of radiotherapy in cancer of the lung in a comprehensive way. The contributors mostly come from centres in the British Isles but there are also some from Holland, America, Japan, Finland, and New Zealand. The book therefore has a definite international flavour.

This book is one of the 'Modern Radiotherapy' Series, designed to give the established clinician up-to-date knowledge of advances in this field. The contributors are from groups of pathologists, cytologists, physicians, diagnostic radiologists, radiobiologists, and radiotherapists.

Mr. Cleland, the only surgical contributor, writes on the place of surgery in the treatment of cancer of the bronchus. He considers that fewer than 20 per cent of all cases are suitable for surgical excision.

The use of adjuvant chemotherapy and hyperbaric oxygen is discussed at some length. All who are concerned with the treatment of patients suffering from carcinoma of the bronchus will find much of value in this book. As a reference volume it will take pride of place.

Intestinal Absorption and its Derangements. Edited by A. M. DAWSON, St. Bartholomew's Hospital, London. 9¾ × 7½ in. Pp. 161. Illustrated. 1971. London: British Medical Journal, B.M.A. House. £2.

THIS volume contains the papers which were presented at a symposium organized by the Royal College of Pathologists and delivered in London in February, 1971.

The papers cover a wide range, from carbohydrate digestion and absorption to microbiology and immunology.

Protein, iron, fat, and salt and water absorption are all discussed at length. There is a comprehensive list of references at the end of each chapter.

This is a most useful volume for gastro-enterologists. Surgeons who are interested in ulcerated colitis and Crohn's disease will find this a valuable reference book.

Tumors of Bone and Cartilage. Vol. 5. By HARLAN J. SPJUT, M.D., Texas; HOWARD D. DOFFMAN, M.D., New York; ROBERT E. FECHNER, M.D., Texas; and LAUREN V. ACKERMAN, St. Louis. 10 × 7¾ in. Pp. 454. Illustrated. 1971. Washington: Armed Forces Institute of Pathology. No price given.

THIS atlas of tumour pathology is Volume 5 in the second series, and is devoted to tumours of bone and cartilage. A team of pathologists too numerous to mention has been responsible for this excellent book.

Nearly 500 pictures illustrate this atlas and all are of a high quality, but the photomicrographs are superb. The common tumours and the rare ones are all described. Osteoid osteoma is discussed in detail and is well illustrated. Synovial cysts and aneurysmal bone cysts are described and illustrated.

This is an excellent atlas which all pathologists and orthopaedic surgeons will want to possess. A first-class production.

Les Entretiens de Bichat 1971. Edited by P. L. CHIGOT, Trousseau, and A. BELLIN, Bichat. 8½ × 6¾ in. Pp. 408. 1971. Paris: Expansion Scientifique Française. No price given.

IN this book the papers given at the annual conference in Bichat Hospital have been gathered together. As usual there were sessions in general surgery, with eight subdivisions, radiology, gynaecology, and sundry others. As there are about 80 articles dividing 400 pages between them, each article averages a few pages. This allows for no more than rather short summaries. If there were discussions they certainly are not given. There are no illustrations and no references to the relevant literature. Consequently the group of potential buyers of this book will probably be limited to those who actually attended the conferences. In a way this is a pity, for the subjects chosen are certainly topical and cover a wide range. It seems probable that they would arouse keen interest if the nature of these articles could be changed; the great fame of some of the contributors would certainly guarantee that. As it is, the book is no more than a rudimentary attempt at recent advances in surgery and allied subjects.

An Aid to Clinical Surgery. By PETER R. SCOTT, M.B., B.S., F.R.C.S., F.R.C.S. (Edin.), F.R.A.C.S., F.A.C.S., Melbourne. 9½ × 7½ in. Pp. 324 + x, with 60 illustrations. 1971. Edinburgh: Churchill Livingstone. £4.

THIS is a useful book for the student, although its size is rather too large for comfortable reading in a chair. The text is concise and lucid and the illustrations—line drawings—are clear and informative. Much of the subject-matter is considered in relation to commonly encountered symptoms, such as upper abdominal pain, rectal haemorrhage, or nipple discharge.

The price of this book is reasonable.

Clinical Organ Transplantation. Edited by R. Y. CALNE, M.A., M.S., F.R.C.S., Professor of Surgery, University of Cambridge. 9 × 6 in. Pp. 539 + xi. Illustrated. 1971. Oxford: Blackwell Scientific Publications. £8.

THIS book is born of popular demand, for in many countries organ transplantation is becoming more common as the years go by.

Professor Calne is the right person to edit such a book as this, for his experience in kidney and liver transplantation is second to none. He has collected a band of contributors all of whom are known for their interest in the many-sided problem of organ transplantation.

The book is divided into seven parts. Part 1 deals with the general considerations, such as allograft reaction, immunosuppression, organ preservation, tissue typing, and cancer and transplantation. Part 2 is concerned with kidney transplantation, including living-donor nephrectomy, pathology, complications, long-term care and follow-up, and the results of operation.

Part 3 deals with liver transplantation, including the selection of donors, the technique of liver transplantation, haematological management, and postoperative care.

Part 4 is devoted to heart transplantation and describes the operative technique. There are less than 200 cardiac transplants reported from the world literature at the present time.

Part 5 is concerned with lung transplantation. There are far less lung transplants than heart transplants, although the first successful reimplantation of the right lung was carried out over 20 years ago. The technical problems are the main cause of a large number of graft failures.

In Part 6 other organs such as the pancreas, the endocrine organs, and the alimentary tract are considered as possible transplantable organs. Part 7 is devoted to the question of ethics, the law, and the future, and Professor Calne is at his best dealing with these knotty problems.

This volume is a practical guide to organ grafting and it will prove of great value to all those scientists and surgeons who are interested in organ transplantation.

The Polycythemic Disorders. By BARUCH MODAN, M.D., D.Ph., Tel Aviv. $9\frac{3}{4} \times 6\frac{1}{2}$ in. Pp. 177+ix. Illustrated. 1971. Springfield, Ill.: Charles C. Thomas. $26.

THIS is an important monograph which comprises a review of the aetiological, clinical, therapeutic, laboratory, and epidemiological features of the various forms of polycythaemia.

The book is divided into four parts. Part 1 is concerned with the regulation of erythropoiesis and a classification of the polycythaemic disorders. Part 2 deals in considerable detail with polycythaemia vera. The treatment of this disease is not crystallized at present. Some pathologists still believe in phlebotomy, because there are no complications. Others believe in suppression of the bone-marrow. Many substances have been advocated, including benizol, Fowler's solution, Thiotepa, uracil mustard, and Daraprim. Radioactive phosphorus has also been tried.

In Part 3 secondary polycythaemia comes under review, and Part 4 is concerned with pseudopolycythaemia and benign erythrocytosis. Special attention is paid to the nature and degree of association between polycythaemia vera and leukaemia, and to the association with other entities, particularly renal and pulmonary disorders, and benign and malignant neoplasms.

Some excellent photomicrographs are included in this volume.

The author is to be congratulated on writing this monograph because he has covered the subject of polycythaemia disorders in a most interesting way.

There is a very comprehensive list of 849 references at the end of the book.

Diagnosis and Treatment of Abdominal Abscesses. By IRVING M. ARIEL, M.D., F.A.C.S., New York, and KIRK K. KAZARIAN, M.D., New York. 9×6 in. Pp. 322+xxiii. Illustrated. 1971. Edinburgh: Churchill Livingstone. £8.

THIS book presents a comprehensive survey of the various abdominal abscesses and their treatment. The whole wide field comes under consideration, from subphrenic to pelvic abscesses.

The picture has completely changed since Barnard's classic description of the surgical aspects of subphrenic abscess in 1908. Today with the use of antibiotics, modern laboratory tests, radioactive scanning, and improved techniques the diagnosis and treatment of abdominal abscesses have vastly improved and the mortality rate is low.

The various chapters in this book deal with every facet of abdominal abscesses, including those arising from the genito-urinary tract and the female genital organs.

The pros and cons concerning the use of drainage tubes and wicks are discussed at length.

The illustrations throughout the book are well produced and informative.

A useful reference volume.

Angiography. Techniques and Procedures. By JOSEPH E. WHITLEY, M.D., and NANCY O'NEIL WHITLEY, M.D., North Carolina. Pp. 122+x. 1971. Missouri: Warren H. Green. $12.50.

TODAY angiography is one of the essential branches of special diagnostic radiology. This large monograph with an excellent atlas of clear angiograms will be most useful to all clinicians who are interested in vascular diseases or conditions. Neurosurgeons depend to a large extent on cerebral angiograms for the exact orientation of various tumour formations.

Angiography of ischaemia is an important aid in the diagnosis of diseased blood-vessels.

This monograph with its excellent angiograms will take its place as one of the essential books in any medical library.

As a reference volume it could not be bettered.

A Textbook of Nursing. A Compendium of Nursing Knowledge. Eighteenth edition. By EVELYN PEARCE. Pp. 800+xxxvii. Illustrated. 1971. London: Faber & Faber. £3.

IT is sad that Evelyn Pearce did not see this eighteenth edition published, but she died just before it came out. For nearly 35 years Miss Pearce had been concerned in teaching the principles of nursing to a large number of student nurses. Miss Pearce wrote five other books on anatomy, and instruments, and a medical and nursing dictionary. Her name was well known among the medical profession as well as by generations of student nurses.

This eighteenth edition has been entirely revised and rewritten, though the basic pattern of the book has been maintained.

An important new feature is the inclusion of thirty-eight distinguished contributors, all specialists in their particular fields.

Although this textbook does not contain a large number of illustrations, the ones that are included are excellent.

There can be no doubt whatever that this textbook will still retain pride of place in the nursing world.

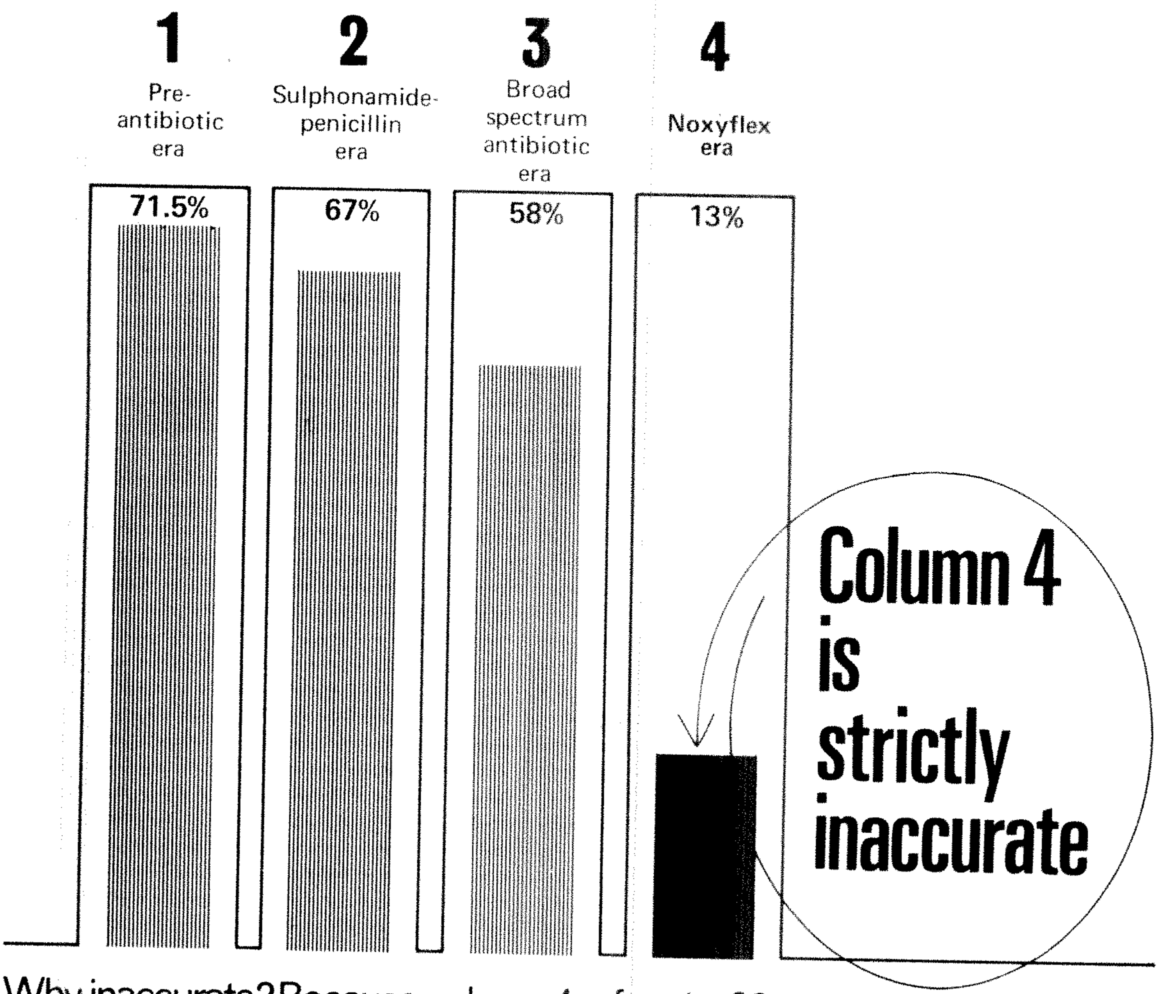
Mediastinoscopy. Edited by OTTO JEPSEN and H. RAHBEH SØRENSEN, Odense. 10×7 in. Pp. 167. Illustrated. 1971. Odense: Odense University Press. $16.50.

THIS volume contains the proceedings of an international symposium which was held at the Odense University in Denmark in June, 1970.

Mediastinoscopy was devised by Professor Carlens of Stockholm in 1959; it is a method of exploration of the superior mediastinum employing a mediastinoscope and biopsy. Its use is mainly in the assessment of resectability in cancer of the lung. It may also be used in the evaluation of sarcoidosis and carcinoma of the stomach.

This book covers the whole range of usefulness of mediastinoscopy and there is an excellent bibliography on this subject covering the years 1959–69.

The graph below compares mortality rates due to faecal peritonitis, era by era.
It is not pedantically accurate because its sources differ. But the point is fairly made.



Why inaccurate? Because column 4 refers to 23 cases of faecal peritonitis which were treated successfully with Noxyflex. But the *3 deaths which occurred were due to causes other than peritonitis - as post-mortem revealed. **The mortality rate due to peritonitis can therefore be regarded as zero.**

* The whole graph, and the causes of the deaths referred to are the subject of the new Noxyflex folder "Why three deaths?" You will receive at least one copy!

When bacterial contamination of the peritoneum is diagnosed or suspected: **Noxyflex**

Geistlich Chester

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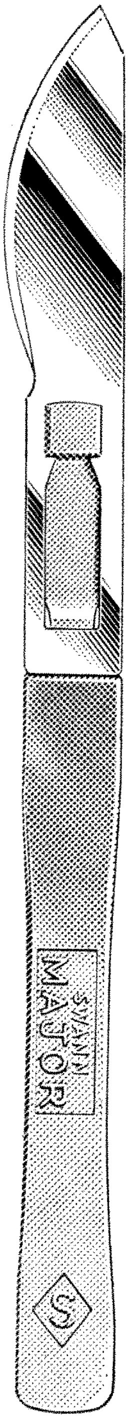

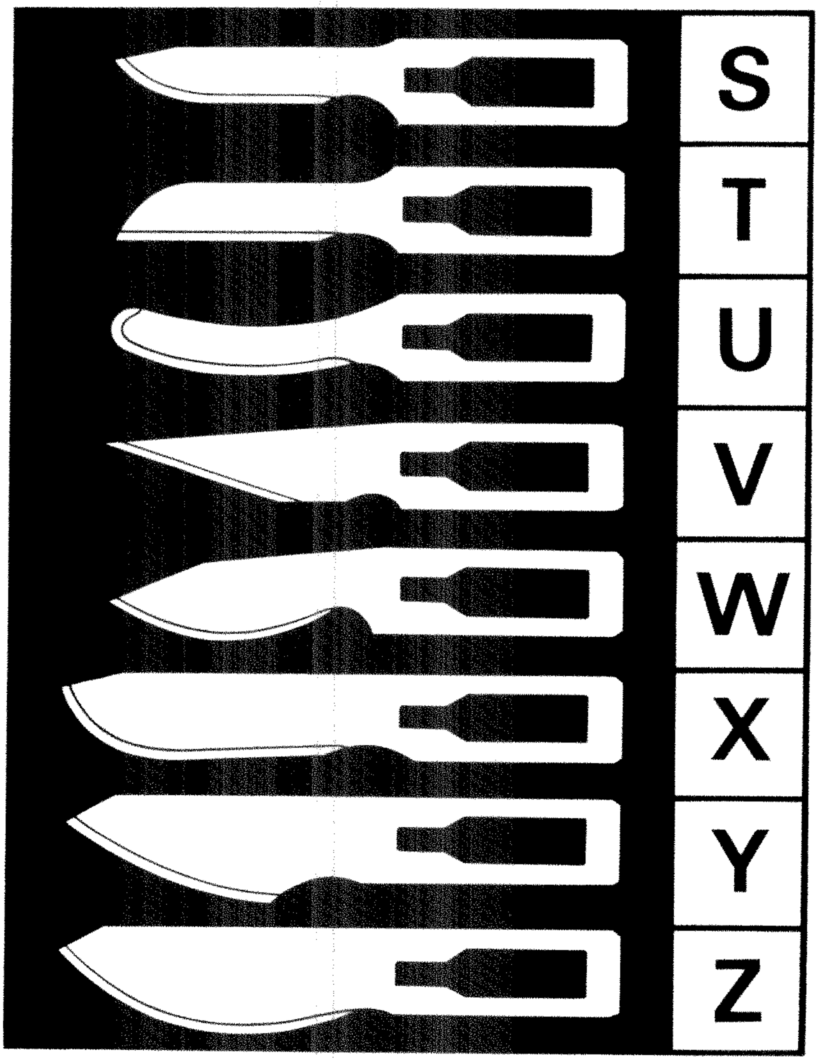

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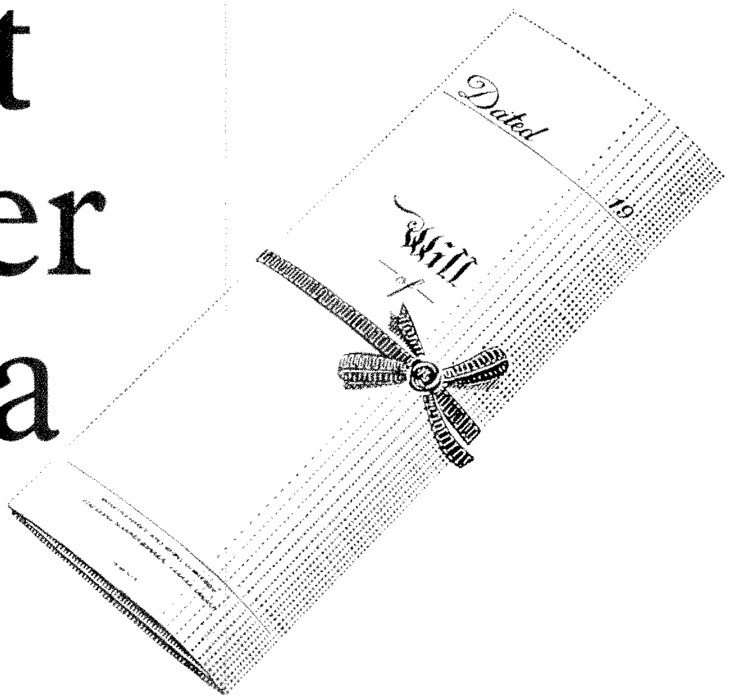

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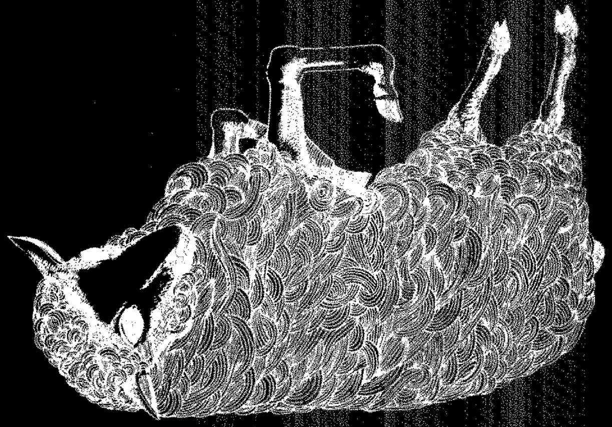

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CONTENTS

ORIGINAL PAPERS

PAGE

SIR CECIL WAKELEY - 417

SIMULTANEOUS FLOW AND PRESSURE MEASUREMENTS IN INTERMITTENT CLAUDICATION *J. D. Lewis, C. Papathanaiou, S. T. Yao, and H. H. G. Eastcott* 418

ATROPHY FOLLOWING TESTICULAR TORSION - *James A. Burton* 422

SECONDARY ENLARGEMENT OF THE MANDIBULAR CORONOID PROCESS *P. A. Bramley and J. E. DeB. Norman* 426

MUSCLE BLOOD-FLOW FOLLOWING INSERTION OF A BY-PASS VEIN-GRAFT IN FEMOROPOPLITEAL OCCLUSIVE DISEASE *Graham Bell and Douglas W. Short* 429

THE RESULTS OF 101 OPERATIONS FOR SYMPTOMATIC HIATUS HERNIA - *C. J. Magarey* 432

THE MOVEMENTS OF THE ADULT *ASCARIS LUMBRICOIDES* - *Milroy Paul* 437

BACTERIAL CONTENT OF THE GASTRIC JUICE - *A. B. Macgregor and P. W. Ross* 443

A METHOD OF REPAIR OF MYELOMENINGOCELES - *Carys M. Bannister* 445

PYLORIC FUNCTION AND GALL-STONE DYSPEPSIA - *A. G. Johnson* 449

A MODIFICATION OF THE FINNEY PYLOROPLASTY - *C. Wastell* 454

AORTO-ENTERIC FISTULAE: AN UNCOMMON COMPLICATION OF ABDOMINAL AORTIC ANEURYSMS *J. P. D. Reckless, I. McColl, and G. W. Taylor* 458

AORTO-CAVAL FISTULAE: AN UNCOMMON COMPLICATION OF ABDOMINAL AORTIC ANEURYSMS *J. P. D. Reckless, I. McColl, and G. W. Taylor* 461

NON-GANGRENOUS ISCHAEMIC COLITIS - *Alastair R. Brown* 463

AN ASSESSMENT OF THE VALUE OF MEASURING UNCOLLECTED GASTRIC SECRETION DURING ROUTINE SECRETION STUDIES IN MAN - *C. W. Venables* 473

TWO UNUSUAL LEG ULCERS - *A. N. Fawcett and D. A. Harrison* 478

ROUTINE OPERATIVE ARTERIOGRAPHY IN ARTERIAL EMBOLECTOMY *G. E. Mavor, M. G. Walker, and D. P. Dhall* 482

CARCINOMA OF COLON SIMULATING CROHN'S DISEASE - *B. J. Stoodley and C. V. Mann* 484

PROSTATECTOMY AND DEEP-VEIN THROMBOSIS *A. N. Nicolaides, E. S. Field, V. V. Kakkar, A. J. Yates-Bell, S. Taylor, and M. B. Clarke* 487

SHORT NOTES OF RARE OR OBSCURE CASES

HYDATID DISEASE OF THE SPLEEN - *M. Torbati* 489

SUBCUTANEOUS RUPTURE OF THE BREAST: A SEAT-BELT INJURY - *D. S. Eastwood* 491

RUPTURED ANGIOMATOUS SPLEEN PRESENTING AS A SEVERE COAGULATION DEFECT *R. C. Heading, D. B. L. McClelland, A. E. Stuart, and T. Hamilton* 492

VISCERAL NEUROFIBROMATOSIS - *Bernadette Curry and Norman Gray* 494

REVIEWS AND NOTICES OF BOOKS

Management of Constipation—ed. *Sir Francis Avery Jones and Edmund W. Godding.* Conférences de Séméiologie Chirurgicale, vol. 5—*Jean Mouïel and Claude Regensberg.* Handbook of Orthoptic Principles—*G. T. Willoughby Cashell and Isobel M. Durran.* Pädiatrischer EKG-Atlas—*J. Stoermer and W. Heck.* A Text-book of X-ray Diagnosis—ed. *S. Cockrane Shanks and Peter Kerley.* Actions of Alcohol, vols. 1 and 2—*Henrich Wallgren and Herbert Barry III.* An Atlas of the Anatomy of the Ear—*Branislav Vidić and Ronan O'Rahilly.* Critical Surgical Illness—ed. *James D. Hardy.* Clinical Heart Disease—*Samuel Oram.* Vascular Disorders of the Intestine—ed. *Scott J. Boley.* Color Atlas of Cancer Cytology—*Masayoshi Takahashi.* Clinical Otology: An International Symposium—ed. *Michael M. Paparella, Albert Hohmann, and John S. Huff.* Concepts of Disease—ed. *Joel G. Brunson and Edward A. Gall.* Aspirin, Platelets and Stroke. Background for a Clinical Trial—ed. *Williams S. Fields and William K. Hass.* Care of the Surgical Cardiopulmonary Patient—ed. *William E. Neville.* Spinal Dysraphism. Spina Bifida Occulta—*C. C. Michael James and L. P. Lassman.* Basic Skills for Surgical Housemen—*Kenneth C. Calman.* Biological Tissue in Heart Valve Replacement—ed. *M. I. Ionescu, D. N. Ross, and G. H. Wooler.* The Complete Handbook for Medical Secretaries and Assistants—*Robert Lee Dennis and Jean Monty Doyle.* Ergebnisse der Bluttransfusionsforschung—ed. *M. Matthes, N. Kleine, and L. P. Hollander.* Geburtshilfliche Operationen—*Heinrich Martius and Gehard Martius* 497

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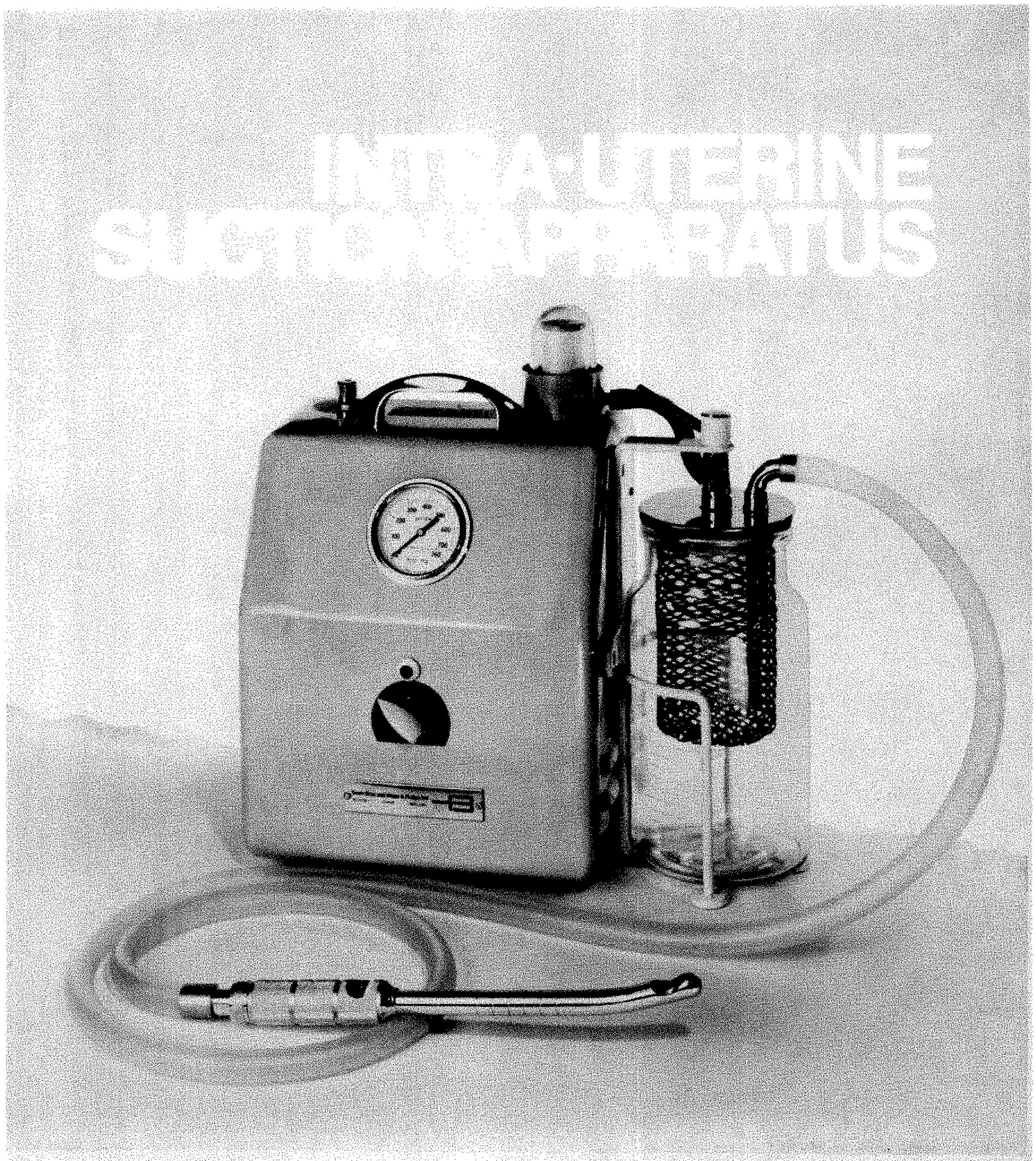

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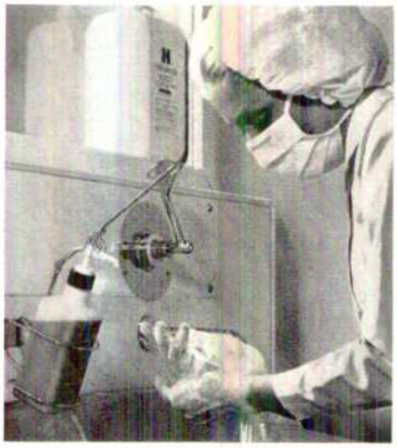

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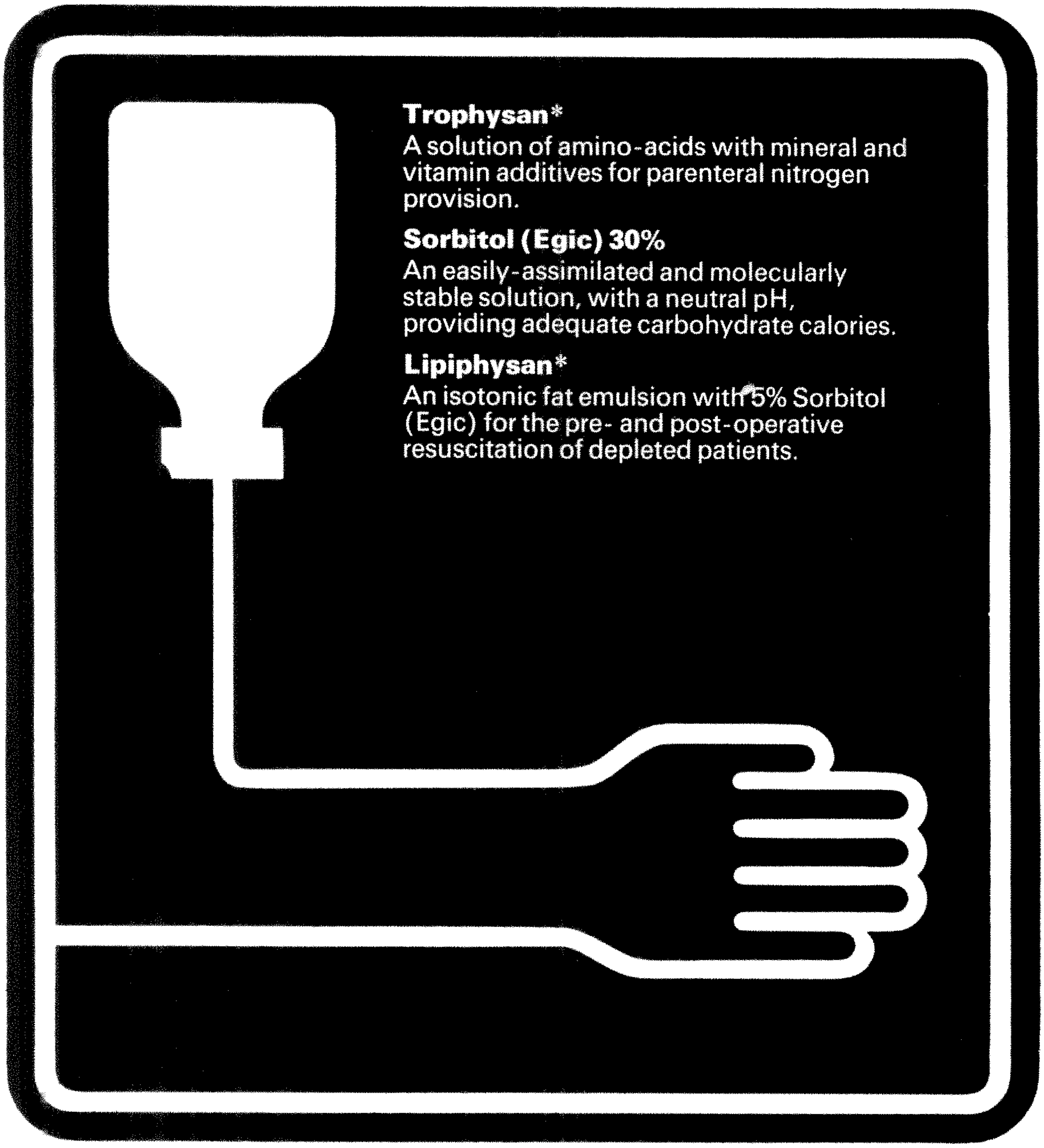

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THE
BRITISH JOURNAL OF SURGERY

Vol. 59 JUNE, 1972 No. 6

SIR CECIL WAKELEY, Bt., K.B.E., C.B.

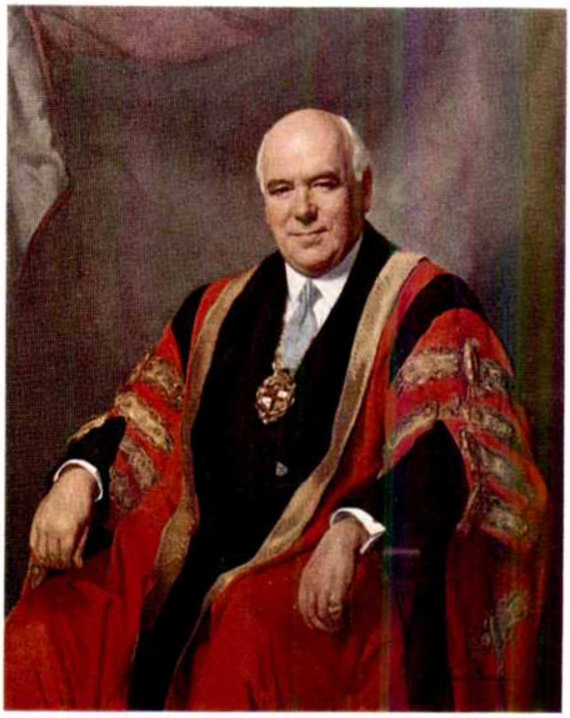
On 24 May, 1972, Sir Cecil Wakeley retired from his office as Editorial Secretary of THE BRITISH JOURNAL OF SURGERY. Some phrases are used so frequently that their meaning becomes dulled, but no alternative will suffice other than to describe this occasion as 'the end of an era'.

Mr. Wakeley was elected to the Editorial Committee in 1933 and to the Executive Committee in 1937. Surgeon Rear-Admiral Wakeley became Editorial Secretary in 1941 and now after thirty-one years the well-loved figure of Sir Cecil Wakeley, Baronet, has attended his last Executive Committee meeting.

Readers of the JOURNAL will be aware of Sir Cecil's multitudinous activities which must have absorbed much of even his indefatigable energy. These were described in a special article in the JOURNAL to commemorate a quarter of a century of service as Editorial Secretary and they need not be related again on this more sorrowful occasion. Nevertheless, the appreciation of the many high offices which he has held and the devotion which he has given to each one of them leaves the ordinary mortal with an overwhelming admiration for the dedication which his whole life has exemplified.

How, one may ask, with all these demands upon his services, has he been able to carry the immense burden which the secretaryship of the JOURNAL entails and how has he been able to do so with the impression that this was his only preoccupation and that he had no other distractions? The question is unanswerable but the facts are these: For thirty-one years Sir Cecil has visited the offices of the JOURNAL once a week and generally more often than that. Last year three hundred and seventy-five articles (more than one for each day of the year) were submitted for approval and, as was his wont, Sir Cecil read them all before circulating them to the appropriate member of the Editorial Board. Furthermore, his remarkable memory enabled him to discuss any article which he might have read some months before with comprehension and critical appraisal.

In addition to this he has taken on the sometimes tedious task of reviewing many of the books presented to the editorial office. In an average year Sir Cecil will have reviewed more than a hundred books with a clarity of perception which might well be emulated by the more discursive reviews in other journals. Last year his total was one hundred and fifty.



Photograph of the painting of Sir Cecil Wakeley which hangs in the Royal College of Surgeons of England (*painted by James Gunn in June, 1957*).

THE BRITISH JOURNAL OF SURGERY has been notable for its insistence on the philosophy of understatement rather than hyperbole and this is what Sir Cecil himself would have wished. It is in keeping with this philosophy to say that Sir Cecil will be missed. He will be missed not only because of his devotion to the duties of his office, for his undeviating service to the objectives of surgery, and his untiring activities in its interest, but because he is a friendly man of kindly understanding, a lovable man, radiating cheerfulness. From the Editorial Committee we bid farewell with grateful thanks to Cecil Wakeley—friend and counsellor.

ORIGINAL PAPERS

SIMULTANEOUS FLOW AND PRESSURE MEASUREMENTS IN INTERMITTENT CLAUDICATION

BY J. D. LEWIS, C. PAPATHANAIOU, S. T. YAO,* AND H. H. G. EASTCOTT
BLOOD FLOW LABORATORY, ST. MARY'S HOSPITAL, LONDON

SUMMARY

In a series of 12 normal and 68 atherosclerotic patients a relationship between flow and pressure changes following moderate exercise correlates well with the anatomical level of the disease. Both flow and pressure studies provide a good objective assessment of the extent of the disease and of the functional results of reconstructive surgery.

MEASUREMENTS of haemodynamic alterations of pressure and flow following exercise in patients suffering from intermittent claudication are essential in achieving a better understanding of the pathophysiology of the disease.

Resting flow values in patients with an occlusion or stenosis of the major vessels in the lower limb have been shown to be of little diagnostic or prognostic value (Landowne, 1942; Edholm, Howarth, and Sharpey-Scharer, 1951; Hillestad, 1963; Yao, Needham, and Irvine, 1970). In order to demonstrate the presence of arterial lesions it is necessary to produce a period of hyperaemia in the limb such that any factor which may limit the arterial inflow via the main vessels or through the collaterals will be revealed. This hyperaemia occurs following ischaemia or, more physiologically, following exercise which produces maximal dilatation of the muscle's intrinsic vascular bed. Reactive hyperaemia following a period of total inflow occlusion is a simple and reproducible method but has mechanical and physiological drawbacks.

The measurement of ankle systolic pressure by means of ultrasound has been shown to be a simple and safe procedure (Yao, Hobbs, and Irvine, 1968). The resting ankle pressure is reduced by the presence of occlusive arterial disease affecting the major vessels (Winsor, 1950; Strandness and Bell, 1965; Carter, 1968; Yao, Hobbs, and Irvine, 1969). This fall of pressure is related to the severity of the disease process (Sumner and Strandness, 1969; Yao, 1970). Furthermore, post-exercise pressure changes are directly related to the severity of the disease and these changes are reproducible (Yao, 1970).

Reliability of measuring muscle blood-flow using the ^{133}Xe-clearance technique has been well established (Lassen, Lindbjerg, and Munck, 1964; Lindbjerg, 1967). Changes in post-exercise clearance have been demonstrated to correlate with the anatomical level and the severity of the occlusive process.

The present study was designed to investigate the relationship between flow and pressure changes occurring in normal limbs and in the limbs of patients who experience intermittent claudication following moderate exercise. The changes of pressure and flow were recorded simultaneously using the Doppler ultrasound and ^{133}Xe-muscle-clearance methods. An indication of the value of objective assessment following reconstructive surgery will be demonstrated. These pressure/flow changes will also be correlated with the anatomical level of the disease.

Table I.—PATIENTS STUDIED GROUPED ACCORDING TO THE ARTERIOGRAPHIC EVIDENCE OF THE LEVEL OF DISEASE

Patients and Level of Disease	*No. of Limbs*
Normal adults (age 30–80 years)	12
Patients with atherosclerotic arterial disease	
Superficial femoral artery	14
Femoropopliteal artery	16
Isolated iliac artery	7
Multiple-segment disease	17
Pre- and postoperative studies	14
Total	80

MATERIALS

Eighty limbs of 75 patients were studied. Twelve limbs were normal and had neither clinical nor ultrasound evidence of arterial disease in either limb. The age range was 30–80 years. The other 68 limbs were of patients who presented with intermittent claudication and were classified according to the anatomical level of the disease as determined by arteriography. A further group of patients who were undergoing reconstructive surgery was examined both before and after operation. *Table I* tabulates the number of limbs according to the anatomical level of the lesion.

METHODS

1. Doppler Ultrasound.—A transcutaneous flow-velocity meter (Parks Doppler Model 806) was used as in the technique described by Yao and others (1969). By placing the flow probe over the dorsalis pedis or posterior tibial arteries a sphygmomanometer cuff was applied just above the ankle. During deflation of the cuff the return of the flow signal indicated the level of the systolic pressure at the ankle.

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[*] Present address: Department of Surgery, School of Medicine, Wayne State University, Detroit, Michigan, U.S.A.

A pressure index was obtained by comparing the ankle and brachial pressures.

2. ^{133}Xe Muscle Clearance.—Muscle bloodflow was measured using the ^{133}Xe-clearance technique as described by Lassen, Lindbjerg, and Dahn (1964); 0·5 mc. of ^{133}Xe dissolved in isotonic saline was injected into the centre of the lateral head of the gastrocnemius muscle of the limb under study, the site having been defined by palpation with the muscle actively contracted. Clearance of the isotope was measured with the Pitman 235 isotope localization monitor. The scintillation probe fitted with a shield was centred over the injection site and was just in contact with the limb but did not distort the skin. Its position was marked for ease of probe replacement. The probe was supported in a clamp and counting could be carried out both in the upright and horizontal positions.

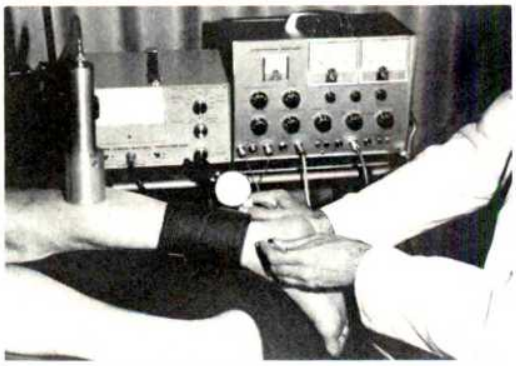

FIG. 1.—Technique of patient monitoring using ultrasound and a Pitman ratemeter.

The particular feature of the ratemeter used was the provision of a percentage scale. Thus, having obtained an initial reading in counts per second, it was possible to adjust the ratemeter so that this count corresponded to 100 on the percentage scale, this then being taken as the starting point for the resting count. The maximum counting rate was 3000 counts per second with time constants of 2 and 12 seconds. Counts were recorded on a linear scale and curves of clearance were drawn.

All patients rested in a supine position for a period of half an hour before any recordings were made. An initial count in counts per second was obtained and converted to 100 on the percentage scale; 4–5 minutes of the resting count were then recorded. The count rarely dropped below 98 per cent, and during this period the resting pressure was also measured. A standard exercise test was used employing a treadmill (Jaeger-Ergotest) without incline set at a constant speed of 4 km. per hour and subjects walked to their maximum walking distance, i.e., the point at which they were forced to stop because of claudication, or they were stopped at 5 minutes.

On completion of the exercise the subjects returned to the supine position. Readings were obtained within a few seconds of stopping the exercise. Recording of ankle systolic pressure was performed simultaneously with muscle clearance until both returned to the pre-exercise level. *Fig.* 1 demonstrates the arrangement of the apparatus.

RESULTS

In all the normal limbs at rest the ratio of the ankle to brachial pressure was equal to or greater than 1; in all the limbs with evidence of arterial disease the ratio was less than 1.

To correlate with the changes of percentage of muscle clearance the ankle-pressure changes were also expressed as a percentage of the resting pressure. The clearance curves were plotted on a linear scale; absolute flow values have not been calculated. *Fig.* 2 demonstrates a typical curve obtained from a normal limb. The ankle pressure showed no change or only a small initial rise following exercise. The Xe-clearance curve showed that during the period of moderate exercise 80 per cent or more of the injected dose was cleared from the muscle and that little further clearance at the end of the exercise period occurred. The curve reached a resting state within 2 minutes in all the normal limbs which were studied.

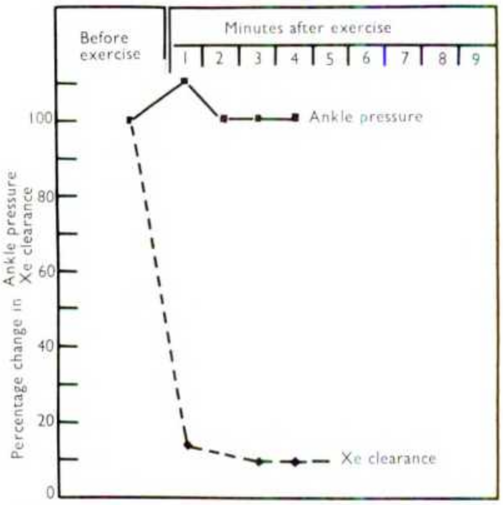

FIG. 2.—Curves showing percentage ankle-pressure change and Xe clearance following 5 minutes' exercise in a normal subject (*Case* R. L., aged 65 years; branchial pressure, 140 mm. Hg; ankle pressure, 140 mm. Hg; initial count, 2400 counts per second; maximum walking time, > 5 minutes).

In all the cases where occlusive arterial disease was present the resting ankle pressure was less than the brachial pressure. Following exercise the Xe-clearance and the ankle-pressure changes departed from the normal pattern. Different types of pressure/flow patterns were observed. When the disease involved a single segment such as a superficial femoral artery occlusion of long duration the changes from normal were only slight. However, when the disease was of recent onset these changes were characterized by a drop of 50 per cent following exercise with recovery to the resting level after 6 minutes. Clearance was reduced to 50 per cent of the resting level during the period of exercise and a further 20 per cent decrease occurred in the next 3 minutes; there was a period of continued hyperaemia before the rise of ankle pressure (*Fig.* 3). A similar situation was seen with an isolated iliac artery lesion (*Fig.* 4).

The flow and pressure patterns obtained from patients with two segments of disease showed more pronounced changes in both parameters (*Fig.* 5). In the presence of femoropopliteal arterial disease the pressure dropped to 40 per cent of the resting level and remained low for a period of 3 minutes, returning to the resting level 8 minutes after exercise. The clearance of Xe during the exercise period (lasting for 5 minutes) was much reduced, 85 per cent remaining at the end of walking, and then there was a period of rapid clearance which lasted for 8 minutes. Again the maximum clearance occurred before the ankle pressure began to return to the pre-exercise level.

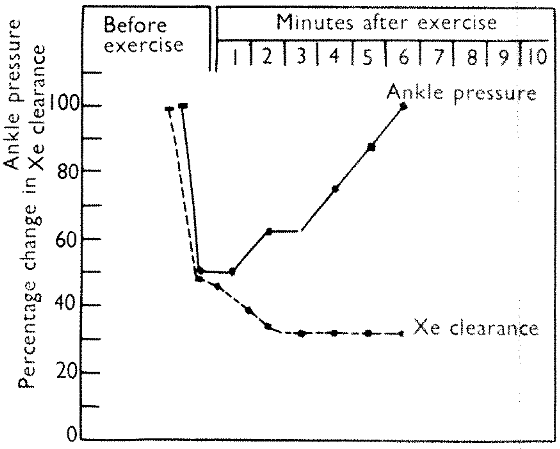

FIG. 3.—Clearance and pressure curves in single-segment disease (*Case* J. S., with a short history of left superficial femoral occlusion; brachial pressure, 120 mm. Hg; ankle pressure, 80 mm. Hg; initial count, 2800 counts per second; maximum walking time, 3 minutes).

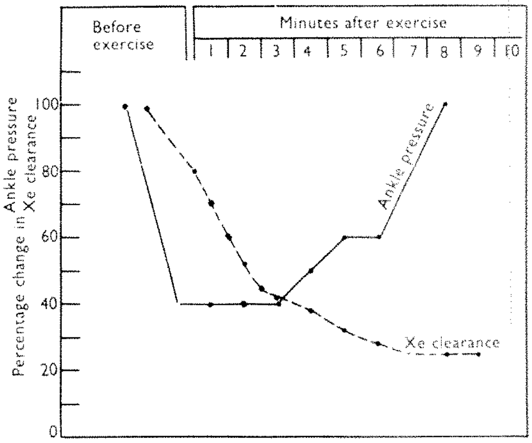

FIG. 5.—Clearance and pressure curves in double-segment disease (*Case* F. D.; left femoropopliteal occlusion; brachial pressure, 180 mm. Hg; ankle pressure, 100 mm. Hg; initial count, 2100 counts per second; mamxium walking time, 5 minutes).

An example of multiple-segment disease where the more severe clinical disability is reflected in the objective measurements is shown in *Fig.* 6. Not only was the maximum walking time reduced markedly but also a greater pressure gradient was seen between the ankle and brachial levels. The pressure dropped to zero after exercise and remained so for 4 minutes and the recovery time was prolonged. At the same time there was minimal clearance of Xe in the initial period followed by a prolonged post-exercise hyperaemia with a return to the resting level 14 minutes after walking had ceased. A similar reciprocal relationship between the Xe-clearance curve and the recovery of ankle pressure was present as seen in the preoperative tracings in *Fig.* 7, where the clearance again increased before there was any marked rise of ankle pressure.

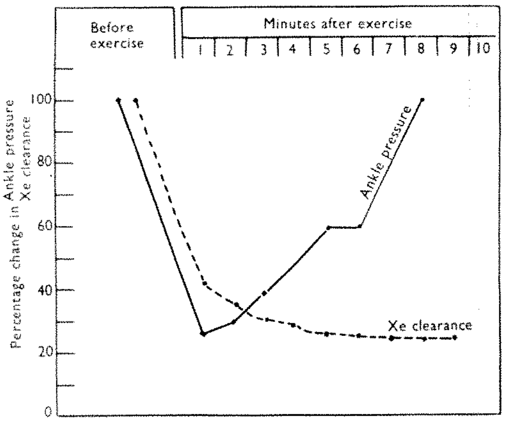

FIG. 4.—Clearance and pressure curves in single-segment disease (*Case* I. M.; left iliac stenosis; brachial pressure, 110 mm. Hg; ankle pressure, 80 mm. Hg; initial count, 2000 counts per second; maximum walking time, 5 minutes).

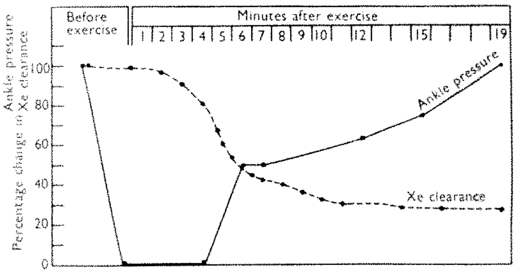

FIG. 6.—Clearance and pressure curves in multiple-segment disease (*Case* E. F.; left common iliac occlusion and superficial femoral artery stenosis; brachial pressure, 140 mm. Hg; ankle pressure, 40 mm. Hg; initial count, 2900 counts per second; maximum walking time, 1 minute).

Both methods provided good objective assessment of the results of surgical treatment of arterial disease. *Fig.* 7 demonstrates the clearance and pressure changes before and after reconstructive surgery in a patient with aorto-iliac occlusion. The preoperative curves indicated moderate disease with delayed recovery of both indices. After successful aorto-femoral artery bifurcation grafting the pressure/flow pattern had reverted to normal. *Fig.* 8 shows the results obtained in a patient with severe two-segment disease which was converted to a single-segment lesion by surgery. The patient had an iliac artery occlusion plus a femoropopliteal artery occlusion and the inflow was increased by insertion of a femoro-femoral cross-over graft which resulted in marked subjective improvement. This was confirmed by the improvement of the pressure and flow patterns although some impairment remained. The benefit of changing a multiple lesion to a single lesion is well documented by these studies.

Fig. 9 demonstrates the distribution of the Xe-clearance patterns according to the anatomical level of the disease.

DISCUSSION

In the normal limb the blood-flow through muscle tissue during a period of moderate exercise is such that there is a minimal post-exercise hyperaemia and little or no change in the distal pressure. Normally a slight increase is seen. These facts were confirmed by the Xe-clearance curves and ankle-pressure patterns obtained in the normal subjects in this study. Maximum clearance occurred during the exercise period with minimal post-exercise hyperaemia and the resting level was reached within 2 minutes. These findings confirm that muscle blood-flow is always adequate during a period of moderate exercise in normal limbs.

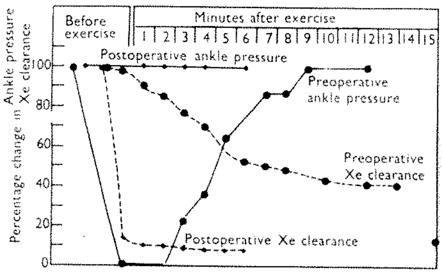

FIG. 7.—Pre- and postoperative curves showing reversion to a normal pattern following an aortofemoral bifurcation graft (*Case* F. A.; aorto-iliac disease corrected with an aortofemoral bifurcation graft. Before operation: brachial pressure, 160 mm. Hg; ankle pressure, 80 mm. Hg; initial count, 2800 counts per second; maximum walking time, 1 minute 15 seconds. After operation: brachial pressure, 150 mm. Hg; ankle pressure, 150 mm. Hg; initial count, 2800 counts per second; maximum walking time, 4 minutes).

In the presence of arterial occlusion an increased resistance to flow is present. Flow in the limb during or after exercise is distributed inversely according to the resistance: maximum resistance to flow is provided by an occlusion in the major artery; minimal resistance occurs in the muscle bed proximal to the diseased segment. With the demand by the proximal exercising muscle the resistance is lowered so that there is a fall of the distal pressure. Patients with a single anatomical level of occlusion in this study all showed a fall of distal ankle pressure together with a reduced muscle clearance of 50 per cent. When there are two anatomical levels of occlusion the picture becomes more complex. Following exercise, blood-flow has to traverse two collateral networks which have a relatively high resistance to flow as compared with the normal inflow tract. A profound drop of ankle systolic pressure and cessation of muscle clearance in the initial period were the common findings. This pattern invariably indicates the presence of severe arterial insufficiency.

The method of measuring muscle blood-flow using ^{133}Xe clearance has been widely applied for studying the effect of occlusive vascular disease affecting the lower limb (Lassen and others, 1964; Lassen and Kampp, 1965; Lindbjerg, 1965, 1967). The method has shown good correlation with venous occlusion plethysmography and with direct blood-flow measurements in the isolated gastrocnemius muscle of the cat (Lassen and others, 1964; Prerovski, Kjellmer, Tonnesen, and Lindbjerg, 1967). Using the ^{133}Xe-muscle-clearance method Alpert, Larsen, and Lassen (1968) were able to show a similar ability to distinguish between single- and multiple-segment disease by using the clearance patterns obtained following exercise. The changes of ankle systolic pressure measured by digital plethysmography in patients with occlusive arterial disease have also been reported by Strandness and Bell (1965).

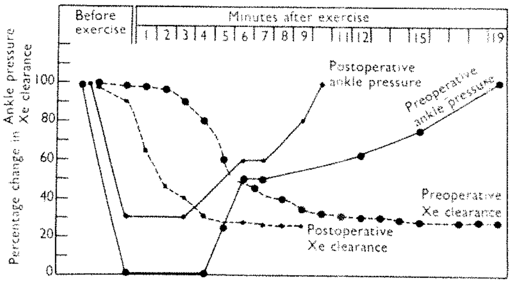

FIG. 8.—Pre- and postoperative curves with single-segment correction in double-segment disease (*Case* E. F.; details of the preoperative state are shown in *Fig.* 6. After a femorofemoral cross-over graft: brachial pressure, 140 mm. Hg; ankle pressure, 100 mm. Hg; initial count, 2700 counts per second; maximum walking time, 4 minutes).

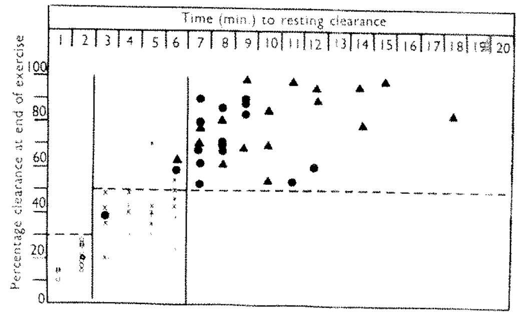

FIG. 9.—Distribution of Xe clearance related to the anatomical level of disease: ×, superficial femoral; i, isolated iliac; ●, femoro-popliteal; ▲, aorto-iliac; ○, normal limb.

The present study has demonstrated the relationship between Xe clearance from the calf and the ankle-pressure changes occurring in the lower limb using two independent techniques but measured simultaneously. Previous work (Yao, 1970) has shown the ability to separate normal legs from those with single- and multiple-segment disease using the ultrasound technique to measure ankle pressure alone before and after exercise. The present work has shown that there is also a good correlation between the clearance patterns using radioactive Xe and the anatomical levels of the disease, with clear distinctions between normal legs, and those with single- and multiple-segment disease. In patients with intermittent claudication this shows that progressively less flow occurs during the exercise period, as represented by the percentage clearance of Xe at the end of this period, and that with more extensive disease the onset of the hyperaemia becomes increasingly delayed and of greater duration. When there was extensive disease the flow was grossly inadequate, sometimes ceasing, and the subsequent recovery was very delayed. The relationship between calf Xe clearance and ankle pressure following exercise is constant and reproducible. In the presence of a stenosis or occlusion there was a fall of both flow and pressure distal to the lesions following a period of exercise. The magnitude of such a fall in both parameters was related to the anatomical level and to the extent of the disease process, being least in single-segment disease and more pronounced as the number of segments involved increases or the disease extends proximally. With extensive disease there is little or no clearance from the calf muscle during or for some minutes after the cessation of exercise, this being associated with a profound and prolonged drop in ankle pressure. The converse is seen in localized disease.

The sequential relationship between flow in the calf and pressure at the ankle following exercise in claudicants has recently been studied by Sumner and Strandness (1969) using venous occlusive plethysmography. Distal pressure measured simultaneously at the ankle by a strain gauge placed around the toe was found to have an inverse relationship with the calf blood-flow. Three types of pressure and flow patterns were obtained which correlated well with the anatomical level and severity of the disease. As in their study an inverse relationship between pressure and flow was also demonstrated in the present report. The onset of maximum clearance (being directly related to the maximum hyperaemic flow) appeared to commence and reach the maximal level before any appreciable rise in ankle pressure occurred. Thus the changes in the two parameters are related to each other and in the same way to the extent of the disease process.

Successful reconstructive surgery converts these clearance patterns to normal and is an indication of the value of this method for assessing the results of surgery. It is apparent that useful information about the effect of the arterial lesion may be obtained from the study of the clearance curves without the need for the measurement of absolute flow values. Because of the simplicity of the Doppler ultrasound method and its close relationship with muscle clearance the Doppler ultrasound method of measuring systolic pressure would appear to be the method of choice as a non-invasive technique to study the functional status of the occlusive process.

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ATROPHY FOLLOWING TESTICULAR TORSION

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SUMMARY

A personal series of 17 cases of torsion of the testis collected over a 3½-year period is reviewed. The incidence is seen to be low in the general population but misdiagnosis is common in the acute condition. The relevant embryology, histology, and signs and symptoms of the condition are described. A number of the patients had unilateral testicular atrophy following a previously misdiagnosed torsion years earlier. Their subsequent management is described. The differential diagnosis is briefly mentioned.

Surgical textbooks would have us believe that torsion of the testis is not a common condition. Indeed, Wheeler and Clark in 1952 collected only 9 cases out of 40,000 admissions to an American hospital. In a further study of 100,000 admissions to a general hospital over a 13-year period only 10 cases of torsion were seen and treated. Reviews from this country would suggest a higher incidence than this and it would perhaps be more correct for the textbooks to state that the condition is fairly uncommon but is much more likely to be incorrectly diagnosed than correctly diagnosed and treated. The situation is really quite serious, for if the condition is not recognized for what it is at the first consultation it may well be too late to initiate effective treatment at the second or subsequent consultation even if it is then recognized. In one of the studies mentioned previously the time at which hospital presentation was made ranged between 24 hours and 6 months, i.e., in all cases the condition had been present certainly longer than 20 hours.

Over the past 3½ years, both in hospital and student health practice, I have been impressed by the number of times that I have seen the acute condition incorrectly diagnosed and also by the results of misdiagnosis years previously in men with unilateral testicular atrophy. As medical officers to a student health service of 5500 students, we have an annual intake of some 1500 new students, about 70 per cent of whom are male. The students register with us as their general practitioners and we therefore receive their National Health Service record from the family doctor. We thus draw on this large number of practices from all over the country each year. We do not undertake routine medical examination of all new students and the real incidence of atrophy following torsion in this population is therefore unknown. From the figures quoted previously it will be apparent that the number of cases of testicular torsion that any one general practitioner may see in a year or even in a lifetime of practice will be very small. This preamble might serve to explain the origin of the cases presented here.

The condition of torsion was first described by a Frenchman, Delasiauve, in 1840, who found gangrenous changes in an undescended right testis which he had mistaken for a strangulated hernia. At operation he noted that the blood-supply to the testis had been compromised by the torsion of the cord. The condition was first described in this country some 50 years later (Nash, 1893).

EMBRYOLOGY

It may be helpful at this stage to review the relevant embryology since this will help in understanding the condition and the rationale of its treatment.

Between the third and ninth months of foetal life the retroperitoneal testis descends from a lumbar to a scrotal position and follows the preformed pathway of the processus vaginalis through the anterior abdominal wall into the scrotum.

During its entire descent it lies dorsal to the posterior peritoneum of the abdominal cavity and the processus vaginalis but ventral to the posterior lining fascia of the abdominal cavity. The descent occurs as a result of (1) differential growth at various levels of the trunk, (2) actual descent, and (3) pull on the inferior pole by the gubernaculum.

On reaching the scrotum it is usually held firmly by the scrotal ligament, which is the remnant of the gubernaculum. Most of the testis becomes surrounded by the tunica vaginalis, but the posteromedial portion remains outside the sac and becomes adherent to the scrotal septum by means of loose areolar tissue. This forms two stabilizing attachments: the scrotal ligament and the extravaginal testicular attachment to the scrotal septum.

Torsion in the normally related testis therefore rarely occurs. The mesorchium is the posteromedial extravaginal attachment of the testis to the scrotal septum. It contains the blood-vessels and the vas deferens. It extends from the superior pole of the testis to approximately 2 cm. from the inferior pole. The tail of the epididymis is usually a part of the mesorchium and therefore has tunica vaginalis on only a portion of its anterior surface. It has been shown that when torsion occurs the tunica vaginalis invests not only the testis but also the epididymis and the spermatic cord above the attachment of the cord to the testis. This condition is usually found on both sides.

Anatomically, the causes of torsion are:—

1. An unusually capacious tunica vaginalis.
2. Absence of the gubernaculum testis and a posterior mesorchium.
3. Absence of the scrotal ligament.
4. Abnormal length and loose attachment of the intravaginal portion of the cord.
5. A combination of these anomalies with imperfect testicular descent.

A review of the literature reveals that 90 per cent of the patients with torsion of the testis lose the testis: 80 per cent by orchidectomy and 10 per cent by subsequent ischaemic atrophy. The main reason for this excessive wastage is delayed or incorrect diagnosis. This is certainly confirmed by the present series.

HISTORY

In the acute episode there is a sudden onset of severe testicular pain. In most acute cases there is a history of recurrent testicular pain, not of such severity as in the acute episode but affecting the same side, and this is probably due to self-limiting, incomplete torsion previously. Urinary symptoms are usually absent. The patient may present with a history of recurrent pain when actually free from discomfort and it is important to diagnose correctly the origin of the pain if the acute episode is to be avoided later.

SIGNS AND SYMPTOMS

The testis of the affected side is usually drawn up towards the inguinal canal and will be tender to a variable degree.

A diagnostic physical sign in recurrent cases is a transversely lying testis when the patient is examined standing up. In the acute case, if the patient is examined standing the testis of the other side will probably be found to be lying transversely also. The onset of the pain may be related to varying degrees of trauma, riding a bicycle, or falling in the bath, or may awaken the patient from sleep. Determination of the position of the epididymis may be helpful. In torsion it will usually be found in some position other than the posteromedial position in relation to the testis. Elevation is said to accentuate the pain in torsion and to relieve it in epididymitis (Prehn's sign). The pain may be cited as being in the scrotum or may be experienced as referred pain along the ilio-inguinal nerve distribution. This is particularly important to recognize in intermittent cases as this seems to be one of the clues to the correct diagnosis which is frequently misinterpreted. The pain is usually very severe and is of sudden onset. It becomes more severe and within an hour or so the testis starts to swell and the scrotum of the affected side becomes red and oedematous. This is the most misleading of all the physical signs and gives rise to the most frequent diagnosis of epididymitis. Interestingly, the longer the torsion is not recognized the more it comes to look like an epididymitis, which lulls the doctor into a false sense of security. He thus exhibits antibiotics and waits. This is then the beginning of the end as far as the testis is concerned. After several hours the patient usually develops a low-grade pyrexia which again falsely confirms the doctor's suspicions of an infection. In some of the cases of proved torsion that I have seen there has been pyuria and microscopic haematuria in a sterile urine. In 2 acute cases there was also an acute mucoid urethral discharge, probably a feature of congestion. Dysuria and frequency, however, were not present except in 1 case during the acute episode.

THE MECHANISM OF TESTICULAR INFARCTION

Ormond (1938) showed that the first effects of rotation of the testis are flattening of the veins of the cord and partial obstruction of the venous return; then as the rotation continues there is obliteration of the veins followed by obliteration of the artery. The effect on the testis depends on the degree of rotation. If there is incomplete obliteration there will be congestion and oedema, especially of the epididymis which is more distensible than the testis. If venous return is entirely obstructed congestion is greater and necrosis occurs in a short time. Prompt infarction occurs if the artery is obliterated.

Dog experiments have shown the following results:—

1. Spermatogenic cells were slightly damaged after 2 hours, severely damaged after 4 hours, and eliminated after 6 hours of ischaemia.
2. Leydig cells were severely damaged after 8 hours of ischaemia and eliminated after 10 hours.
3. Ten hours or more of ischaemia resulted in nearly complete fibrotic replacement of the testis.

At this point it should be recalled that the time of presentation at hospital of the cases quoted previously ranged between 24 hours and 6 months.

The following are summaries of the case histories in the present series. The first 8 cases are of acute torsion seen in both hospital and student health practice, the remainder being non-acute problems at the time seen.

CASE REPORTS

Case 1.—J. K., aged 15 years. This patient presented complaining of sudden onset of left testicular pain 3 hours previously whilst in bed. He had a 6-month history of intermittent pain on the same side which had been presented to the doctor but had not been recognized. On examination acute torsion was present and was manipulated. Bilateral fixation was done later.

Case 2.—R. H., aged 19 years. This patient presented complaining of sudden onset of left testicular pain 1 hour previously following a fall in the bath. On examination he had a very swollen, red, tender scrotum requiring intravenous morphine to allow palpation. The testis was very high in the scrotum. It was manipulated with immediate descent and relief of the pain. The testis was normal the next morning apart from a small secondary hydrocele. The patient was readmitted later for bilateral fixation.

Case 3.—K. D., aged 23 years. This patient was admitted complaining of right testicular pain of 1 hour's duration. A twist could be felt in the cord and this was manipulated. The patient subsequently had bilateral fixation.

Case 4.—T. L., aged 16 years. This patient was seen 6 hours after he had experienced acute onset of left testicular pain whilst standing at a bus stop. The testis was manipulated and subsequently both sides were fixed. A large mesorchium was found at operation.

Case 5.—C. B., aged 21 years. This patient presented complaining of left testicular pain of 36 hours' duration. The testis was manipulated and subsequently fixed. The patient emigrated 6 weeks later so that no follow-up has been possible.

Case 6.—R. N., aged 22 years. This patient developed acute right testicular torsion whilst on teaching practice. He was taken to hospital where he was given paracetamol and ampicillin and sent home by ambulance. *En route* the pain became worse and he was seen 3 hours after onset when the testis was manipulated and subsequently fixed. Urine examination at time of the acute episode showed: epithelial cells, +; leucocytes, ++; red blood-cells, +; hyaline casts, +; the urine was sterile on culture.

Case 7.—A. B., aged 20 years. This patient had experienced sudden onset of left testicular pain 4 hours previously. On examination there was a tender swelling at the upper pole of the testis. This was clinically diagnosed as a torsion of the hydatid of Morgagni, which was proved at operation.

Case 8.—D. H., aged 17 years. This patient presented complaining of sudden onset of right testicular pain 4 days previously. This had been treated at this time as an infection. On examination a very swollen and oedematous scrotum was seen. The patient had a temperature of 37° C. on admission. At operation the testis was necrotic and was removed. The other side was fixed.

Case 9.—C. H., aged 20 years. This patient presented with a history of intermittent right testicular pain over the previous 4 years. On examination both testes were found to be lying transversely. These were fixed and there has been no further pain.

Case 10.—I. F., aged 20 years. This patient presented with a history of intermittent left testicular pain, the right testis having become atrophic following a 'right epididymitis' at the age of 15 years. The remaining testis was lying transversely and was fixed. There has been no further pain.

Case 11.—J. C., aged 24 years. This patient presented complaining of intermittent right testicular pain for 6 months. The left testis was atrophic and the right side was fixed as this was lying transversely. There has been no further pain.

Case 12.—J. S., aged 21 years. This patient presented complaining of intermittent left testicular pain on walking for 3 weeks. The pain was referred along the ilio-inguinal nerves and disappeared on lying down. The testes were lying transversely and he has had no further pain following bilateral fixation.

Case 13.—B. M., aged 21 years. This patient presented with right testicular atrophy following 'epididymo-orchitis' at 15 years. The patient was seen on the third day of the episode at hospital where this diagnosis was again made. Examination showed a transversely lying left testis which had not been fixed. This was then done.

Case 14.—J. H., aged 22 years. This patient presented complaining of left testicular pain following a vacation job which had involved lifting. No hernia was present. The right testis was atrophic following a torsion at the age of 13 years which had been diagnosed as such and had been treated conservatively. It had been hoped 'that the resolution of his large hydrocele would fix the testicle to the scrotum to prevent a recurrence'. The left testis was fixed urgently at the age of 22 years.

Case 15.—M. P., aged 22 years. This patient presented with right testicular atrophy. He had had a painful swelling of the right testis at the age of 14 years and had been given chloramphenicol. He had then developed some dysuria and had been sent to hospital where it was thought that he had a 'cellulitis of the scrotum' and chloramphenicol had therefore been continued for a further 5 days. When next seen 10 days after the onset, the swelling had become much larger. The swelling had then been aspirated but no fluid had been obtained. Subsequently it had been incised, when again no fluid had been found. The patient had been readmitted 10 days later for exploration when a necrotic testis had been found and removed. The correct diagnosis had then been made and it had been suggested that he should wait and see if pain developed on the other side and if it did, he should be admitted urgently for fixation. He had had no pain, but underwent prophylactic fixation the week after he had been seen on the present occasion.

Case 16.—J. L., aged 21 years. This patient complained of intermittent left testicular pain over a 2-year period and was found to have bilateral transversely lying testes which were subsequently fixed at operation.

Case 17.—D. A. B., aged 19 years. This student complained of a painful swollen right nipple of sudden onset. He had a tender subareolar plaque. On questioning about testicular swelling he said he had not noticed any since he had had 'orchitis' at the age of 16 years. He now has an atrophic right testis, and a transversely lying left testis. The diagnosis in hospital at that time had been 'non-specific orchitis' and it had been hoped that it would settle on antibiotics. This was undoubtedly a missed torsion.

DISCUSSION

In Angell's (1963) series of 16 acute cases all had a fever which ranged from 36·7° C. (99° F.) to 39° C. (103° F.). Dysuria and urethritis were absent in all the cases. In only 2 acute cases in the present series where the testes were necrotic was a fever seen (*Cases* 8, 15). In 1 case there was a history of dysuria and this was only in the acute episode (*Case* 6). In the acute cases a mucoid discharge commonly appeared at the urethral meatus and this was probably a congestive effect.

In Angell's (1963) series those cases that were admitted with 'epididymitis' and subsequently were seen to have torsion were 7 in number. These had the urine cultured, only 1 of which contained pus cells, and all the specimens were sterile. In the present series 2 of the 3 acute cases that had the urine examined immediately after manipulation had pyuria; one also had microscopic haematuria. Both these patients had previously taken an aspirin-containing compound and the urinary findings may be simply the result of this. When re-examined 24 hours later the urines contained no such cells and remained sterile throughout.

DIFFERENTIAL DIAGNOSIS

1. **Acute Epididymitis and Orchitis.**—In epididymitis the pain is not so sudden or so severe as in torsion. There is usually evidence of infection in the urine or prostate, or a history of recent urethritis.

In epididymitis the tenderness is maximal at the epididymis whereas in torsion the whole mass is uniformly tender. There is usually tenderness and swelling of the vas deferens in epididymitis whereas in torsion this may not be a feature. Furthermore, at the age at which torsion is common, epididymitis is uncommon.

2. **Mumps Orchitis.**—There will be no previous history of mumps. There may be a history of recent parotitis, but mumps in adults and adolescents may present initially as orchitis. However, in mumps orchitis the swelling does not involve the cord.

3. **Hydrocele, Spermatocele, and Haematocele.**—The first two of these should not present much difficulty in the differential diagnosis. In traumatic haematocele a torsion may be present as well and careful examination is required clinically or subsequently at operation.

4. **Strangulated Hernia.**—Intestinal obstruction will supervene as will clinical shock.

5. **Thrombosis of the Pampiniform Plexus.**—Here there are signs of haematoma and a history of slow development of the pain.

6. **Testicular Neoplasm.**—The history will usually rule out torsion as the cause of the pain and swelling.

7. **Torsion of the Hydatid of Morgagni.**—Swelling is much less than in testicular torsion and the tenderness is localized to the upper pole of the testis. In the only 2 cases that I have seen the infarcted hydatid could be clearly observed beneath the skin as a pea-sized, black mass.

MANAGEMENT

From the cases quoted it is clear that the management in the majority of acute cases could be improved. The correct management depends initially on the doctor of first contact making the correct diagnosis or at least suspecting the condition.

Having made the correct diagnosis in the acute case, the testis must be untwisted immediately and fixed so that the condition does not recur. The opposite side should be similarly fixed since the abnormality is bilateral.

The testis may be untwisted at urgent operation or may be manipulated into the normal position and subsequently fixed electively. Manipulation is described below. Where the testis is obviously non-viable, orchidectomy is the only course, but the opposite side should undergo prophylactic fixation.

In recurrent cases bilateral fixation is the only way of conserving the testes and avoiding the acute episode.

In the acute cases in this series it was possible to manipulate the affected testis into the normal position and therefore restore its blood-supply. This has obvious advantages. It immediately relieves the patient of his symptoms, the pain disappears dramatically, and the testis descends in the scrotum. It is effected by rotation of the testis on the affected side, towards the midline, i.e., clockwise on the left side and anticlockwise on the right side when viewed from the front.

This is advantageous to the patient when awaiting anaesthesia and converts the operation from an emergency to an elective procedure. Intravenous morphine was necessary in 1 case only. Even under narcotic analgesia there was no doubt from the physical signs that the testis had been untwisted.

There are no fatal cases of torsion of the testis recorded in the literature, the most serious and earliest complication of the condition being necrosis following misdiagnosis.

Acknowledgements.—I should like to record my thanks to Mr. D. J. Robertson, Surgeon, Royal Hospital, Sheffield, for his help in treating these patients and for his encouragement in the production of this paper.

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SECONDARY ENLARGEMENT OF THE MANDIBULAR CORONOID PROCESS

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SUMMARY

Enlargement of the coronoid process of the mandible is a rare cause of limited jaw movement.

Primary causes fall into two categories: benign tumours and developmental hyperplasia.

Two cases of clinically important enlargement of the coronoid process secondary to other long-standing causes of difficulty in opening the mouth are described.

It is suggested that significant appositional bone growth secondary to abnormal stresses mediated by the tendon of the temporalis muscle does occur.

IF the coronoid process of the mandible becomes enlarged its anterior surface may strike the posterior surface of the malar process of the maxilla causing an obstruction to mouth opening. Attention to this unusual cause of limited mouth opening was first drawn by Shackleford and Brown (1943). Since that time at least 25 other cases have been reported. Osteoma, osteochondroma, hyperplasia, exostosis, and developmental enlargement are all mentioned as primary causes for coronoid enlargement.

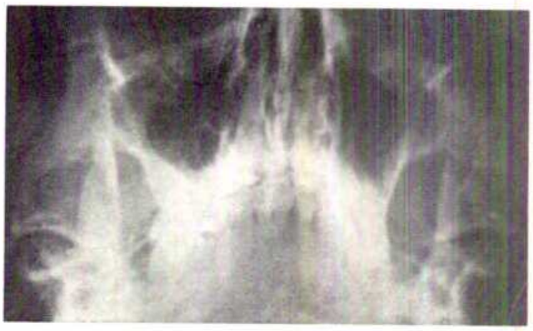

FIG. 1.—*Case* 1. Occipitomental radiograph showing enlargement of both coronoid processes of the mandible. The right side is much larger than the left.

Two cases are presented here which suggest that significant enlargement of the coronoid process of the mandible may occur secondary to another cause of limited movement of the mandible. It will be contended that secondary enlargement of the coronoid process should be considered as a possible complication in cases of long-standing limitation of movement due to other causes.

CASE REPORTS

Case 1.—D. G. was a 24-year-old pharmacist who had been perfectly fit and had had regular and uneventful dental treatment over the years. Neither he nor his dental surgeon had ever noticed any limitation of jaw movement until February, 1965. At this time he had developed an 'abscess' in relation to a left mandibular molar tooth. Although the tooth was extracted under general anaesthesia the inflammatory swelling increased, as did the pain and trismus. The patient was admitted to hospital for drainage of the submandibular abscess. He was

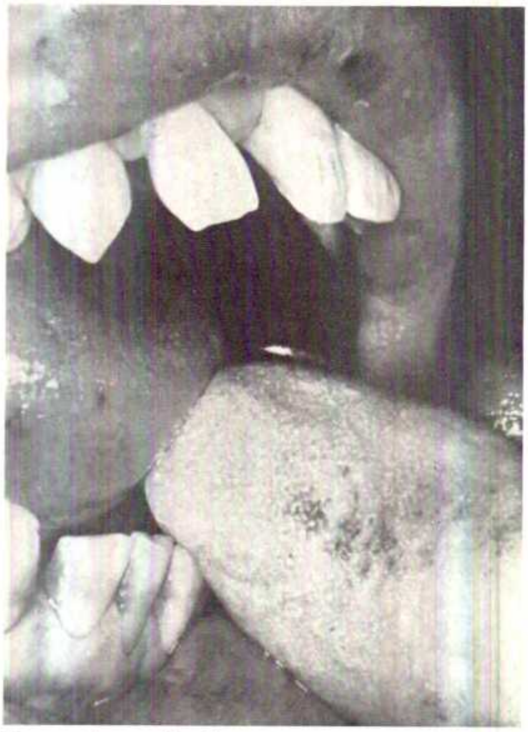

FIG. 2.—*Case* 1. Mouth opening of 35 mm. obtained after removal of the right coronoid process.

discharged after 7 days but with minimal jaw movement. A course of short-wave diathermy followed, together with active and passive jaw exercises, over several months but with little effect on jaw opening. In the autumn of 1965 he was readmitted to hospital for two further dental extractions and jaw manipulation under anaesthesia. No improvement in jaw movement was obtained. Manipulative exercises were continued on an out-patient basis.

The patient next presented for dental treatment in October, 1969, in another town. His new dental surgeon was unable to undertake treatment on account of difficult access and he was referred for investigation.

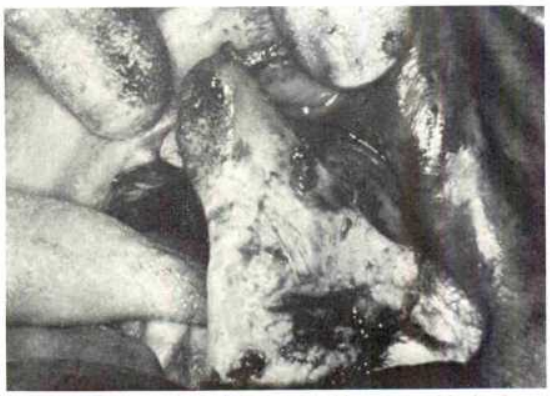

FIG. 3.—*Case* 1. The enlarged coronoid process with the facet on its anterior border.

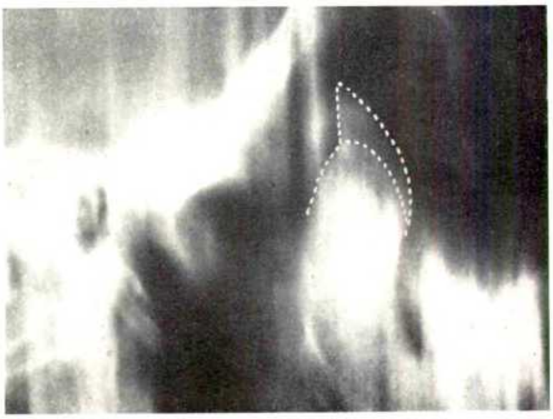

FIG. 5.—*Case* 2. Tomogram of the left coronoid process. The area of new bone formation is outlined.

We first saw this patient in March, 1970. He was a healthy-looking young man with no facial asymmetry or oral abnormalities. Maximal opening of the mouth was 17 mm., measured between the tips of the upper and lower incisor teeth. There was deviation to the right side on protrusion of the mandible. Radiographs suggested that both mandibular joints were not abnormal but that there was enlargement of both coronoid processes, the right being much larger than the left (*Fig.* 1).

A diagnosis of impeded jaw movement due to right-sided coronoid enlargement was made.

OPERATION.—The right mandibular coronoid process was removed via the intra-oral route under endotracheal anaesthesia. As a mouth opening of 35 mm. was obtained the left coronoid process was not touched (*Fig.* 2). Post-operative progress was uneventful and the patient was discharged on the fifth day. In the period following operation the patient practised mouth opening using wooden tongue spatulae. One year later full jaw movements had been maintained.

SPECIMEN.—The specimen of the enlarged coronoid process (*Fig.* 3) was lacking in distinction. It had a facet on its anterior border which articulated with a similar facet palpable at operation on the posterior aspect of the zygomatic process of the maxilla.

MICROSCOPIC APPEARANCE.—Histological sections (*Fig.* 4) showed an enlarged coronoid process of normal tissue with a fatty marrow. The growth appeared to be due entirely to normal bone apposition. No special features were present. There was no evidence of chondroid bone or cartilage.

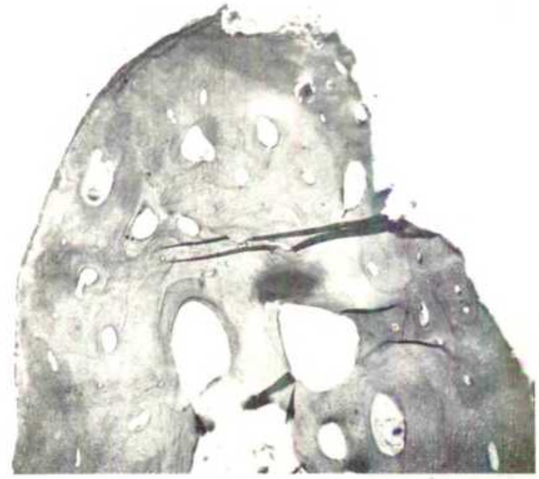

FIG. 4.—*Case* 1. Photomicrograph showing normal tissue structure, enlargement being entirely caused by normal bone apposition. (× 23.)

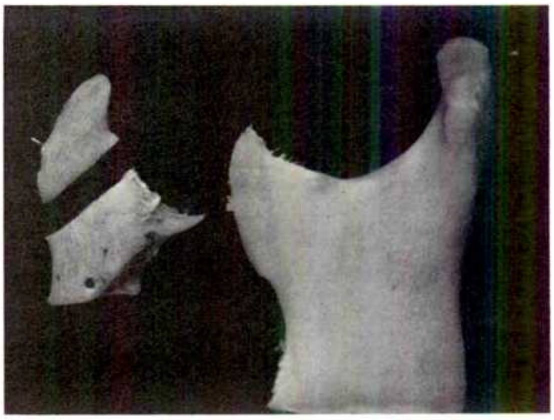

FIG. 6.—*Case* 2. Operative specimen shown adjacent to a specimen taken from a normal subject of similar age, build, and sex.

Case 2.—J. H., a 17-year-old girl, had an attempted extraction of the left maxillary third molar tooth in 1964. The tooth was apparently dislodged into the temporal fossa but was recovered at a second operation through an incision in the scalp transverse to the direction of the fibres of the left temporalis muscle. After the dislodgement of the tooth she had difficulty in opening the mouth. After the operation for the recovery of the tooth, jaw opening was minimal. Six weeks later the patient was readmitted for manipulation of the jaw under general anaesthesia as she was still unable to open her mouth. She was again admitted 4 months later for a similar manipulation and intensive physiotherapy. Short-wave diathermy and jaw exercises were continued on an out-patient basis for several months.

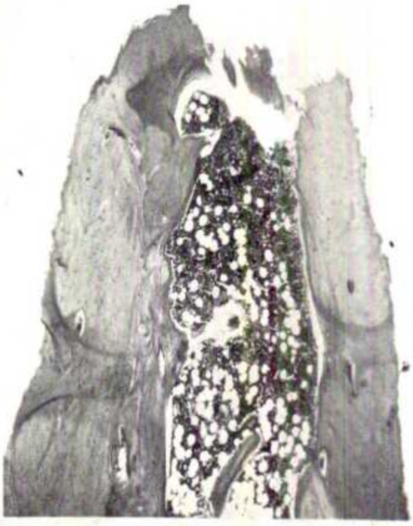

FIG. 7.—*Case* 2. Photomicrograph showing enlargement caused by lamellar and non-lamellar bone apposition. There is rimming with osteoblasts. Haemopoietic bone-marrow is present. (× 23.)

In April, 1967, the patient had some mandibular teeth extracted using a transalveolar approach, in addition to a further attempt at jaw manipulation under general anaesthesia. In February, 1970, she presented complaining of generalized toothache. She was admitted to hospital and 10 grossly carious teeth were removed with great difficulty. The incisal opening at this time was less than 1 cm.

On 6 April, 1970, we saw this patient for the first time. The incisal clearance was less than 1 cm. and the mandible deviated to the left side on protrusion. A 5-cm. long scar was present on the left temporoparietal region. There was no apparent cause for the limitation of mandibular movement other than the presumed shortening by fibrosis of the left temporalis muscle.

Radiographs (*Fig.* 5), however, suggested an overgrowth of the left coronoid process. New bone formation appeared to be sitting on the original outline of the coronoid process like a dunce's cap.

A diagnosis of limited jaw movement caused by left-sided temporalis shortening was made. It was also recognized that hypertrophy of the left coronoid process might be a complicating factor.

OPERATION.—In order to by-pass the effects of the shortened temporalis fibres and at the same time to relieve the possible physical obstruction of the enlarged coronoid process, a left mandibular coronoidectomy was carried out by the intra-oral route under endotracheal anaesthesia. The fibres of the temporalis were freed from the coronoid process with little improvement in opening. Removal of the coronoid process, however, resulted in considerably increased opening. The patient failed to persevere with exercises in the postoperative period and it was necessary to manipulate the jaw under general anaesthesia on the eighth postoperative day.

The patient failed to attend for further appointments and has been lost to follow-up.

SPECIMEN (*Fig.* 6).—The coronoid process was elongated and a conical portion of bone rather like a cap was seen at the tip of the process.

MICROSCOPIC APPEARANCE (*Fig.* 7).—Sections showed lamellar bone of the coronoid process with haemopoietic marrow, some non-lamellar bone apposition on external surfaces, and in some places there was rimming by osteoblasts. The tip showed remnants of the temporalis muscle attachment.

The coronoid process seemed to have enlarged by appositional growth; no cartilage or chondroid bone was present.

DISCUSSION

The coronoid is recognized to be one of the 'muscular' processes of the mandible. The temporalis is an extremely powerful muscle with a tendinous insertion into and around the coronoid process. It is not unreasonable to postulate that abnormal stresses transmitted by the temporalis muscle could result in appositional bone growth at the point of its insertion. Well-known examples of this are 'Rider's spur' and the Pellegrini-Steida syndrome where there is excessive bone formation at the insertion of the adductor longus and the adductor magnus respectively in some devoted horsemen.

Animal experiments emphasize the relationship between temporalis function and coronoid size. Sarnat and Engel (1951) showed that the coronoid process of the growing monkey became larger, thicker, and extended above the zygomatic arch following condylectomy on the ipsilateral side. They concluded that this was the result of the unopposed action of the temporalis not counterbalanced by condylar growth and support. Washburn (1947) resected the temporalis in rats but preserved the coronoid process on the same side. After 3–5 months he found the coronoid process to be absent. Similar work by Avis (1959), who resected portions of the temporalis on one side in young cats, showed that the process on the operated side was smaller than that on the unoperated side.

In the present *Case* 2 it is suggested that the surgical interference to remove the displaced wisdom tooth resulted in scarring and shortening of the temporalis muscle-fibres which were the original causes of the inability to open the mouth. Repeated attempts to open the mouth by manipulation under anaesthesia and by active and passive physiotherapy served merely to stress the tendinous insertion of the temporalis muscle with resulting functional hyperplasia of bone. That this secondary growth of bone was of clinical significance was noted at operation. Jaw movement was obtained not after detachment of the temporalis insertion but after removal of the enlarged coronoid process. The significance of the presence of haemopoietic marrow in the coronoid process at this age is not known.

In *Case* 1 we postulate a similar mechanism of secondary coronoid hyperplasia, but with less direct evidence.

There was no histological evidence of primary tumour growth.

Symptoms relating to developmental hyperplasia are usually detected at puberty with a gradually increasing inability to open the mouth.

Case 1 had reached the age of 24 with no difficulties with jaw movement until the infective episode. Then over a period of 5 years he had manipulations under general anaesthesia and much active and passive physiotherapy. When we saw him in 1970 both coronoid processes were enlarged, but the right was much larger than the left. Histological examination confirmed that appositional bone growth accounted for the enlargement. We were not able to establish whether the other areas of insertion of the masticatory muscles were subject to secondary hyperplasia.

In both cases the absence of chondroid bone suggests that the process of hypertrophy of the coronoid had been slow.

The 26 cases of coronoid enlargement reported in the literature are all of primary origin: either some form of benign tumour or developmental hyperplasia. There is little agreement on the criteria for the histological diagnoses of these cases, being variously described as exostosis, osteocartilaginous exostosis, osteochondroma, and osteoma, with little justification in some of the cases.

Nickerson, Graft, and Sazima (1969) have made a useful and critical review of the problem with an extensive survey of the literature.

Incontrovertible examples of true primary tumours, however, do exist, such as the osteoma reported by Lewars (1959) and the osteochondroma reported by Levine, Chessen, and McCarthy (1957). These illustrate the true nature of the tumour group. They are unilateral, appearing mostly in males over a wide age range. They are sometimes productive of facial asymmetry and are characterized by a mushroom-shaped mass which virtually fills the space between the zygomatic arch and the temporal bone.

Developmental hyperplasia accounts for the other group of primary enlargements. Good examples are described by Lyon and Sarnat (1963), Rowe (1963) and Nickerson and others (1969). Developmental hyperplasia is bilateral, confined to males, and starts at puberty. The coronoid process, although enlarged, retains its normal form.

In addition to these two primary groups of enlarged coronoid process of the mandible we suggest that enlargement can be due to functional hyperplasia secondary to other causes of inability to open the mouth fully. It is important to consider this possibility in the differential diagnosis of the causes of impeded jaw movements.

Acknowledgements.—We wish to thank Professor J. J. Hodson for the histological studies and reports, and Mr. R. Cousins for his photographic work.

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MUSCLE BLOOD-FLOW FOLLOWING INSERTION OF A BY-PASS VEIN-GRAFT IN FEMOROPOPLITEAL OCCLUSIVE DISEASE

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SUMMARY

Muscle blood-flow has been measured by the local clearance of ^{133}Xe in 32 patients (34 limbs) following arterial replacement with a by-pass vein-graft for atherosclerotic occlusive disease affecting the femoropopliteal segment.

In 27 cases (29 limbs) in which the graft was functioning satisfactorily there was a marked improvement in muscle blood-flow with a return to within normal range in most instances. In 5 patients the graft occluded within 3 months of operation and in these cases there was no significant alteration in the muscle blood-flow following operation. The measurement of muscle blood-flow therefore provided objective corroborative evidence of the success or failure of the procedure.

Seventeen of the group had muscle blood-flow measurements carried out at 3-monthly intervals for a year or more after operation. The postoperative flow tended to remain stable throughout this period, and did not show any tendency to return to the preoperative levels as has previously been reported for thrombo-endarterectomy. This lends further support for the view that in reconstructive surgery for femoropopliteal occlusive disease the long-term results are better with by-pass vein-grafts than with thrombo-endarterectomy.

THE blood-flow through a tissue can be measured by injecting a radioactive substance directly into the tissue and measuring the rate of disappearance of the isotope. This technique was introduced for the measurement of the blood-flow through the calf muscle in man by Kety (1949), who used the isotope ^{24}Na. Subsequently, Lassen (1964) showed that the radioactive inert gas ^{133}Xe had several advantages over ^{24}Na as the radioactive tracer.

The xenon-clearance technique has been shown to be useful in the detection of peripheral arterial disease (Lassen, Lindbjerg, and Munck, 1964; Lindbjerg, 1965; Webster, 1966; Bell and Short,

1968) and in the postoperative assessment of patients following surgery (Garcia Del Rio, Welsh, and Repetto, 1969; Bell and Short, 1971).

PATIENTS STUDIED

Thirty-two patients with atherosclerotic occlusive disease of the femoropopliteal artery have been studied. Two patients had a vein-graft inserted in both legs and thus 34 limbs had blood-flow measurements before and after operation.

The level of the occlusion present is shown in *Table I*. The grafts were inserted across the diseased segment and ranged between 12·5 and 35 cm. in length. A minimum diameter of 4 mm. was considered desirable and with 3 exceptions this was achieved.

Table I.—LEVEL OF ARTERIAL OCCLUSION IN 32 PATIENTS (34 LIMBS)

Lesion	*No. of Legs*
Occlusion of superficial femoral artery, either partial or complete	18
Occlusion at the adductor magnus hiatus	10
Stenosis at the adductor magnus hiatus	3
Occlusion of the popliteal artery	3

In 5 patients the graft failed within the first 3 months. At the follow-up 1 year after operation 22 limbs were available for study, 3 patients having been lost to follow-up and 4 patients being within a year of operation. Of this group, 4 developed late occlusion of the graft and 1 patient developed stenosis at the proximal end of the vein-graft with a return of symptoms. This left for study 17 limbs who were symptom-free at the end of 1 year.

METHODS

Muscle blood-flow was measured from the local clearance of ^{133}Xe as described by Lassen and others (1964); 30–60 μc. of ^{133}Xe dissolved in 0·1–0·2 ml. of 0·9 per cent saline were injected directly into the anterior tibial group of muscles. The radioactivity was detected using a NaI crystal connected to a ratemeter and recorder. Following the injection of ^{133}Xe the arterial inflow to the limb was occluded and the patient was asked to exercise his ankle. The exercise was continued until the patient was forced to stop on account of ischaemic pain; in each case a minimum of 60 movements was carried out and the ischaemic period was never less than 2 minutes.

Following release of the cuff a clearance curve was obtained and the muscle blood-flow (M.B.F.) was calculated using the formula:—

$$\text{M.B.F.} = D \times 161 \text{ ml. per 100 g. per min.,}$$

(Lassen and others, 1964), where D is the decrease in 1 minute of a tangent drawn to a logarithmic plot of the clearance curve.

From each curve the following three calculations were made:—

1. The peak blood-flow (P.B.F.).
2. The time taken from release of the occluding cuff to reach this peak blood-flow.
3. The duration of peak blood-flow.

By drawing a tangent to the logarithmic plot of the clearance curve at any moment in time a D factor can be calculated for that time and a flow pattern obtained. In the present paper the flow patterns illustrated were made from blood-flow calculations at minute intervals after release of the occluding cuff.

RESULTS

In 5 patients the graft failed within the first 3 months. In all these cases the postoperative blood-flow at 3 months showed no statistically significant change from the preoperative levels (*Table II*). The pre- and postoperative blood-flow results in the remaining 27 patients (29 limbs) in whom a vein-graft was functioning satisfactorily at 3 months are shown in *Table III*. The peak blood-flow increased by 77 per cent, the duration of peak blood-flow was reduced by 46 per cent, and the time from release of the occluding cuff to reach peak blood-flow was reduced by 73 per cent ($P < 0·001$ in all 3 cases).

Table II.—PRE- AND POSTOPERATIVE MUSCLE BLOOD-FLOWS IN PATIENTS WITH A FAILED VEIN-GRAFT (5 LIMBS)*

TIME	PEAK BLOOD-FLOW (ml. per 100 g. per min.)	TIME TO PEAK BLOOD-FLOW (min.)	DURATION OF PEAK BLOOD-FLOW (min.)
Before operation	24·7 ± 5·9	1·4 ± 1·5	2·9 ± 3·0
After operation	22·5 ± 5·1	2·0 ± 1·8	2·8 ± 1·5

* Mean ± S.D.

Table III.—PRE- AND POSTOPERATIVE MUSCLE BLOOD-FLOWS IN PATIENTS WITH A SUCCESSFUL VEIN-GRAFT (29 LIMBS)*

TIME	PEAK BLOOD-FLOW (ml. per 100 g. per min.)	TIME TO PEAK BLOOD-FLOW (min.)	DURATION OF PEAK BLOOD-FLOW (min.)
Before operation	30·6 ± 12·9	1·5 ± 0·7	2·8 ± 1·2
After operation	54·2 ± 14·1*	0·4 ± 0·2†	1·5 ± 0·6†

* Mean ± S.D.

† $P < 0·001$.

Table IV.—POSTOPERATIVE MUSCLE BLOOD-FLOW IN PATIENTS WITH A SUCCESSFUL VEIN-GRAFT (29 LIMBS) COMPARED WITH THAT IN NORMAL SUBJECTS (68 LIMBS)*

PATIENTS	PEAK BLOOD-FLOW (ml. per 100 g. per min.)	TIME TO PEAK BLOOD-FLOW (min.)	DURATION OF PEAK BLOOD-FLOW (min.)
Normal group	55·9 ± 12·7	0·5 ± 0·3	1·1 ± 0·4
Postoperative group	54·2 ± 14·1	0·4 ± 0·2	1·5 ± 0·6

* Mean ± S.D.

When the postoperative results in the group with patent grafts are compared with the muscle blood-flow results obtained from a group of 36 normal subjects (68 limbs) of the same age-group who had no clinical evidence of peripheral arterial disease, there is a close correlation between the two groups (*Table IV*).

The muscle blood-flow patterns before and after surgery for the successful group are shown in *Fig. 1*. The postoperative flow pattern is compared with that of the normal group in *Fig. 2*. The postoperative blood-flow pattern closely resembles that of the normal group.

At the follow-up 1 year after operation 17 out of the 22 limbs available for study were symptom-free and clinically the graft was functioning satisfactorily.

Fig. 3 illustrates the mean peak muscle blood-flow results at 3, 6, and 12 months after operation. It is apparent, in general, that the increase in muscle blood-flow is well maintained during the first post-operative year.

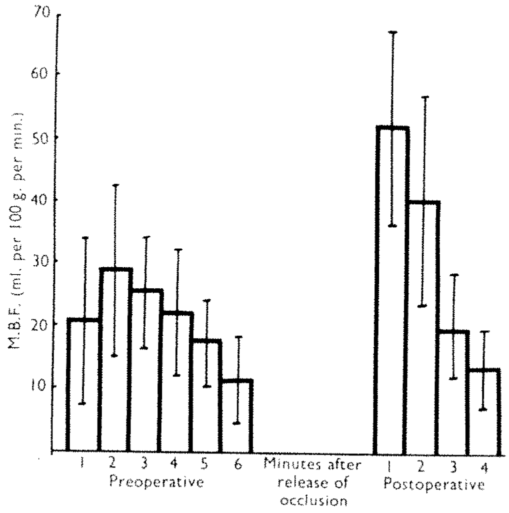

FIG. 1.—Pattern of muscle blood-flow (M.B.F.) calculated at minute intervals after the release of the cuff. Comparison of the pre- and postoperative flow patterns in 29 limbs with a patent graft (mean ± S.D.).

DISCUSSION

In most instances it is not difficult on clinical grounds to determine whether a graft is functioning or not, particularly when distal vessels are patent and pedal pulses are palpable. It is not so easy to determine clinically how well a graft is functioning or to be certain that no inherent defect is present which might lead to early failure. Angiography provides a useful assessment of the anatomical function of a vein-graft, especially when it is performed at the time of insertion of the graft, but it is not suitable as a routine follow-up procedure. The measurement of muscle blood-flow by the ^{133}Xe-clearance technique not only has the merit that it is less traumatic and is easily performed on out-patients, but also it is a more direct and more accurate measurement of the adequacy of blood-supply to the limb in the management of intermittent claudication (Alpert, Larsen, and Lassen, 1968). Alterations in postoperative muscle blood-flow as shown by ^{133}Xe studies may be an indication for further angiography.

In the series reported here there was a good correlation between the clinical picture and the muscle blood-flow estimations. In the 5 patients whose graft failed there was no significant improvement in the blood-flow following operation (*Table II*).

In the 29 limbs with an open graft at 3 months only 3 failed to show a rise in muscle blood-flow. One of these 3 patients had stenosis of his graft demonstrated by arteriography and developed a late occlusion of the graft. In the second case the pre-operative peak muscle blood-flow was 67·6 ml. per 100 g. per minute and this falls well within the normal range (in 68 limbs in patients over 40 years of age the mean peak muscle blood-flow was 55·9 ml. per 100 g. per minute, S.D. ± 12·7).

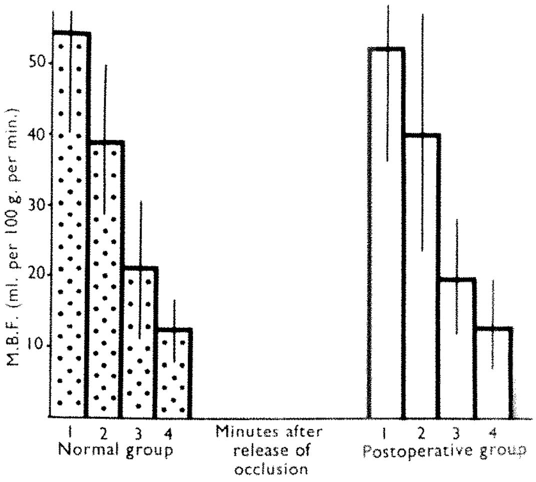

FIG. 2.—Postoperative muscle blood-flow (M.B.F.) in patients with a successful graft (29 limbs) compared with that in normal subjects (68 limbs) (mean ± S.D.).

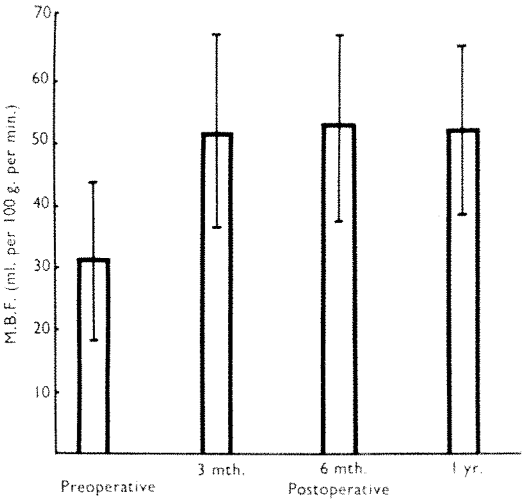

FIG. 3.—Peak muscle blood-flow (M.B.F.) before operation and 3, 6, and 12 months following operation in 17 limbs (mean ± S.D.).

In the third patient the muscle blood-flow following operation remained below the normal range, but there was a dramatic reduction in the time taken to achieve peak blood-flow following ischaemic exercise from a grossly abnormal 3·3 minutes to a normal 0·5 minute. Abolition of this time lag, which is due to slow repressurization of the local vascular bed following removal of the cuff, was accompanied by relief of symptoms. We have had a similar experience following effective thrombo-endarterectomy (Bell and Short, 1971). In the remaining 26 limbs in which the graft functioned well throughout the time under observation the muscle blood-flow remained at approximately normal levels. This supports the view that muscle blood-flow provides objective evidence of the success or failure of the surgical procedure.

In some patients the muscle blood-flow pattern returned to within normal ranges following reconstructive surgery and this is in keeping with the finding of others. Mannick, Jackson, and Coffman (1966), using the local clearance of Na labelled with ^{131}I, found that the clearance after exercise returned to normal following surgery. Snell, Eastcott, and Hamilton (1960), using venous occlusion plethysmography, also found that the pattern of reactive hyperaemia tended towards normal following removal of an arterial occlusion.

In those patients with a patent graft the improvement in muscle blood-flow was well maintained throughout the first postoperative year. Strandness and Bell (1966) have postulated a gradual build-up of muscle blood-flow for several months following surgery. In the present series this was observed in 1 patient. Following operation the peak muscle blood-flow rose from the preoperative level of 20·9 to 32·2, 41·7, and 51·5 ml. per 100 g. per minute at 3, 6, and 12 months respectively. However, in the majority of cases the improvement in muscle blood-flow observed at 3 months was usually well maintained at a constant level throughout the rest of the year. In our previous study (Bell and Short, 1971) it was found that in 50 per cent of cases followed up after thrombo-endarterectomy for femoropopliteal occlusive disease there tended to be a progressive diminution in muscle blood-flow over the first year. This was not found to occur in the present group. This lends support to the view that by-pass vein-grafts functioning satisfactorily will give better long-term results than thrombo-endarterectomy.

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THE RESULTS OF 101 OPERATIONS FOR SYMPTOMATIC HIATUS HERNIA

A COMPARISON OF TWO DIFFERENT METHODS

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SUMMARY

The results of all the operations for symptomatic sliding hiatus hernia carried out by 1 surgeon during 5½ years are reviewed. One hundred and six operations were done and 101 patients were available for review after 6 months to 5 years. The earlier patients in the series underwent transthoracic or transabdominal hiatus hernia repair, and the later patients underwent fixation of the lesser gastric curve to the anterior abdominal wall, as described by Boerema (1969). Before operation the two groups were clinically comparable. There were significantly less clinical failures after the Boerema operation, and less radiological recurrences. This simple and rapid operation is, therefore, preferred to the more complicated procedure.

MANY operations have been described for symptomatic sliding hiatus hernia. They have been reviewed recently by Collis (1970) and Mustard (1970). Similar results have been reported in each case by the originator, with a 4–22 per cent clinical failure rate and 0–10 per cent radiological recurrence. However, many of the operations are complicated and difficult, so that different results may be obtained by other operators. There are few reports of large series of patients treated by other operators, and even fewer attempts to compare different methods.

The results obtained in 101 patients in whom a hiatus hernia was repaired by 1 surgeon using three different operations are reviewed after 6 months to 5 years.

MATERIALS AND METHODS

One hundred and six patients undergoing operations by Mr. H. T. John (Consultant Surgeon, Bath Clinical Area) for symptomatic sliding hiatus hernia, confirmed by barium meal or oesophagoscopy, from 1965 to 1970 are reviewed. Three patients died in the immediate postoperative period of pulmonary embolus or myocardial infarction, and 1 patient died 3 months later of cerebral haemorrhage. A further patient has not been traced since her operation, leaving 101 patients followed up for 6 months to 5 years. Until 1968 all the patients underwent hiatus hernia repair by a transthoracic or transabdominal route, depending on the suspicion of other abdominal disorder. After 1968 most patients underwent Boerema's operation, so that there were three groups of patients (*Table I*): 39 transthoracic repairs, 64 thoracic or abdominal repairs (including the 39 transthoracic repairs), and 37 Boerema operations.

The transthoracic repair was carried out through the bed of the seventh or eighth rib. The lower oesophagus and herniated stomach were mobilized. Up to six thread sutures were placed through the wall of the lower oesophagus, the fundus of the stomach, and the under-surface of the diaphragm. They were then tied, fixing the stomach and lower oesophagus below the diaphragm and restoring the gastro-oesophageal angle. Finally, the crura were approximated behind the oesophagus with thread sutures so as to narrow the hiatus.

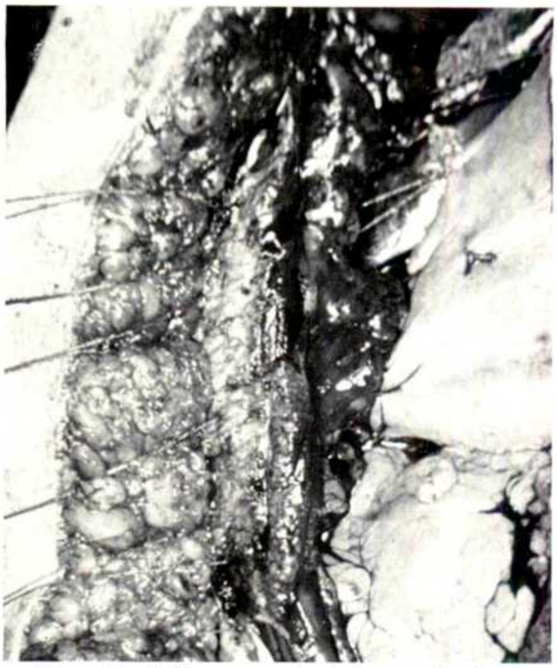

FIG. 1.—For the Boerema operation eight to ten thread sutures are placed in the lesser curve of the stomach and brought out through the rectus 2·5 cm. to the right of the midline incision. The top of this photograph is towards the head of the patient. The stomach is being drawn down from the top right by six sutures (so far) through the rectus sheath which runs down the middle of the picture, beneath the subcutaneous fat and skin on the left of the picture.

Table I.—THE GROUPS OF PATIENTS STUDIED

GROUP	OPERATION	NO. OF PATIENTS				
		1965–7	1968	1969	1970	Total
1. Thoracic	Transthoracic repair of hiatus	24	11	2	2	39
Abdominal	Transabdominal repair of hiatus	14	4	6	1	25
2. Combined	Thoracic or abdominal repair of hiatus	38	15	8	3	64
3. Boerema	Boerema's operation	0	9	6	22	37

The transabdominal repair was carried out through an upper midline incision. The lower oesophagus was mobilized and drawn into the abdomen. The crura were approximated behind the oesophagus to narrow the hiatus, the gastro-oesophageal angle was restored, and the fundus of the stomach was fixed to the diaphragm, all with thread sutures.

The Boerema operation was also carried out through an upper midline abdominal incision. The lower oesophagus was mobilized by digital dissection until at least 5 cm. could be drawn into the abdomen. The crura were usually dissected out and approximated with thread sutures behind the oesophagus to narrow the hiatus, but this step was sometimes omitted and frequently only one or two sutures were used. The subcutaneous fat was cut off the right side of the linea alba, and then eight to ten thread sutures were placed in a row just anterior to the lesser curve of the stomach and each end of each suture was brought out through the abdominal wall 2·5 cm. to the right of the midline (*Fig.* 1). These were tied, so that at least 5 cm. of the lesser curve of the stomach were fixed to the anterior abdominal wall (*Fig.* 2), and the oesophagus was held down into the abdomen under tension. This was the most important step, and Boerema (1969) states: 'The intra-abdominal oesophagus and upper part of the

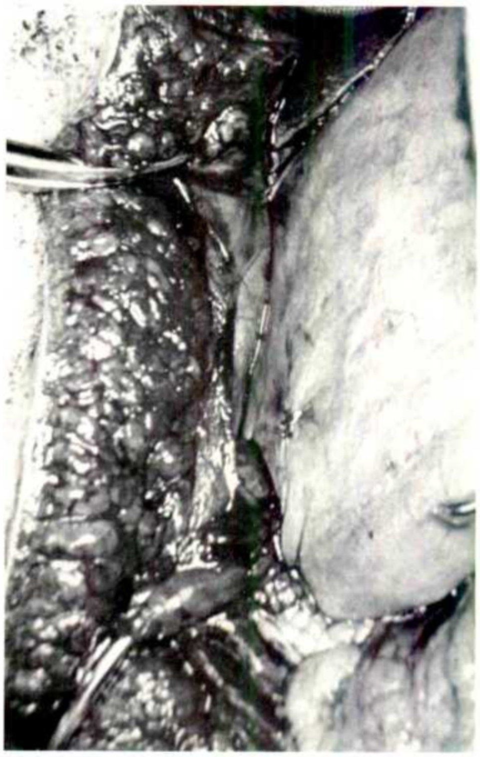

FIG. 2.—The Boerema operation is completed by tying the sutures, thus fixing the lesser curve of the stomach to the anterior abdominal wall. The top of this photograph is towards the head of the patient. The stomach has been drawn over from the right, and is separated from the anterior abdominal wall (on the left) by the peritoneum which is displayed by two artery forceps. A little of the left lobe of the liver is seen at the top of the picture.

lesser curvature must feel like a very tense cord, extending from the hiatus close along the under surface of the liver to the anterior abdominal wall one inch to the right of the median line.' The fundus of the stomach was left free to roll up under the diaphragm, automatically restoring the gastro-oesophageal angle.

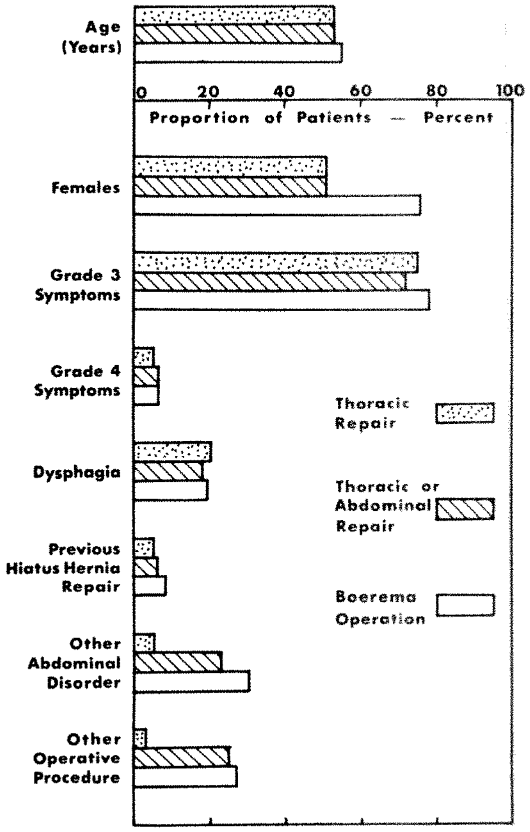

FIG. 3.—Preoperative clinical features of the patients grouped according to *Table I*. The length of each column represents the proportion of patients in each group with each clinical feature, except for the mean age which is shown at the top of the figure.

Preoperative clinical features and any postoperative symptoms at out-patient visits were determined from the hospital notes. The severity of symptoms due to hiatus hernia or resulting from the operation itself was graded retrospectively (*Table II*). For the review all patients were sent questionnaires. They were asked in simple terms to grade the severity of their own symptoms (*Table II*) and to indicate when the symptoms had returned after operation. An unprompted description of the symptoms and any other comments were invited. A patient's general practitioner was approached when any reply was not clear or was not received, and those patients with severe symptoms who had not already been seen were interviewed at the hospital. Satisfactory replies were obtained from 97 of the 101 patients. The results were interpreted by a surgeon (C. J. M.) who had not carried out any of the operations. Only upper gastro-intestinal symptoms or symptoms resulting from the operation itself, such as wound pain or post-vagotomy diarrhoea, were recorded as 'postoperative symptoms'. Dysphagia was usual for up to 6 weeks and therefore was recorded as a symptom only when it lasted for more than 2 months. When a patient with severe recurrent symptoms underwent a further operation for his hiatus hernia it was assumed that his symptoms would have persisted for more than 2 years after the first operation. The results of the second operation were assessed and recorded separately.

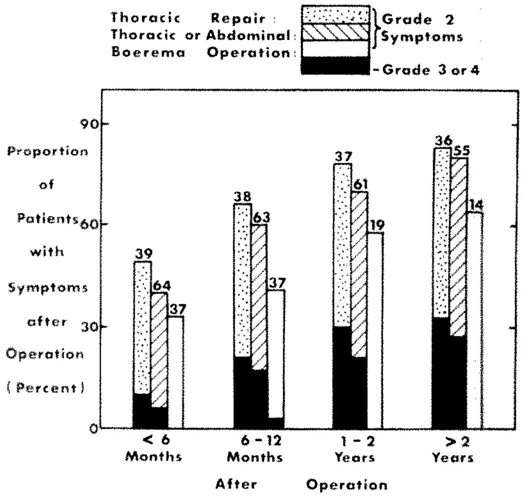

FIG. 4.—Postoperative clinical recurrences in the patients grouped according to *Table I*. The height of each column represents the proportion of patients with recurrent symptoms in each group at each time interval. The number of patients in each group is shown above each column. The severe (grades 3 and 4) symptoms are shown in black, and the mild (grade 2) symptoms are coded according to the group represented.

Table II.—GRADING OF CLINICAL SYMPTOMS*

GRADE	SEVERITY	DESCRIPTION
1	Absent	No symptoms
2	Mild	Symptoms usually relieved by conservative measures
3	Severe	Symptoms resistant to conservative measures
4	Severe	Persistent incapacitating symptoms

* Related to the hiatus hernia or resulting from operation.

All of the patients with severe (grade 3 or 4) recurrent symptoms, many of those with mild (grade 2) symptoms, and all of those who had undergone Boerema operations had postoperative barium-meal studies. A hiatus hernia or gastro-oesophageal reflux in the supine position was considered abnormal, but if it occurred only in the prone position with a bolster under the abdomen it was considered abnormal only when associated with symptoms of reflux. Conversely, when no hiatus hernia or reflux of barium could be demonstrated in patients with severe (grade 3 or 4) symptoms these symptoms were considered not to be due to hiatus hernia or reflux. These symptoms were classed as grade 2 postoperative symptoms for the purpose of analysis to avoid confusion with grade 3 or 4 symptoms due to recurrent hiatus hernia.

RESULTS

The preoperative clinical features of the three groups are compared in *Fig.* 3. There were more females in the Boerema group, but the ages of the patients and the severity of their symptoms were similar. There were less 'other abdominal disorders' discovered in the thoracic group, but as there were more in the abdominal group the incidence in the combined group (7 duodenal ulcers, 5 gall-stones, 2 diverticuloses, and 1 achalasia of the oesophagus out of a total of 64 cases) was similar to that in the Boerema group (4 duodenal ulcers, 5 gall-stones, and 2 diverticuloses out of a total of 37 cases). Likewise, the number of other operative procedures done on the combined group (10 vagotomies, 5 cholecystectomies, and 1 cardiomyotomy out of 64 cases) was similar to that in the Boerema group (3 vagotomies, 5 cholecystectomies, 1 duodenal diverticulectomy, and 1 diagnostic thoracotomy out of 37 cases).

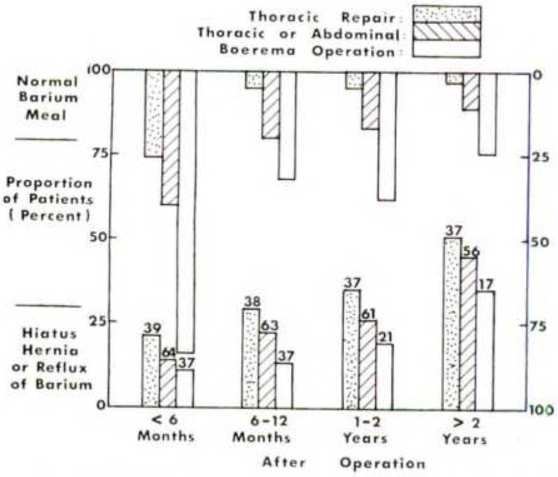

FIG. 5.—Postoperative radiological findings in the patients grouped according to *Table I*. The height of each lower column represents the proportion of patients in each group known to have radiological recurrence. The depth of each upper column represents the proportion known to have normal barium meals. The space between each pair of columns represents the patients who had not had barium-meal studies. The number of patients in each group is shown above each lower column.

The postoperative symptoms of the three groups are compared in *Fig.* 4. Fifty-five of the 64 patients in the combined group were followed up for more than 2 years but most of the clinical recurrences had appeared within a year. In only 6 did symptoms recur after 1 year, 1 of these recurring after 2 years. Ultimately, 15 out of these 55 patients (27 per cent) experienced severe (grade 3 or 4) clinical relapse associated with an abnormal barium meal. At the time of review 14 of the 37 patients in the Boerema group had been followed up for more than 2 years. None of these had severe symptoms associated with an abnormal barium meal, although 1 had grade 3 symptoms (epigastric discomfort, sweating and faintness after meals, and diarrhoea) without radiographic evidence of recurrent hiatus hernia. He had undergone vagotomy and pyloroplasty at the time of his Boerema operation which probably accounts for his symptoms, so they have been classed as grade 2 postoperative symptoms for the purpose of analysis. None of the 5 patients followed up for 1–2 years had severe symptoms, but 1 of the 18 followed up for less than a year had grade 3 symptoms (flatulence, epigastric discomfort after meals, and diarrhoea). She had undergone vagotomy 3 years before her Boerema operation, but she had recurrent hiatus hernia and reflux on barium-meal examination and has been included as a grade 3, severe clinical failure—the only one after a Boerema operation. This clinical failure rate is significantly better than that in the combined group (at 6–12 months, $P < 0{\cdot}05$; at 1–2 years, $P < 0{\cdot}05$; after more than 2 years, $P < 0{\cdot}06$, by the χ^2 test). Only 11 of the 55 (20 per cent) patients in the combined group and 5 of the 14 (36 per cent) in the Boerema group were completely free of symptoms after 2 years, but the rest had only mild symptoms which had been improved by the operation.

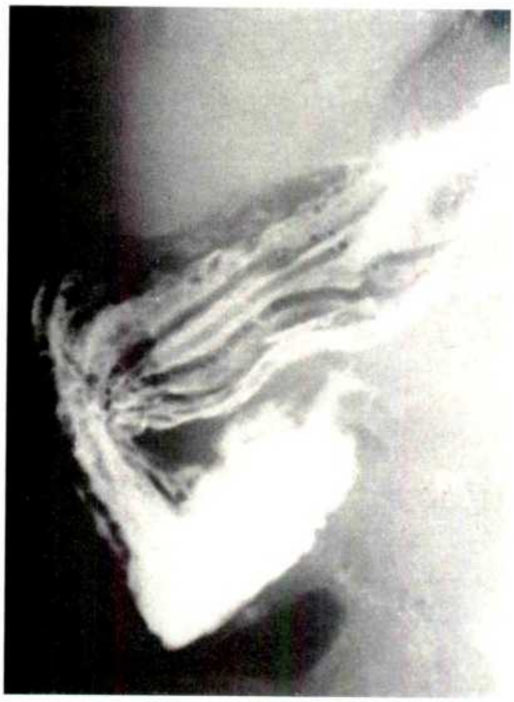

FIG. 6.—Radiological gastric deformity found after the Boerema operation. This is a lateral radiograph of a patient taken during a barium meal more than 2 years after his operation. The top of the picture is towards the head of the patient and his anterior abdominal wall is on the left. The barium within the stomach can be seen extending towards the abdominal wall, showing that the stomach is still fixed there over a length of at least 5 cm.

The barium-meal results are compared in *Fig.* 5. Once recurrent hiatus hernia or abnormal reflux had been demonstrated it was assumed to be present subsequently, so that the results are cumulative. Conversely, when no hiatus hernia or reflux could be shown it was assumed to have been absent since the operation. The results are incomplete because many of the patients with mild or no symptoms did not have a postoperative barium-meal examination, and the investigation of severe symptoms was often delayed. Even so, after 2 years more than half of the patients undergoing thoracic repairs and a third of those undergoing Boerema operations had radiological recurrence; but while many of the former had severe symptoms only 1 in the Boerema group had severe recurrent symptoms. The typical gastric deformity produced by the Boerema operation (*Fig.* 6) persisted for more than 2 years. This seemed to control symptoms, even when reflux of barium could be seen on radiographs.

DISCUSSION

The results of three different operations for sliding hiatus hernia have been compared, but the patients were not randomly allocated so it is important to be certain that other factors did not influence the results. The thoracic and abdominal groups differed clinically because the patients were selected on clinical grounds, and therefore the results of these two approaches cannot be compared. However, it is reasonable to combine these into one group because a similar repair of the hiatus hernia was achieved by each approach. Selection of the patients for the Boerema operation was based on fashion not on clinical grounds so that this group can be compared clinically with the combined group, except for the preponderance of females. The sex of the patients is unlikely to have influenced the results, and comparison of the results obtained in the Boerema group with those in the combined group is valid.

The operations were done to relieve symptoms and therefore the results are best measured by the severity of any postoperative symptoms. This was determined by asking the patients to describe and grade their own symptoms and the replies were interpreted by a surgeon who had not carried out any of the operations. The accuracy was increased by information from general practitioners and by personal interview and radiographic studies of the patients with more severe symptoms. Since the patients in the Boerema group were not followed up for as long as those in the combined group the results have been compared at shorter postoperative periods. At 6–12 months and at 1–2 years there were significantly ($P < 0·05$) less clinical failures in the Boerema group. There were no clinical failures in this group after 2 years, but too few patients had been followed up for this result to reach significance ($P < 0·06$). As the surgeon gained experience with the Boerema operation the results at 6–12 months improved significantly ($P < 0·05$), so that 11 out of the first 16 patients, 5 out of the next 12, and none of the last 9 had postoperative symptoms. Symptoms seldom recurred more than 1 year after thoracic or abdominal repair, and at the time of the review none had appeared more than 1 year after a Boerema operation. It is reasonable to suppose, therefore, that the long-term results of the Boerema operation will improve further as the more recently operated on patients are followed up, and that they will be considerably better than the results obtained in the combined group.

The main value of the radiographic studies was in the diagnosis of symptoms, but all of the patients in the Boerema group had barium meals postoperatively so that a good idea has been obtained of the anatomical result of this operation. Within 6 months only 4 of the 37 had recurrent hiatus hernia and 2 others had recurred when first radiographed after more than 6 months. No hiatus hernia or gastro-oesophageal reflux could be demonstrated in the other 31 patients. This result was not obtained by the insertion of a few stitches in the oesophageal hiatus, because within 6 months there were 9 recurrences in the 29 patients radiographed in the combined group after extensive dissection and repair of the hiatus. The reduction in reflux must, therefore, have been due to the fixation of the stomach to the anterior abdominal wall. It remained fixed for more than 2 years (*Fig.* 6) so that it is likely that the control of reflux will persist. The present 35 per cent (6 out of 17) radiographic recurrence rate after 2 years will improve as more patients are followed up. Seven of the 17 had normal barium meals within 2 years, and the results of the Boerema operation have improved with increased experience. In contrast, the 45 per cent (25 out of 56) known radiographic recurrence rate after 2 years in the combined group is likely to have been worse if the remaining 28 patients had been radiographed. This would confirm, radiologically, the better clinical results of the Boerema operation.

These are the results obtained by one surgeon. Other surgeons may have obtained even better results with another operation, but most other operations described are complicated and require much dissection. Boerema's operation is simple and rapid and is suitable for use even in the elderly and frail (Zeifer, 1968). It achieves all the aims of hiatus hernia repair: closure of the hiatus, infra-diaphragmatic segment of the oesophagus, and acute gastro-oesophageal angle (Collis, 1970; Mustard, 1970), though it seems that the first can be omitted. Boerema's method could be combined with an abdominal repair of the hiatus or another operation (Mustard, 1970), but vagotomy and pyloroplasty did not improve the results in this series. Until another operation has been compared with Boerema's technique in a large group of patients by a surgeon other than the originator of the method, this simple, rapid, and safe operation is preferred.

Acknowledgements.—I thank Mr. H. T. John, Consultant Surgeon, Bath Clinical Area, for allowing me to study his patients, the patients themselves for their co-operation, Dr. S. K. Das for his help in tracing their records, and, in particular, my wife for her patience in typing the many drafts of this paper.

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THE MOVEMENTS OF THE ADULT *ASCARIS LUMBRICOIDES*

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SUMMARY

Deductions made from Makidono's (1956) observations of the movements of ascarids in the small intestine of man and from findings at surgical operations and post-mortem examinations of the positions of ascarids causing clinical disturbances have been used to build a concept of the behaviour of ascarids under normal and abnormal conditions.

THE adult *Ascaris lumbricoides* is the largest nematode parasitic in man, and its movements are easily seen with the naked eye, and yet nothing was known of the modes of movement of this large worm till Makidono (1956) published his *Observations on Ascaris under Fluoroscopy*.

Why were observations under fluoroscopy needed to observe the movements of this large worm? As Makidono observed: 'The ineffectual movements of *Ascaris* in a pan of water are in contrast to the positive progressive locomotion it exhibits in its normal habitat.'

Following the trail created by Fitz (1922), who first visualized ascarids in the gastro-intestinal tract of man during radiographic examinations, Makidono made a series of painstaking and detailed observations on the movements of ascarids in human small intestines. Here for the first time were observations which could not have been made by any other means, because the adult *A. lumbricoides* is formed only in the jejunum of man and can live only in the human body.

Makidono's observations were on ascarids in the small intestine of persons who were unaware of the presence of these worms and who were found on investigation to be harbouring only a few worms each. Makidono's observations relate therefore to ascarids living peacefully and undisturbed in the small intestine of man and which were so few in number that the worms did not impede each other. His observations give a clear picture of the modes of movement of worms living under these conditions. In the present communication Makidono's observations are made the basis for deductions about the mechanics of movements of ascarids in the small intestine.

Much attention has been given in the literature to the clinical disturbances set up by ascarids reaching particular sites. Although the occurrence of ascarids at these sites has been observed at surgical operations or at post-mortem examinations, and descriptions have been published in the literature, these descriptions, accurate though they are, do not give sufficient clues to the chain of events causing the ascarids to take up these positions.

In the present paper the deductions which are made about the mechanics of movements of ascarids living in the small intestine under normal conditions are used to interpret the chain of events leading up to ascarids arriving at unusual sites in the body when conditions are not normal.

MAKIDONO'S OBSERVATIONS

Makidono (1956) made detailed observations on the movement of ascarids in the small intestine in 87 persons, who harboured 588 worms between them. Five of these persons harboured only 1 worm each, three-quarters of the group harboured from 3 to 10 worms each, and only 1 person harboured more than 20 worms.

Ninety-nine per cent of the worms were in the jejunum and ileum, the proportion being 8 : 1 in favour of the jejunum. Ninety-two per cent of these worms were static in the small intestine during the period of observation. These worms were not displaced by intestinal peristalsis, nor could they be dislodged by digital pressures on the abdominal wall made under the guidance of the image on the fluorescent radiographic screen. It was evident that these worms were maintaining their positions in the small intestine by continuous muscular efforts of their own. As Makidono put it: 'The worms resemble fish maintaining their positions in a stream with their heads pointing into the current.'

Makidono observed that in the presence of a large number of worms the mass of worms in the small intestine resembles a bundle of macaroni.

Only 5 per cent of the worms were advancing up the small intestine during the period that they were observed. These worms raised a coil in their bodies as they advanced up the intestine.

Less than 3 per cent of the worms were descending the small intestine during the period that they were observed. Before descending these worms bent backwards upon themselves till their head pointed to the distal end of the intestine, after which they descended the intestine head first.

During earlier examinations Makidono had observed that after an anthelmintic had been administered the bodies of the ascarids became flaccid and that the ascarids were then passively propelled down the small intestines by intestinal peristalsis, their now flaccid bodies being bent into an 'U' with the head and tail ends of the worm pointing to the distal end of the intestine.

SOME DEDUCTIONS ABOUT THE MECHANICS OF MOVEMENTS OF ASCARIDS

Makidono's observation that ascarids which were static in the small intestine directed their head into the current shows that ascarids do not retain their position in the small intestine by attaching themselves by their mouth, which is at the anterior end of the body, to the mucosa of the intestine. On the contrary, he found that the worms maintained themselves in the lumen of the gut pointing their head towards the upper end of the gut.

An *Ascaris* in the small intestine is from time to time being pushed down the small intestine by intestinal peristalsis, and if it is to combat displacement by these peristaltic waves it must make muscular efforts to counteract exactly each wave as it comes along. By directing its head to the proximal end of the gut the *Ascaris* is in a position to counteract each wave of intestinal peristalsis by making movements to advance its body up the intestine.

Makidono observed that ascarids which were advancing up the intestine raised a coil in their bodies as they did so. Why did they do this? To raise a coil in its body the worm would advance the posterior section of its body while keeping the anterior section static. In following this up by advancing the anterior section of its body the worm would thereby have advanced the whole of its body in two phases of movement. By doing this, by advancing half of its body at each phase of its movement up the intestine, the worm is able to use more force in advancing each half section than if it had to advance the whole of its body at one movement.

Movement of a worm up the intestine means advancing against the downward thrusts of the peristaltic waves, and the currents of chyme created by these waves, and the worm would need to make a greater effort to move up the intestine than when it is static and maintaining its position in the intestine.

It is evident from Makidono's observations that no matter whether an ascarid is advancing up the small intestine or whether it is descending the intestine it always moves head first, and that even when it is static and is resisting displacement it combats displacement by making forward movements of its body.

Makidono also observed that regardless of the direction of movement of the *Ascaris* or whether it is static the worm maintains a position in which its body lies extended along the long axis of the small intestine and it curves its body only slightly to conform to the curves of the intestine. By doing this the *Ascaris* presses its body against the walls of the intestine and thus obtains a purchase against which it can make movements to advance its body head first.

The ineffectual movements of ascarids in a pan of water must therefore be due to the worms being unable to secure a purchase on the surface of the pan from which to make their forward movements.

The ridges of the closely set valvulae conniventes of the jejunum would afford an *Ascaris* a better surface to press against and to obtain a purchase from than the smoother walls of the ileum, and this would make the jejunum a more favourable habitat than the ileum. This is confirmed by Makidono's statement that 88 per cent of ascarids observed by him were in the jejunum.

Ascarids in the ileum may therefore be ascarids which were unable to resist effectively being propelled downwards from the jejunum.

ASCARIDS IN THE LARGE INTESTINES

Ascarids passed out in the stools are usually very much alive. Are they ascarids which were living in the colon, or have they passed through the colon enmeshed in the stools?

Ascarids would become more and more enmeshed in the stools towards the distal end of the large intestine where the contents are more and more solid, and worms enmeshed in solid stools would hardly be able to resist being passed out with the stools.

An *Ascaris* in the colon cannot obtain a purchase on the walls of the gut by the expedient of extending its body along the long axis of the gut because of the absence of ridges in the walls of the colon against which the worm could press its body. Moreover the lumen of the colon is so much wider than that of the small intestine that the worm could not get a purchase on its walls efficiently. Thus even in the right colon where the contents of the colon are liquid an *Ascaris* would be unable to make active movements of its own, and it would be swept on with the liquid contents of the right colon.

Surgeons who have dealt with cases of impaction of a mass of ascarids in the ileum by opening the abdominal cavity and massaging the bolus of worms on into the caecum have observed that while the bolus is sometimes expelled in the stools after these operations there are occasions when not a single ascarid is passed out in the stools after such a manœuvre. What could have happened? That it does happen there is no possible doubt.

Cole (1965) relates a case of this kind in which a second operation for intestinal obstruction for adhesions was done 10 days after the first operation. There were no worms in the colon at this second operation. Cole examined the stools passed after operations of this kind and found only ghost worms and fragments of worms' bodies in the stools.

The key to the mystery is to be found in the number of days elapsing after the operation before the stool is passed. If the stool is passed soon after the operation the bolus of worms would be expelled in this stool. If several days elapse before a stool is passed, as might well happen after an abdominal operation, the ascarids in the mass, unable to survive in the colon, perish and their bodies disintegrate so completely that evidence of their presence is to be found only on a microscopic examination of the stools.

It is likely that ascarids perish in the colon because they are unable to nourish themselves on the contents of the colon. Moreover even though they could swallow the liquid contents of the right colon the solid contents of the left colon either could not be swallowed or could be swallowed only with great difficulty.

THE MASSING OF ASCARIDS IN THE SMALL INTESTINE

The number of ascarids which can live in the human small intestine without causing any disturbance from their presence is truly remarkable. Louw (1966) estimated that up to 5000 ascarids can live in the small intestine without causing apparent harm.

The normal content of the small intestine is liquid chyme and the presence of so large a solid object as the body of an adult *A. lumbricoides* could not fail to set up waves of intestinal peristalsis which would be directed to displacing the worm down the intestine.

The fact that up to 5000 ascarids could live in the small intestine without giving a hint of their presence is evidence that the waves of intestinal peristalsis caused by such a large number of worms do not reach the degree of intensity which would result in bouts of acute circumumbilical abdominal colic.

When the number of ascarids in the small intestine is large the fortuitous presence of several ascarids at the same site would excite waves of intestinal peristalsis of a greater intensity than would be the case were these same worms more evenly distributed in the gut. Although these waves of intestinal peristalsis might not be noticed by the host they could be of sufficient intensity to drive ascarids from the more proximal reaches of the intestine down to where a few worms had already aggregated. All the worms would be resisting displacement down the intestine and their bodies would therefore be extended along the long axis of the gut with their heads directed to the proximal end of the gut. This deduction is supported by Makidono's observation: 'in the presence of a large number of worms, X-ray pictures without digital manipulation is sufficient to show that the mass of worms resembles a bundle of macaroni'.

The larger the mass of worms the greater the intensity of the waves of intestinal peristalsis set up from its presence. The mass may become so large that the increased peristalsis is felt by the host as bouts of acute colicky circumumbilical pain. Should the mass of worms be propelled by the peristaltic waves into the caecum the peristalsis and the acute abdominal colic would cease. The worms might then be expelled *en masse* in the stools a day or two later.

The mass of worms may impact in the small intestine as it is being propelled along it, and the mass may then be pushed on again by waves of intestinal peristalsis of an even greater intensity. On the other hand, the mass may impact firmly in the small intestine and remain impacted.

Regardless of whether the impaction of the small intestine is temporary or permanent the complete blockage of the lumen of the intestine by the mass of worms results in a rapid sequence of events which will progress to a fatal termination if the impaction remains.

The firm impaction of a mass of worms in the small intestine may also stretch the walls of the intestine to a degree which results in gangrene of the walls. In the first instance only patches of gangrene occur in the walls. Ascarids emerge through these patches of gangrene into the peritoneal cavity.

THE MIGRATION OF ASCARIDS INTO THE VERMIFORM APPENDIX

The first case to be recorded of the migration of an *Ascaris* into the lumen of the vermiform appendix (Blackadder, 1824) is worth recalling, not only because of its dramatic interest but also because it records the salient features of such a migration with great accuracy.

A man, 41 years of age, was struck down by a bout of excruciating abdominal pain lasting 3½ hours and terminating fatally. At the post-mortem examination an *Ascaris* was found in the lumen of the appendix. The worm had reached the tip of the appendix and only the pointed tail end of the worm projected into the lumen of the caecum.

This case affords clear evidence that the *Ascaris* having entered the appendix had continued advancing into its lumen till it was held up at the tip of the appendix. This appendix was therefore almost as long as the *Ascaris* as only the tip of the worm's tail projected into the caecum. The 3½-hour bout of unrelieved excruciating abdominal pain set up during the migration of the worm into this long appendix caused so much shock that death had resulted from it.

Death from the migration of an *Ascaris* into the lumen of an appendix would be an exceptional event, but in all other respects Blackadder's case records the mode of migration of an *Ascaris* into the appendix and the clinical disturbances resulting from this.

An *Ascaris* propelled into the caecum from the ileum would not be able to make effective movements of its own in the caecum. How then does it come to enter the lumen of the appendix? In Blackadder's case it is recorded that the *Ascaris* had entered the appendix head first. This confirms the deduction which has been made from Makidono's observations that an *Ascaris* can only move with its head forwards. The cases in which an *Ascaris* has entered the lumen of an appendix show that once the head of an *Ascaris* has entered the orifice of an appendix the *Ascaris* continues to advance into the lumen as far as the lumen will permit, which will usually be right up to the tip of the appendix. The deduction that could be made from all this is that the engagement of the head of an *Ascaris* in the orifice of an appendix must be a fortuitous circumstance because of the inability of the worm to make active movements of its own in the caecum, and that once the head of the *Ascaris* has entered the appendix this acts as a stimulus causing the worm to advance through the orifice and to continue advancing into the lumen of the appendix till its advance is held up at the tip or at a constriction in the lumen of the appendix.

The migration of an *Ascaris* into the lumen of an appendix sets up a bout of appendicular colic, and the epigastric or circumumbilical colicky pain from this together with tenderness over the appendix lead to these cases being admitted for operation as acute appendicitis. Examination of such appendices after appendicectomy has been done shows that there is no inflammation of the mucosa of the appendix.

In countries where ascarids are common parasites of man it is not uncommon to find on operating for acute appendicitis an appendix gangrenous at its tip and ascarids in the peritoneal cavity in the neighbourhood of the appendix. In some of these cases an *Ascaris* may be found projecting from the gangrenous tip of the appendix into the peritoneal cavity.

At first sight these findings would suggest that the ascarids had been attracted into the lumen of the appendix by the gangrene at its tip, and that after one *Ascaris* had emerged from the gangrenous tip of the appendix another *Ascaris* in the caecum had been attracted to enter the appendix. Such a view would presuppose that ascarids in the caecum could direct themselves towards the orifice of the appendix. Good reasons have been adduced for rejecting such a view.

A more rational explanation for these findings would be that once an *Ascaris* had entered the lumen of an appendix and had reached the tip of the appendix it would continue to try to move forward against the tip of the appendix. The stretching of the tip of the appendix resulting from this would impair the blood-supply to the tip of the appendix, and this could result in gangrene, an event all the more likely to occur in cases where the blood-supply to the tip of the appendix is poor. Once gangrene of the tip of the appendix occurs the worm continuing to push its head against the soft gangrenous tip of the appendix will push through the tip and emerge from it.

The fact that the worm continues to emerge from the tip of the appendix even after its head has emerged into the peritoneal cavity indicates that the stimulus causing the worm to advance comes not only from the encirclement of the head end of the *Ascaris* by the walls of the appendix, but also from the encirclement of the body of the worm by the walls of the appendix.

Why do other ascarids follow when one worm has emerged into the peritoneal cavity from the gangrenous tip of the appendix? It is likely that the passage of the first worm through the lumen of the appendix by dilating the orifice of the appendix makes the fortuitous engagement of the head of another *Ascaris* in the appendix easy.

The sequence of events postulated for these cases is confirmed by the finding that the mucosa of the appendix in such cases is normal right up to the gangrenous tip of the appendix. There is no pus in the lumen of these appendices.

ASCARIDS IN MECKEL'S DIVERTICULUM

A Meckel's diverticulum could accommodate several ascarids. Viliger (1929) recorded a case in which 64 ascarids had filled a Meckel's diverticulum so tightly that they had stretched its walls to a paper-like thickness.

How does this happen? An *Ascaris* which is ascending or descending the ileum would enter the orifice of a Meckel's diverticulum if this happened to be in its path. As the *Ascaris* could only withdraw its body by bending its anterior end backwards till its head pointed in the reverse direction, an *Ascaris* which had entered a Meckel's diverticulum would be unable to get out of the diverticulum since it would not have sufficient room to bend backwards. It could now only advance up to the tip of the diverticulum and other ascarids entering the diverticulum would have to do the same.

Cases have been recorded of the emergence of ascarids into the peritoneal cavity through the gangrenous tip of a Meckel's diverticulum. The sequence of events would be much the same as in the cases where ascarids emerged from the gangrenous tip of an appendix.

Despite the much wider lumen of a Meckel's diverticulum the escape of ascarids into the peritoneal cavity from its gangrenous tip is not followed by the escape of intestinal fluids into the peritoneal cavity. This must be due to the gangrenous tissue closing on to itself as the *Ascaris* pushes its way out of the diverticulum.

ASCARIDS IN THE BILE- AND PANCREATIC DUCTS

Ascarids in the bile- and pancreatic ducts would have entered these ducts from the duodenum. Makidono's (1956) observations established that the duodenum is not the normal habitat of *A. lumbricoides*. However, ascarids do occasionally reach the duodenum.

They could have been regurgitated into the duodenum from the jejunum during bouts of vomiting caused by the impaction of a mass of worms in the jejunum. Ascarids could also move up into the duodenum and would be likely to do so when the number in the jejunum became large. Louw (1966) stated that the presence of ascarids in the duodenum is strong presumptive evidence of biliary ascariasis. It would be unreasonable to infer from this that ascarids in the duodenum direct their course to the orifice of the duodenal papilla through which they reach the common bile-duct. It is more likely that the presence of ascarids in the duodenum sets the stage for the fortuitous engagement of the head of an *Ascaris* in the orifice of the duodenum papilla, and that should this happen the worm would be stimulated to advance into the ampulla of the bile-duct and from there into either the common bile-duct or the main pancreatic duct.

Observations made on the radiographic fluorescent screen confirm that ascarids enter the common bile-duct or the main pancreatic duct head first. Thus Liang, Wang, Wang, and Liu (1957) observed that an *Ascaris* enters the common bile-duct via the ampulla of the duct and that usually only the *proximal* third of the worm lies in the duct.

Lien (1959) claimed that if one end of the worm is pointed and the other end blunt fixation of the blunt anterior end of the worm at the ampulla of the bile-duct would be evidence that the worm had started to enter the ampulla. He also stated that if the tip of the tail of the worm was left in the duodenum the tail would be seen to move up and down, while the rest of the body of the worm would be fixed.

Ascarids in the Biliary Passages.—From the deductions which have been made about the advance of ascarids into the lumen of an appendix an *Ascaris* which has entered the common bile-duct from the ampulla of the bile-duct would be stimulated to advance up the duct so long as its body is gripped by the orifice of the duodenum papilla, but when the whole body of the worm has passed into the channel of the common bile-duct, that stimulus might cease because of the width of the duct and the worm would remain in the common bile-duct. As was the case with ascarids entering the appendix, once one *Ascaris* has passed through the orifice of the duodenal papilla other worms can follow more easily. Several ascarids may thus enter the common bile-duct, and Wang, Tang, Liu, and Kao (1956) report finding 48 ascarids in a common bile-duct.

Despite its width the common bile-duct could grip the bodies of ascarids sufficiently to stimulate them to advance into the right or the left hepatic duct and from there on into the intrahepatic ducts till they are stopped by the diminishing lumen of the more distal intrahepatic ducts.

Although a normal cystic duct with its spiral valve would not present an easy pathway for an *Ascaris* the dilatation of the cystic duct occurring when the common bile-duct dilates in response to obstruction of the orifice of the duodenal papilla during the passage of an *Ascaris* through it could allow a worm to travel via the cystic duct to the gall-bladder.

Bacteria carried in on the bodies of ascarids could set up suppuration in the biliary tract, and acute inflammation leading to suppuration could occur in the common bile-duct, the intrahepatic bile-duct, and the gall-bladder (Barrera-Ordonez, 1965). A liver abscess from suppuration in the intrahepatic ducts could rupture into the peritoneal, pleural, or pericardial cavity or into viscera within these cavities.

Could ascarids continue to live in the biliary tract? Apparent survival of ascarids for 1 month in the common bile-duct have been reported (Louw, 1966). When an *Ascaris* dies in the biliary tract its body disintegrates. Fragments of its body may form the nuclei for gall-stones (Robinson, 1966). The dead and disintegrating bodies of ascarids in the common bile-duct destroy the ductal mucosa and excite the formation of granulation tissue which becomes firm fibrous tissue stricturing the common bile-duct (Louw, 1966).

Ascarids reaching the intrahepatic ducts disintegrate and disappear, but fertilized ova in the bodies of female worms resist digestion and persist, and these ova stimulate the formation of granulomatous masses in the liver (Anstey, 1966). Segmentation and even embryonation may occur in ova embedded in these granulomatous masses.

Ascarids in the Main Pancreatic Duct.—An *Ascaris* may enter the main pancreatic duct from the ampulla of the bile-duct and should it do so it will move up the duct till it is held by the diminishing calibre of the distal end of the duct. Despite the small diameter of the main pancreatic duct some ascarids have found their way into this duct. Bacteria carried in on the bodies of ascarids and the irritant products from the dead and disintegrating bodies of the worms cause an inflammation of a variable degree of intensity which manifests as acute pancreatitis, subacute pancreatitis, or the formation of a pseudopancreatic cyst.

ASCARIDS IN THE PERITONEAL CAVITY

Deductions have been made as to the events determining the emergence of ascarids from the gangrenous tip of an appendix or a Meckel's diverticulum. Once the ascarids had entered the peritoneal cavity they would be as helpless as ascarids in a pan of water. They would remain close to the place from where they had emerged. Many of these ascarids are found in the pelvis, and it is likely that they were moved there by gravity.

Ascarids may enter the peritoneal cavity through suture lines made at operations on the gastro-intestinal tract as a result of the head of a worm engaging in the suture line. Ascarids may also enter the peritoneal cavity through gangrenous patches in the wall of a small intestine filled to bursting point with ascarids. Ludlow (1927) and Girges (1934) described the emergence of ascarids from the walls of apparently normal small intestine through circular holes a little smaller than the girth of the *Ascaris*. Girges (1934) refers to the suggestion made by Blanchard that these ascarids had nibbled through the mucosa of the small intestine and that this had resulted in a submucous abscess through which the ascarids had pushed their way out. This proposition is not supported by evidence. Moreover the mouth parts of an *Ascaris* are not adapted for biting and as Makidono (1956) observed the worm directs its head into the lumen of the small intestine and away from the mucosa.

Dickson and Cole (1964) provide good evidence for the view that ascarids which emerge from the walls of apparently normal intestine have done so through the softened floors of typhoid ulcers of the ileum.

The emergence of ascarids into the peritoneal cavity from the intestinal tract is not followed by a leak of intestinal content probably because of the closing in of the walls after the worm has passed. Nevertheless the escape of ascarids into the peritoneal cavity is fraught with the danger of peritonitis from bacteria on the bodies of the worms.

An *Ascaris* escaping into the peritoneal cavity could not normally move out of this cavity, but should the head of such a worm engage in the lumen of a tube draining the peritoneal cavity the *Ascaris* would advance along the tube and emerge on to the surface of the abdominal wall. The mechanics of this movement have been deduced from what happens when a worm enters the lumen of an appendix.

An *Ascaris* could not nourish itself in the peritoneal cavity. How long could it survive? Asada (1924) found that adult ascarids could survive for 2 weeks in the peritoneal cavity. When the worm dies in the peritoneal cavity its body disintegrates and disappears, but fertilized ova in the bodies of female worms persist, and if the ova remain together at the site of the worm's body the presence of so many ova in one place excites the formation of a large granulomatous mass. If the worm discharges its ova into the peritoneal cavity these ova became widely dispersed and each ovum becomes encysted in a miliary nodule of granulation tissue resembling the nodules of miliary tuberculosis. Such nodules have been observed and described by Cooray (1951) and de Silva (1957).

SOME OTHER MIGRATIONS OF *A. LUMBRICOIDES*

Many of the other migrations of *A. lumbricoides* can be explained on the basis of the deduction which has been made that if the head of an *Ascaris* engages in an orifice this will act as a powerful stimulus causing the worm to make its way into the orifice and to advance into any channel leading off from it.

Thus, although ascarids carried in the stools to the rectum are usually expelled in the stools, occasionally an *Ascaris* emerges from the anus by active movement of its own. How does this occur? If an *Ascaris* in the rectum chances to get its head engaged in the upper end of the anal canal the worm will be stimulated to advance into and push through the lumen of the closed anal canal till it has emerged from the anus.

The sudden emergence of an *Ascaris* from the nostril by active movements of the worm is the result of the head of an *Ascaris* entering the nostril and thereby being stimulated to emerge from the nostril. This unheralded occurrence shows that ascarids have reached and remained in the nasal passage without giving any hint of their presence there.

The sudden emergence of an *Ascaris* from the orbit medial to the eyeball is a very rare occurrence (Van Rensburg and Kark, 1958). In this case the head of an *Ascaris* in the nasal passages enters the orifice at the lower end of the lacrimal duct and this stimulates the worm to ascend the lacrimal duct and lacrimal sac, from where it emerges by pushing its way out through the softened walls of the lacrimal sac, after these walls have become inflamed by bacteria carried into the sac on the body of the worm.

The emergence of an *Ascaris* from the external auditory meatus is another rare event; the head of an *Ascaris* in the nasopharynx enters the orifice of the auditory tube and this stimulates the *Ascaris* to enter the auditory tube and the middle ear, from where it emerges by perforating the ear-drum, after the ear-drum has become softened by inflammation in the middle ear from bacteria carried in on the bodies of the worms.

These two events occurring suddenly indicate that ascarids reaching the nasal passages and the nasopharynx are not noticed by their host. Oschner, de Bakey, and Dixon (1949) describe cases of sudden suffocation from the impaction of ascarids in the larynx. These ascarids must have remained unnoticed in the laryngopharynx for some time.

Occasionally an *Ascaris* in the laryngopharynx may slip down the larynx and trachea and become impacted in an intrapulmonary bronchus, causing a lung abscess by inflammation from bacteria on the body of the worm.

These events indicate that ascarids in the pharynx or the nasal passages give no hint of their presence. How did they get there? They could have been projected into the laryngopharynx during vomiting. If ascarids in the pharynx and nasal passages are not felt by the host it would follow that ascarids could have ascended from the stomach by muscular efforts of their own, and that the movements of the worms making this ascent would not have been noticed.

Ascarids which had entered the oesophagus would be stimulated to ascend the oesophagus and pharynx from the contact of the walls of the oesophagus and pharynx with the bodies of the worms. The worms would have come from the stomach. There have been no studies on the lines of Makidono of the movements made by ascarids to travel from the jejunum into the duodenum and the stomach; nor have there been studies on the movements of ascarids in the stomach. Although the stomach is not the normal habitat of *A. lumbricoides*, ascarids occasionally live in the stomach, and Girges (1934) records finding large numbers of ascarids there.

Ascarids have been found in the lumen of an acutely inflamed uterine tube (Maxwell, 1924; Sterling and Guay, 1936). Ascarids could reach the uterine tube by emerging from the anus and ascending the vagina and uterus or they could enter the uterine tube through its abdominal orifice from the peritoneal cavity. Both these routes are, however, somewhat improbable.

Ascarids have been found in the urinary bladder of both male and female hosts. It is just possible that an ascarid emerging from the anus could have ascended through the female urethra to the urinary bladder, but this route would not be practicable in the case of a male subject. In the male, ascarids in the bladder have emerged from the external urethral meatus after traversing the male urethra and this would be explicable on the basis of the head of the worm engaging in the internal urethral meatus. Girges (1934) suggests that ascarids reach the urinary bladder through vesico-intestinal fistulae and he states: 'Ascarids may be seen passing through fistulae into the urinary and genital tract.' This would explain how ascarids might reach a uterine tube.

The most remarkable migration of ascarids was that recorded by Boettiger and Werne (1929), who found 2 ascarids at a post-mortem examination. One *Ascaris* was in the right ventricle and the other extended from the right ventricle to the pulmonary artery. These ascarids could have made their way into the inferior vena cava from the liver or from the peritoneal cavity, but there was no evidence of this at the post-mortem examination, and there the matter rests to this day.

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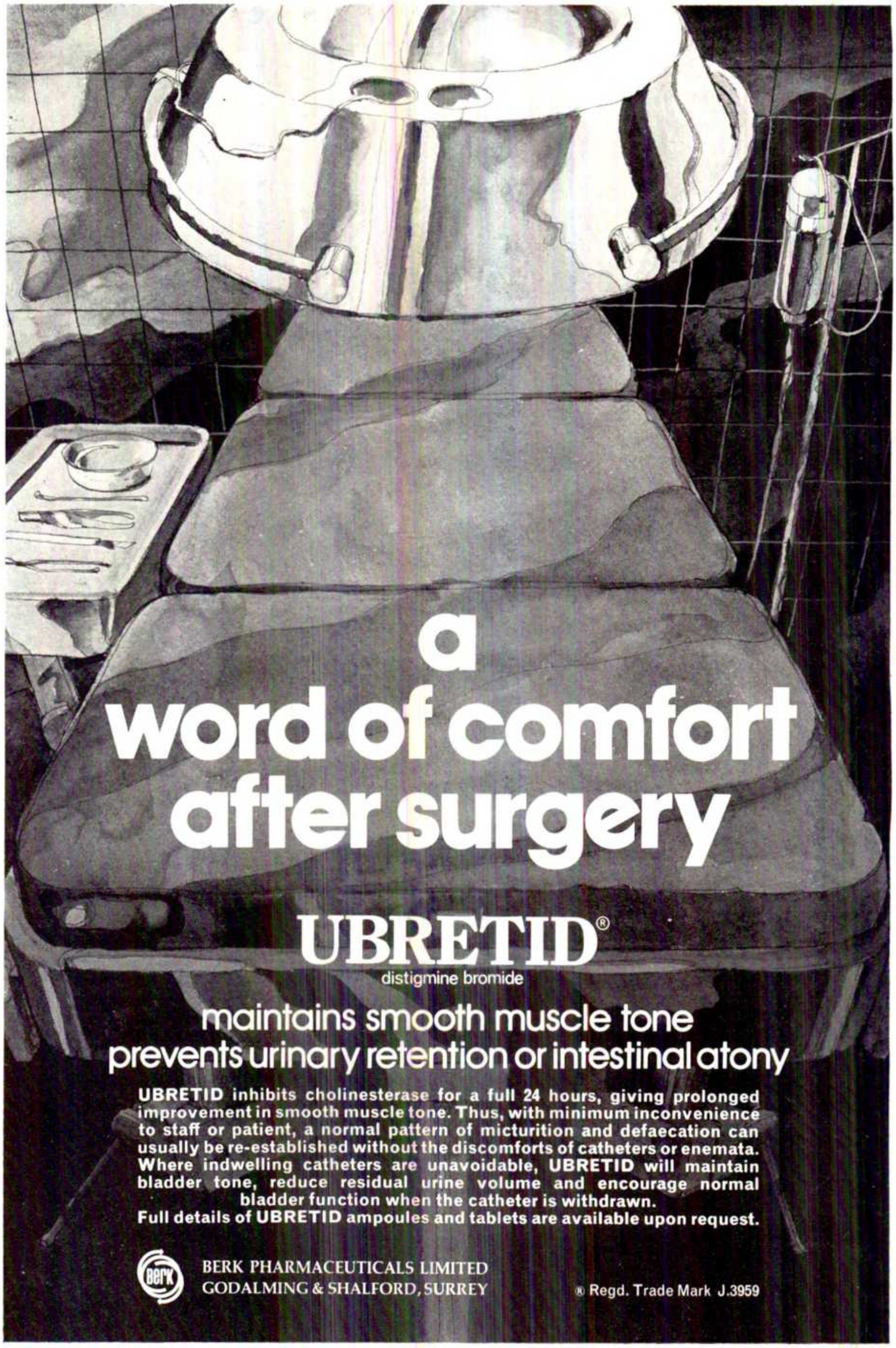

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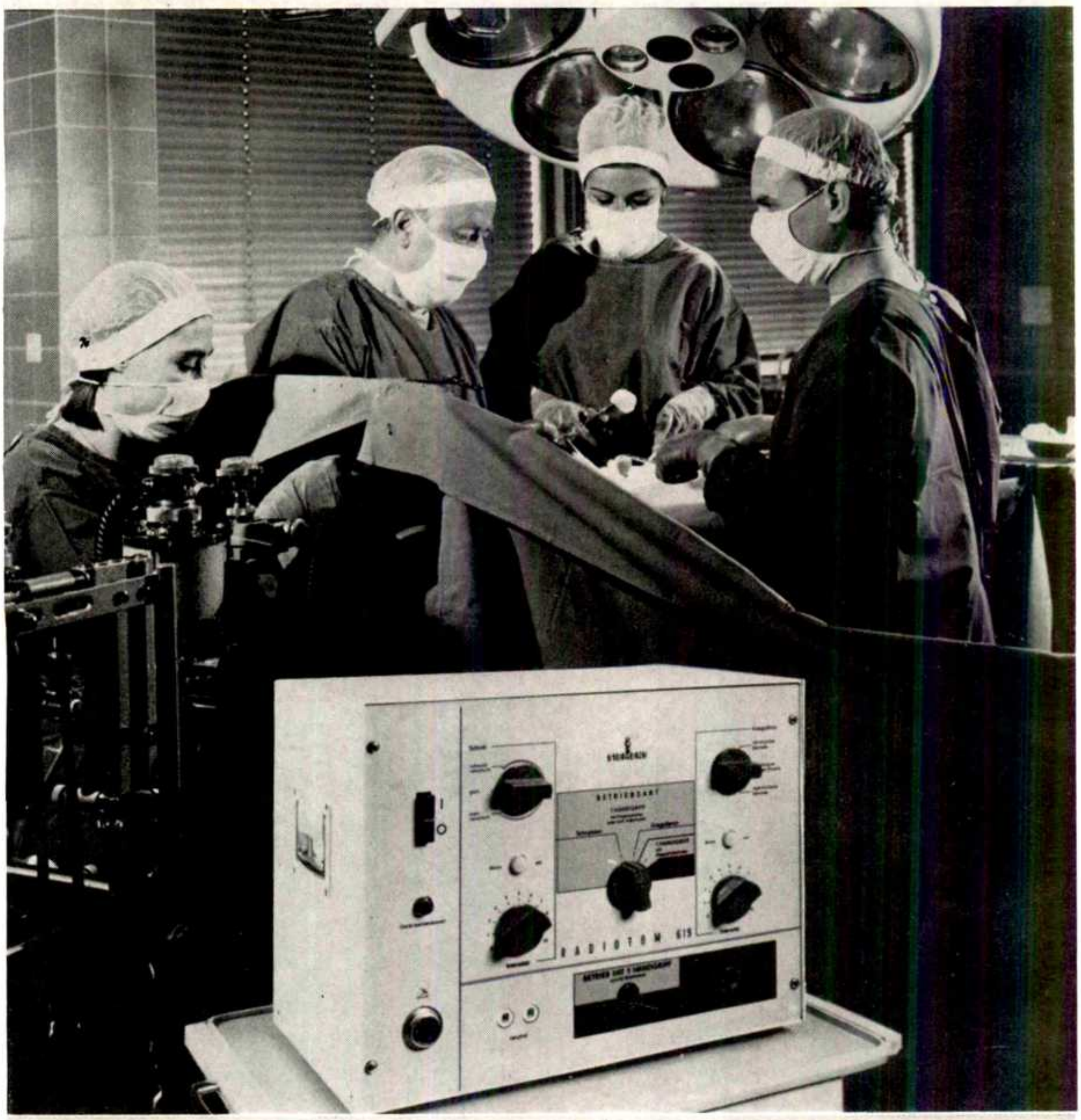

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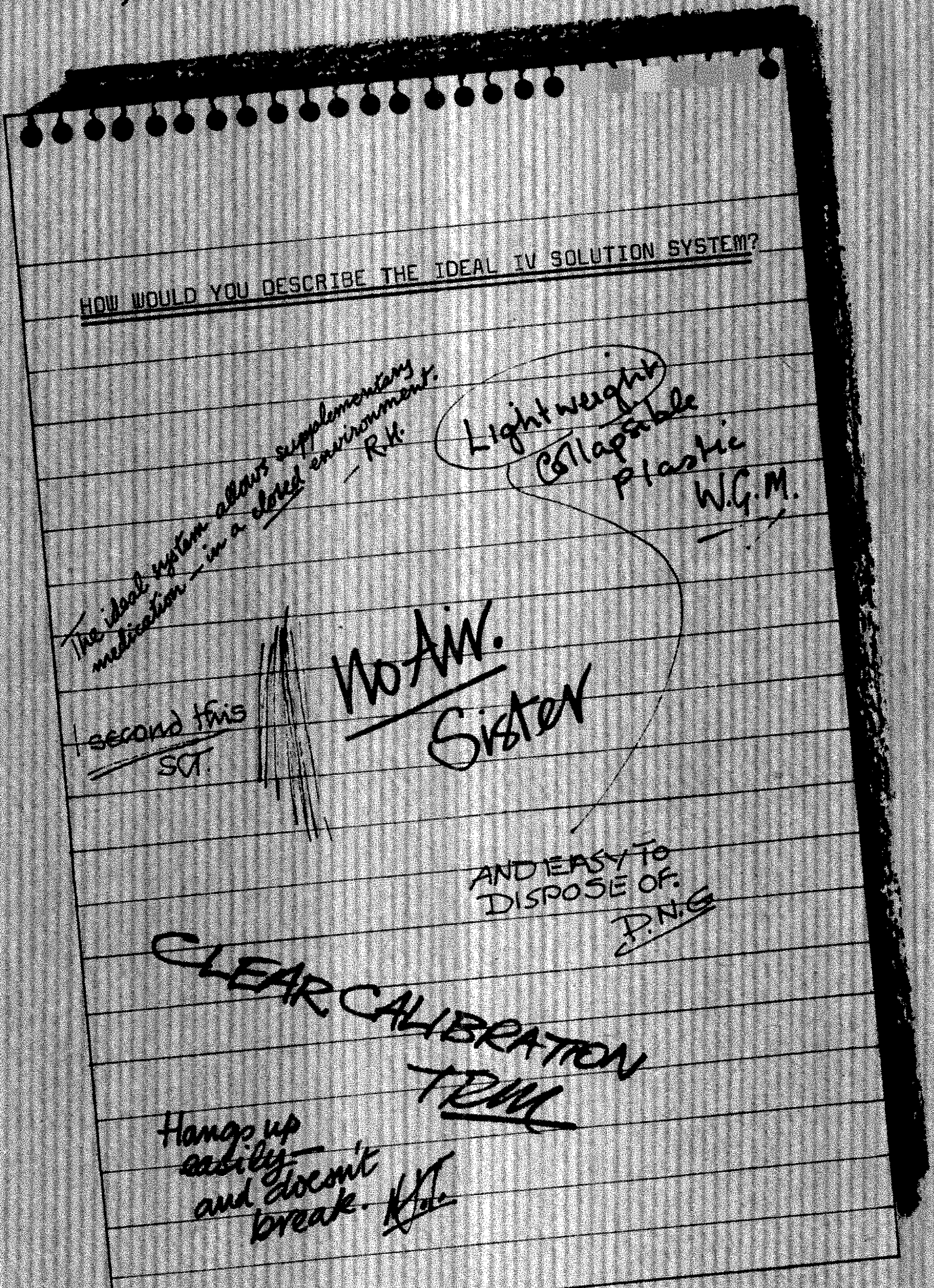

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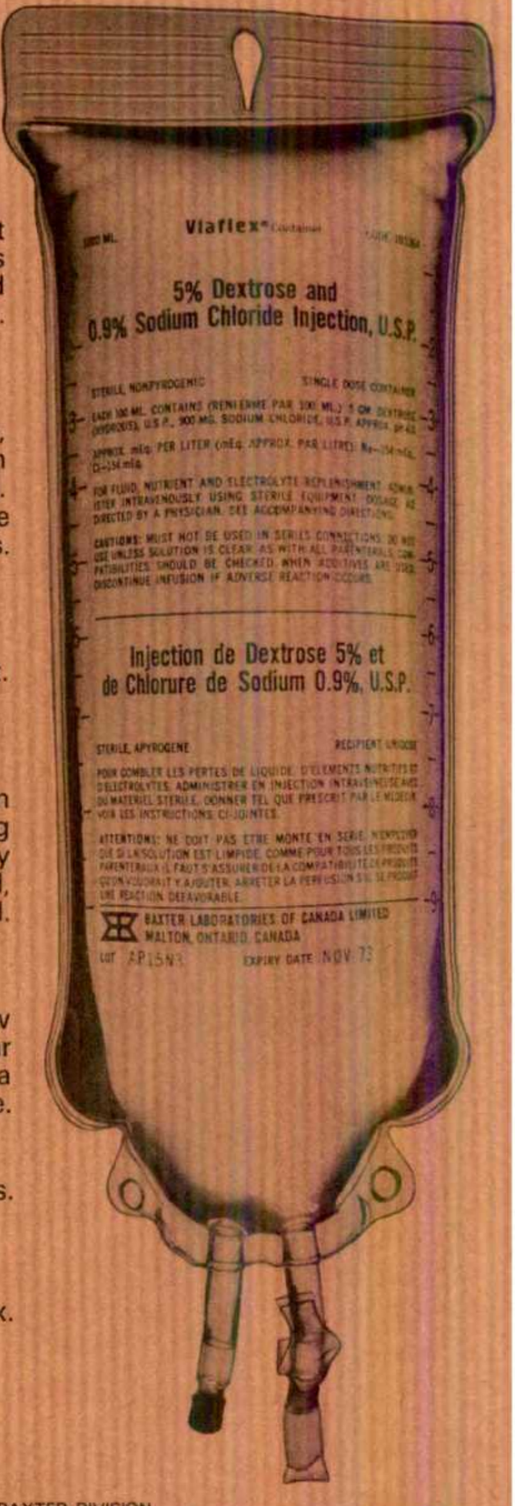

BACTERIAL CONTENT OF THE GASTRIC JUICE

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SUMMARY

A survey has been made of the bacteria present in the gastric aspirate obtained from 280 preoperative and postoperative secretion studies. In the preoperative group viable bacteria were isolated from 41 per cent of patients, whereas in the postoperative group they were isolated from 73 per cent. The nature of the bacterial flora also differed in the two groups.

It is suggested that infected stomach contents may cause local sepsis following gastric surgery and that loss of the acid barrier may allow infection by pathogenic bacteria of the gut, producing postoperative diarrhoea.

ALTHOUGH several authors have investigated the bacterial content of gastric juice (Seley and Colp, 1941; Barber and Franklin, 1946; Schwabacher, Salsbury, and Loosemore, 1959; Irvin, Donaldson, and Smith, 1967; Drasar, Shiner, and McLeod, 1969) wide variations have been reported in the proportion of patients who have viable bacteria in the stomach, and little is known of the clinical significance of this. A prospective study conducted in the Department of Clinical Surgery, Edinburgh University, on the acid levels and bacterial content of the stomach in patients with peptic ulceration has been completed and the results are now presented.

MATERIALS AND METHODS

Specimens of gastric juice were taken from all patients who underwent Peptavlon secretion studies. After an overnight fast each patient had a polythene Ryle's tube passed and a specimen of gastric juice aspirated with a sterile syringe. This was sent for bacteriological examination. A second specimen was obtained in a similar fashion at the end of the fast and this was also processed bacteriologically. After neutralization of the specimens two blood-agar and two MacConkey plates were inoculated; one of each was incubated aerobically at 37° C. for 24 hours and the remaining two were incubated anaerobically at 37° C. for 48 hours. All organisms growing on the plates were identified by a Gram-stain, cultural characteristics, and biochemical reactions (Cruickshank, 1965), and the following species were isolated: *Candida* spp., *Escherichia coli*, *Staphylococcus aureus*, *Staphylococcus albus*, alpha-haemolytic streptococci, beta-haemolytic streptococci, *Streptococcus faecalis*, anaerobic streptococci, pneumococci, *Neisseria pharyngis*, *Proteus* spp., diphtheroid bacilli, lactobacilli, *B. anthracoides*, and *Clostridium welchii*.

Results in the postoperative group were obtained at follow-up secretion studies performed at least 2 months after operation.

RESULTS

Two hundred and eighty tests were performed; 181 on preoperative and 99 on postoperative patients. In the preoperative group 143 patients had duodenal ulcers, 5 had gastric ulcers, 2 had gastric carcinomas, and there were 31 miscellaneous diagnoses including hiatus hernia, cholelithiasis, and pyloric stenosis. Eighty-four of the 181 patients (41 per cent) had viable bacteria in the stomach and 108 bacterial growths were obtained. Growths were obtained from 4 of the patients with gastric ulcers, from both patients with gastric carcinomas, from 56 (39 per cent) of the cases of duodenal ulcer, and from 22 (71 per cent) of those with miscellaneous diagnoses.

Table I.—PREOPERATIVE GASTRIC FLORA AND ACID LEVELS FROM 181 PATIENTS

GASTRIC FLORA	ACID LEVELS (mEq./l.)				
	0–10	11–20	21–30	31–50	>50
Total No. of tests	15	32	41	79	14
No growth	1	12	26	47	11
Candida spp.	3	7	5	19	3
Esch. coli	1	1	2	1	1
Staph. aureus	1	1	2	—	—
Staph. albus	2	7	2	2	—
Alpha-haemolytic streptococci	5	4	2	1	—
Beta-haemolytic streptococci	1	—	1	—	—
Strept. faecalis	1	1	—	2	—
Anaerobic streptococci	1	1	1	1	—
Pneumococci	4	2	4	—	—
N. pharyngis	2	2	1	1	—
Proteus spp.	—	—	1	—	—
Diphtheroid bacilli	1	—	1	1	—
Lactobacilli	1	—	—	—	—
B. anthracoides	—	—	—	2	—
Cl. welchii	2	1	—	—	—
Total No. of growths	25	27	22	30	4

Organisms most frequently isolated were those of the *Candida* group, especially from the high acid secretors, whereas in the lower acid ranges organisms such as alpha-haemolytic streptococci, *Staph. albus*, pneumococci, and neisseriae were more common. Fifteen different groups of organisms were isolated (*Table I*). Ten (9 per cent) of the 108 growths were heavy, 34 (31 per cent) moderate, and 64 (59 per cent) scanty.

In the postoperative group, in which the majority of the 99 patients underwent vagotomy with a drainage procedure, there was a marked rise in the proportion of patients from whom bacterial growth was obtained and a considerable change in the proportions of organisms isolated (*Table II*). Whereas in the preoperative group growth of bacteria was obtained from 41 per cent of the patients, growth in the postoperative group was obtained from 73 per cent. Most patients in the latter group had acid levels of 0–10 mEq./l. compared with 30–50 mEq./l. in the preoperative group. The total number of growths from the 72 patients in the postoperative group was 145. The organism most commonly isolated was *Esch. coli*, although *Candida* spp., *Strept. faecalis*, *Staph. albus*, and alpha-haemolytic streptococci were commonly isolated, generally from those patients who had very low acid levels.

Bacteriological studies were conducted on the gastric juice of 46 patients both pre- and postoperatively in order to investigate the effect of surgery on the gastric flora of the same patient. The results are shown in *Table III*, and it can be seen that in terms of growth or no growth 22 of the 46 patients had postoperative findings which differed from the preoperative ones.

Table II.—POSTOPERATIVE GASTRIC FLORA AND ACID LEVELS FROM 99 PATIENTS

GASTRIC FLORA	ACID LEVELS (mEq./l.)				
	0–10	11–20	21–30	31–50	>50
Total No. of tests	66	17	9	5	2
No growth	14	2	4	5	2
Candida spp.	14	7	2	—	—
Esch. coli	28	2	—	—	—
Staph. aureus	6	3	1	—	—
Staph. albus	9	5	—	—	—
Alpha-haemolytic streptococci	10	2	1	—	—
Beta-haemolytic streptococci	3	—	—	—	—
Strept. faecalis	17	3	1	—	—
Anaerobic streptococci	3	1	—	—	—
Pneumococci	7	—	1	—	—
N. pharyngis	2	1	—	—	—
Proteus spp.	6	—	—	—	—
Diphtheroid bacilli	3	—	—	—	—
Lactobacilli	—	3	—	—	—
B. anthracoides	—	—	—	—	—
Cl. welchii	2	2	—	—	—
Total No. of growths	110	29	6	—	—

Table III.—PRE- AND POSTOPERATIVE GROWTH OF ORGANISMS FROM THE GASTRIC JUICE OF 46 PATIENTS

Growth of Organisms	*No. of Patients*
No growth pre- or postoperatively	10
No growth preoperatively but growth postoperatively	21
Growth preoperatively but no growth postoperatively	1
Growth pre- and postoperatively	14
Total	46

The most common difference was that growth was obtained from the postoperative specimens of the gastric juice, no growth having been obtained preoperatively. Furthermore, of the 14 patients whose pre- and postoperative specimens both produced growth, only 2 retained postoperatively the same organisms which had been cultured preoperatively. In 12 patients the flora was different, many coliforms and *Strept. faecalis* organisms being cultured from the postoperative specimens. Also, whereas growth from the preoperative specimens was mostly scanty, growth postoperatively was generally heavier.

DISCUSSION

That a wide variety of bacteria can survive in the stomach has been established by several authors. The proportion of patients with duodenal ulcers in whom this has been reported varies widely, however, though most authors are agreed that there is a very high incidence in patients with gastric ulcers and tumours (Seley and Colp, 1941; Barber and Franklin, 1946; Bach-Nielsen and Amdrup, 1965).

Barber and Franklin (1946) reported that 100 per cent of patients with duodenal ulcers had sterile gastric juice; Högman and Sahlin (1956) found 74 per cent; Seley and Colp (1941) reported 63 per cent; and Bach-Nielsen and Amdrup (1965) recorded only 30 per cent. In the present series 61 per cent of patients with duodenal ulcers had sterile gastric contents. These variations are very wide and are probably related to differing sampling and culture techniques.

It has been shown that there is an association between bacterial growth and various levels of acidity. In the present series this is demonstrated by the wide variety of bacteria grown from those patients with levels of between 0 and 20 mEq./l. compared with the comparatively few grown at levels above 20 mEq./l.

The possibility of local sepsis developing from infected gastric contents at operation was investigated by Bach-Nielsen and Amdrup (1965), but in only 9 out of 176 patients in their series was there any evidence that this had occurred. In the present series this was a possibility in only 1 patient, a 64-year-old man who had a laparotomy performed for abdominal pain and who was found to have a gastric carcinoma. Coliforms, predominantly *Esch. coli*, were grown from his postoperative gastric aspirate and a short period later he developed a wound infection from which similar bacterial species were cultured. His preoperative sample had yielded a light growth of *Esch. coli*. *Staph. aureus* or beta-haemolytic streptococci were isolated from 6 patients preoperatively but none of these developed postoperative sepsis, however.

The second point of interest in these results is the large number of organisms such as *Proteus* spp., *Esch. coli*, and *Strept. faecalis* which was cultured from postoperative samples compared with the small number of those obtained preoperatively. Because postoperative studies were not conducted until at least 2 months after operation this shows that persistence of these organisms in the stomach is not a temporary phenomenon due to regurgitation of intestinal contents during the phase of paralytic ileus, but is a more permanent sequel to upper gastrointestinal surgery. The reason for this is not clear at present, though the small numbers of patients with a high residual acid output did not have the same tendency to harbour coliform organisms as those with a very low acid output and it would appear, therefore, that the level of acid output is more important than regurgitation of small-bowel contents into the stomach.

Diarrhoea following upper gastro-intestinal surgery is probably due to a variety of causes. One of these may be that the loss, or partial loss, of the sterilizing barrier of the hydrochloric acid of the stomach renders this group of patients more susceptible to infection by small doses of pathogenic bacteria which would not be harmful to the normal person. Howie, Duncan, and Mackie (1953) suggested that diarrhoea following upper gastro-intestinal surgery may be bacterial in origin.

CONCLUSIONS

Two main points are made in this paper: first, that infected stomach contents may lead to local sepsis postoperatively and, secondly, that the loss or partial loss of the hydrochloric acid barrier of the stomach may facilitate infection by pathogenic gut bacteria.

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A METHOD OF REPAIR OF MYELOMENINGOCELES

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SUMMARY

We believe that it is possible in the majority of myelomeningoceles to achieve a satisfactory repair of the lesion. To achieve dural closure the mobilization must be extensive and this can only be done if the anatomy of the myelomeningocele is thoroughly understood. Large skin defects can be closed with primary wound healing provided that the skin is mobilized extensively. To do this it is essential that the subcutaneous layer be retained intact to maintain the blood-supply to the skin. Only exceptionally large lesions require relieving incisions, skin-grafts, or swinging of skin-flaps.

IN recent years increasing interest has been shown in the treatment of myelomeningoceles, and early repair of the lesion is now commonly undertaken in many centres. In general, repair is not easy because it is difficult to identify structures in the grossly abnormal and variable anatomy of the myelomeningocele and because a large skin defect has to be closed. The aims of operating early are to preserve functioning neural tissue and to prevent bacterial invasion of the cerebrospinal axis. To maintain asepsis it is essential that neither the dura nor the skin suture lines should break down; this occurs all too commonly at present, with tragic results for the infant. Although many methods of repair of myelomeningoceles have already been described (Sharrard, Zachary, Lorber, and Bruce, 1963; Ingraham and Matson, 1969; Gurdjian and Thomas, 1970) the purpose of this paper is to report a procedure which permits adequate closure of both the dura and the skin. It is based on experience gained at early operation on 120 infants with myelomeningocele admitted to the Neurosurgical Unit of the General Infirmary at Leeds between October, 1966, and December, 1970.

ANATOMY OF THE MYELOMENINGOCELE

If the lesion is to be operated on successfully it is essential that the surgeon has a thorough understanding of the anatomy of the myelomeningocele, especially of the areas adjacent to normal tissue. It will be recalled that a myelomeningocele may present either as a protruding cyst or as a neuroplaque flush with the surface of the back; in either case the anatomical arrangements of the tissues are the same and there is no difference in the surgical approach.

Deep to the myelomeningocele the vertebral bodies may be normal or, especially at the thoracolumbar junction, wedged to form a kyphus (*Fig.* 1A) (Barson, 1970). The pedicles are rotated outwards to form a shallow gutter of which the lateral dimension is two or three times that of the normal spinal canal.

Dura lines the gutter and the lateral protrusion formed by the pedicles. It also covers part of the dorsal muscles before being reflected posteriorly into the dome of the cyst. At the points of reflection the dura is covered by skin and joins it at a variable distance from the summit of the cyst to form a thin membrane attached to the circumference of the neuroplaque.

The spinal cord, after leaving the spinal canal at the upper limit of the myelomeningocele, passes dorsally and comes to lie immediately beneath the dura. It then flattens out into the disk-shaped neuroplaque whether this lies in the dome of the cyst or flush with the back (*Fig.* 1). Spinal nerves arise from the deep surface of the neuroplaque and cross the underlying cavity which is filled with cerebrospinal fluid (C.S.F.). They then penetrate the dura and leave the spinal gutter through the intervertebral notches.

At the lower limit of the neuroplaque, depending on the spinal level of the lesion, either the spinal cord is re-formed or the nerve-roots arising from it gather together to form the cauda equina (*Fig.* 1).

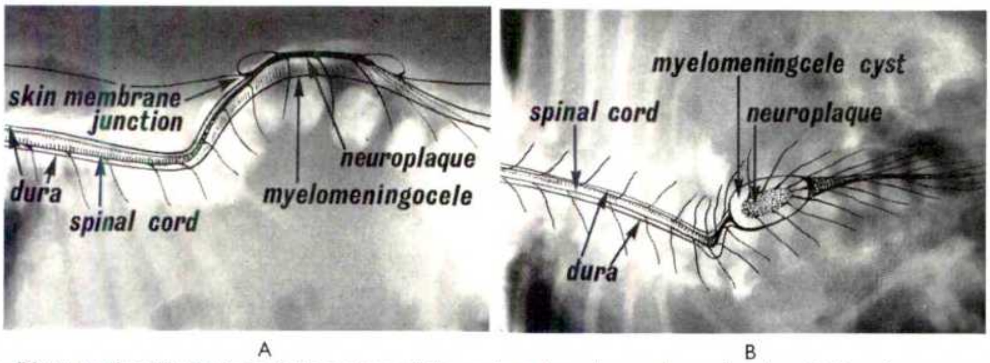
OPERATIVE PROCEDURE

Our aim is to operate on the infants within 8 hours of birth and this is usually achieved.

The umbilical vein is cannulated and any blood shed during the operation is replaced; the usual blood-loss is about 40 ml. We believe transfusion is necessary even in infants in good nutritional status, as wound healing occurs best if the postoperative haemoglobin is maintained at normal levels.

The anaesthetized baby is laid prone on a hot-water blanket. The myelomeningocele and a wide area of surrounding skin are cleaned with a soapy cleansing fluid; chemical antiseptics and alcoholic solutions are avoided because of the risk of damaging functioning neural tissue in the neuroplaque. To prevent mechanical damage to the neuroplaque the cleansing fluid is poured over the myelomeningocele—swabs are never used.

Skin hooks are placed in the skin at the proposed limits of the incision. Tension on the hooks supports the skin while an outline of the incision is scratched with a scalpel. The incision should always be planned to lie vertically because transverse and to a lesser extent oblique incisions are subjected to considerable stress by inevitable movements of the trunk during the healing period. It is stress of this kind which contributes significantly to delayed wound healing and even separation of the edges. At the lateral borders of the myelomeningocele the incision lies as close as possible to the skin–membrane junction but any abnormally thin or thickened skin must be excised because of its poor healing qualities. At the upper and lower limits of the incision triangles of skin are sacrificed to prevent unsightly bunching when the wound is sutured (*Fig.* 2).



A B

FIG. 1.—Diagrammatic representations of the anatomy of the myelomeningocele superimposed on lateral (A) and anteroposterior (B) radiographs of the spine.

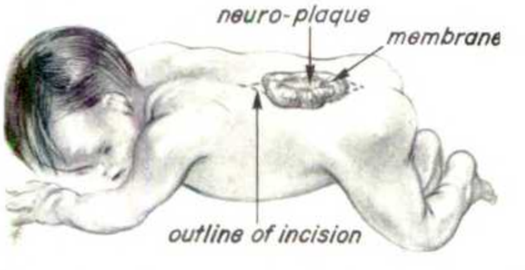


FIG. 2.—The dotted line indicates the position and extent of the skin incision.

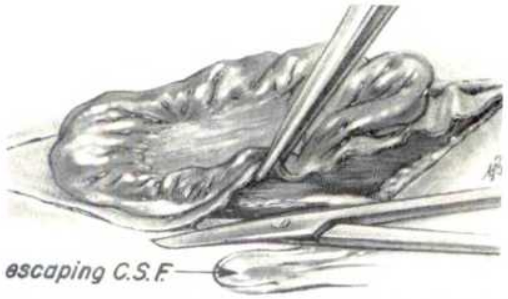


FIG. 3.—The incision at the skin–membrane junction enters the cyst of the myelomeningocele and C.S.F. escapes.

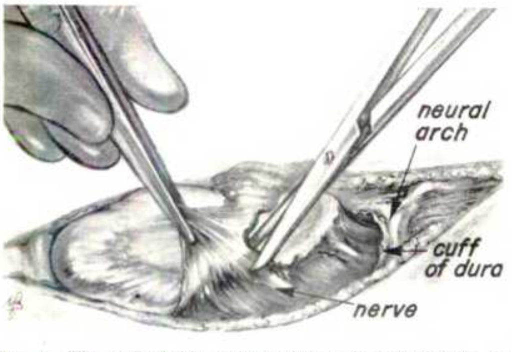


FIG. 4.—The cuff of skin and membranes is excised from the neuroplaque.

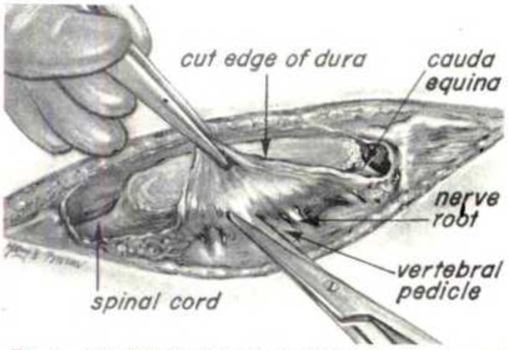


FIG. 5.—The dura has been dissected from the dorsal muscle and medially a band of fibrous tissue attaching the dura to the dorsal surface of the vertebral body is being divided to give adequate medial mobilization of the dura.

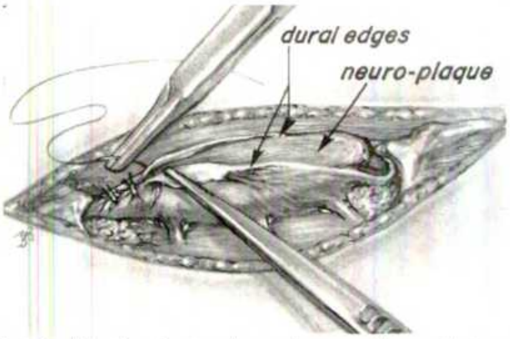


FIG. 6.—The dura is sutured over the neuroplaque with interrupted cat-gut sutures.

The incision is started laterally on each side with a scalpel and completed with scissors (*Fig.* 3) while the skin is pulled taut with hooks. The incision usually passes through the dura and provided that the myelomeningocele cyst has not previously ruptured C.S.F. escapes and the cyst deflates (*Fig.* 3). The skin and dura are divided together on each side until the points are reached where the dura starts to funnel inwards to join the dural sac in the spinal canal above and below the myelomeningocele. Beyond these points the skin and subcutaneous tissues are incised down to the deep fascia covering the dorsal muscles. Then the skin and underlying subcutaneous tissue, starting at the apices of the triangles, are dissected off the deep fascia and reflected towards the skin–membrane junction. As this is approached great care must be taken not to damage the underlying dura and the neural elements. The dura is uncovered as far as the skin–membrane junction and then divided. It is necessary to emphasize the care needed in making these divisions because of the proximity of the underlying neural elements which must not be damaged (*Fig.* 1). When these dural divisions have been made the neuroplaque is free of all surface attachments but it still has attached a cuff of skin and membrane. This cuff is excised from the neuroplaque (*Fig.* 4), but beforehand several filmy vascular adhesions passing from the membrane to the dura covering the dorsal muscles must be coagulated and divided. If the cuff of skin and membrane are left there is a risk that an intrathecal inclusion dermoid may develop in later years (Van Gilder and Schwartz, 1967). After excision of the cuff the neuroplaque is attached to spinal cord elements only and is laid on the dura lining the spinal gutter.

The next step is the mobilization of the dura so that it can be sutured over the neuroplaque to close the dural sac. It is our experience that provided the mobilization is extensive enough there is always sufficient dura to close the sac. The mobilization is started close to the cut edge of skin on each side by making an incision through the dura and the tissues lying superficial to the deep fascia of the dorsal muscles (*Fig.* 5). The line of the incision is kept close to the skin edge until the points are reached where the dura funnels into the spinal canal at the upper and lower ends of the myelomeningocele. The dura and its underlying tissue are dissected off the deep fascia of the dorsal muscles and reflected medially (*Fig.* 5). It is important to reflect the dura covering the muscle together with some underlying tissue because the dura is usually very thin and tears easily; the dura lining the spinal gutter is much thicker and stronger. Within the spinal gutter the dura is attached by several strong fibrous tissue bands to the dorsal surface of the vertebral bodies and these bands must be divided to achieve adequate medial mobilization (*Fig.* 5). The extradural fat lying in the spinal gutter must not be entered as it contains numerous blood-vessels of which large veins especially are easily damaged and bleed profusely. If any bleeding does occur it must be controlled by coagulation without damage to the nerve-roots as they emerge from the dura (*Fig.* 5). The attachment of the upper dural funnel to the laminae of the last complete neural arch is divided, and the dural edges are drawn together and sutured. The lower dural funnel seldom presents a clearly seen attachment for division, and at this end the dural edges are easily brought together.

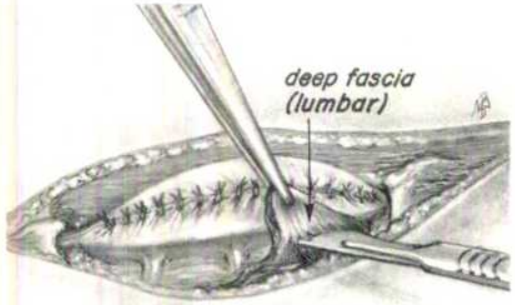


FIG. 7.—A flap of lumbar fascia is dissected from the dorsal muscles.

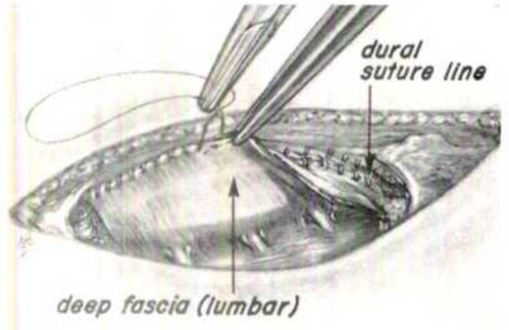


FIG. 8.—The lumbar fascia is sutured over the dural repair.

Interrupted chromic cat-gut sutures are used to evert the edges of the dura (*Fig.* 6). A continuous suture is never used, and unabsorbable suture materials are unsatisfactory because they are often extruded through the wound at a later stage with the risk of wound infection.

If the myelomeningocele lies in the lumbar region a flap of lumbar fascia may be used to give additional protection to the dural suture line. A flap is raised on one side, turned across the midline to cover the dural suture line, and stitched to the lumbar fascia on the opposite side (*Figs*. 7, 8). In the thoracic and sacral areas it is not usually possible to raise a satisfactory flap because the fascia is thin and tenuous.

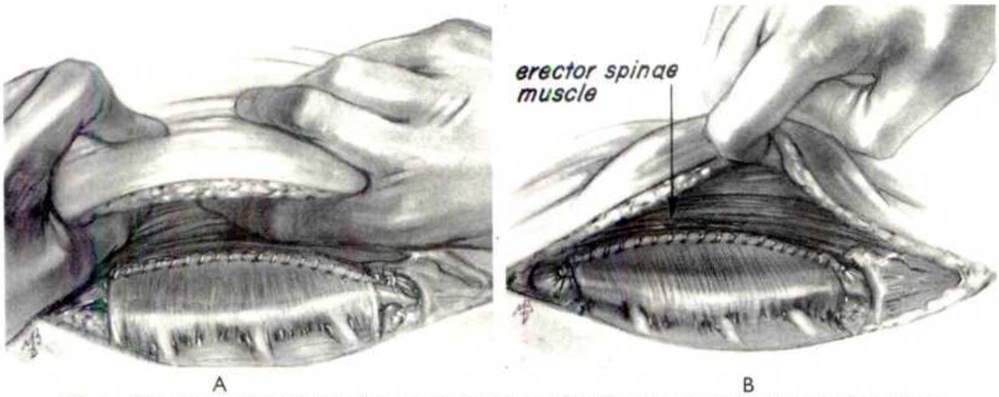


FIG. 9.—The skin together with its subcutaneous layer is mobilized by finger dissection from the deep tissue.

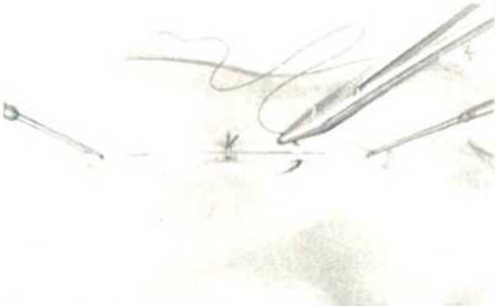


FIG. 10.—The skin incision is pulled taut with skin hooks and sutured with interrupted stitches.

Except in exceptionally large lesions it is always possible to mobilize the skin sufficiently to close the the skin defect, but since it must be mobilized very extensively and sutured under tension it is essential that its blood-supply should be preserved. The blood-supply to the skin arises from a network of vessels lying in the corium fed by arteries from the underlying muscles. When the feeding vessels are divided posteriorly the blood-supply depends on the anterior vessels. It is, therefore, essential that the skin be mobilized with the whole of its subcutaneous layer intact. Sharp dissection with a scalpel or scissors inevitably leads to the plane of dissection lying within the subcutaneous layer; blunt dissection by a finger in the subcutaneous fat strips the skin and the whole of the underlying subcutaneous layer without the use of excessive force (*Fig*. 9 A). On either side the plane between the subcutaneous layer and the deep fascia needs to be entered by sharp dissection, but once entered all further dissection is done with the index finger (*Figs*. 9 A, 9 B). Remarkably little bleeding is produced. Mobilization of the skin is carried out in all directions; only inferiorly do bands of fibrous tissue attaching the skin to the dorsal surface of the lower dural funnel require division. The exact extent of the mobilization should be no more than is necessary to close the defect. To test whether sufficient mobilization has been carried out the skin hooks are placed at the apices of the wound and pulled taut. If the skin edges at the centre of the wound can be brought together without undue tension then mobilization is adequate.

The suturing is started in the centre of the wound (*Fig*. 10). The skin edges are brought together without overlap using interrupted fine silk sutures on an atraumatic needle. The stitches are placed close together near the skin edges to minimize stitch tension.

POSTOPERATIVE MANAGEMENT

After the operation the baby is nursed prone for 10 days. The day after the operation the wound is inspected and any fluid collection under the mobilized skin is aspirated to prevent tension on the suture line. The sutures are removed on the tenth postoperative day.

Acknowledgements.—I wish to thank Mr. R. Myles Gibson for permitting me to operate on these patients and for his constant encouragement. I would also like to express my special thanks to Miss Mary Brown for the drawings used to illustrate this article.

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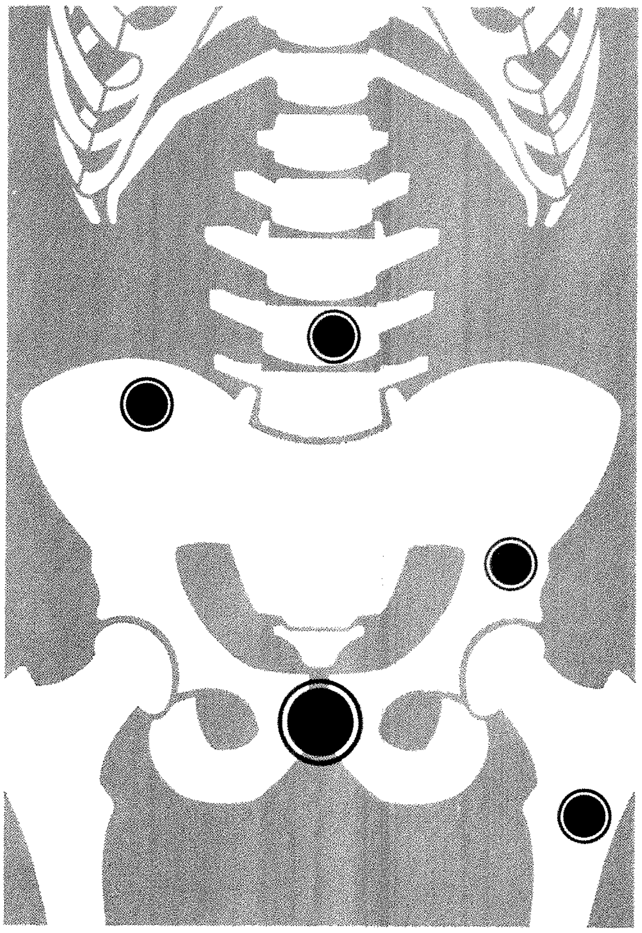

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PYLORIC FUNCTION AND GALL-STONE DYSPEPSIA*

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SUMMARY

Pyloric function was studied by means of a modified pyloric regurgitation test in which regurgitation was assessed both radiologically and biochemically. Forty-two tests were performed in 40 patients from six clinical groups: those with gall-stones with and without dyspepsia; those after cholecystectomy with and without persistent dyspepsia; and those with normal radiographs with and without dyspepsia. A close correlation was found between a history of flatulent dyspepsia and the detection of pyloric regurgitation in each matched pair of groups and in the series as a whole ($P < 0.001$). The time at which regurgitation occurred appeared to be significant. Regurgitation was not observed in symptomless subjects.

FLATULENT dyspepsia is a well-known symptom complex which has been defined by Rhind and Watson (1968) as follows: 'Epigastric discomfort after meals, a feeling of fullness so that tight clothing is loosened, eructation, with temporary relief and regurgitation of sour fluid to the mouth with heartburn.' Hess (1965) describes it as a sensation of fullness, slight nausea, and tension, especially after particular food, and points out that the discomfort cannot be provoked by palpation.

The relationship between these symptoms and gall-stones has been a subject for discussion for many years and it has been increasingly realized that cholecystectomy fails to relieve the symptoms in a proportion of cases. Maingot (1956) states, 'cholecystectomy has little or no effect in curing the unpleasant symptoms of flatulent dyspepsia'. Rhind and Watson (1968) found that 30 per cent of patients were no better after operation and 70 per cent were either cured or improved. Bodvall (1964) also found that one-third of his patients had persistent postoperative flatulent dyspepsia.

The problem was put into perspective by Price (1963), who found that amongst women between 50 and 70 years of age in an urban general practice there was an equal incidence of these symptoms in those with a normal and those with an abnormal cholecystogram, and he concluded that the relationship between the symptoms and gall-bladder disease was coincidental.

Any theory of the aetiology of flatulent dyspepsia must take all these observations into account. Rains (1964) points out that these symptoms are essentially related to the stomach rather than to the biliary tract and it is, therefore, in disordered gastroduodenal function that the link between these groups of patients is likely to be found. Capper, Butler, Kilby, and Gibson (1967) found a close corrrelation between a history of flatulent dyspepsia and the regurgitation of barium through the pylorus in radiological studies of patients with gall-stones. It was decided, therefore, to test the reproducibility of these findings with reference to patients with gall-stones and to those with a normal cholecystogram and barium meal by using a modified pyloric regurgitation test (P.R.T.).

MATERIALS AND METHODS

Forty-two tests were performed in 40 patients from three clinical groups, each group being matched with equivalent controls. Two patients were tested before and after cholecystectomy.

Group A: Preoperative patients with gall-stones and flatulent dyspepsia; 14 patients (10 female, 4 male); average age of 48 years.

Controls for group A: Preoperative patients with gall-stones and *no* flatulent dyspepsia; 6 patients (5 female, 1 male); average age of 42 years.

Group B: Patients after cholecystectomy with persistent flatulent dyspepsia; 3 patients (all female); average age of 60 years.

Controls for group B: Patients after cholecystectomy with *no* flatulent dyspepsia; 6 patients (4 female, 2 male); average age of 48 years.

Group C: Patients with a normal cholecystogram and barium meal and flatulent dyspepsia ('radiological negative dyspepsia'); 9 patients (4 female, 5 male); average age of 42 years.

Controls for group C: Patients with a normal cholecystogram and barium meal and *no* flatulent dyspepsia; 4 patients (2 female, 2 male); average age of 40 years.

The control patients for group C were under investigation for intermittent mild upper abdominal pain and did not have any of the symptoms under discussion. The stomach, pylorus, and duodenum were macroscopically normal either on barium meal or at subsequent operation in all but 1 patient in whom the pylorus was thought to be 'thickened'. Any patients with active duodenal ulceration or scarring were excluded from the study. (It will be seen that the controls were well matched for sex ratios and average age except in group B where 1 patient of 71 years affected the average.)

Method of Assessment of Symptoms.—A patient was considered to have flatulent dyspepsia if three or more of the following symptoms were present consistently up to the time of testing. They were considered to have no flatulent dyspepsia when none of the symptoms was present. The patients were interviewed and the history, being the more subjective part, was taken before the test started:—

Symptoms.—

Flatulence

1. Repeated belching.
2. Full-feeling after a normal-sized meal.
3. Inability to finish a normal-sized meal.

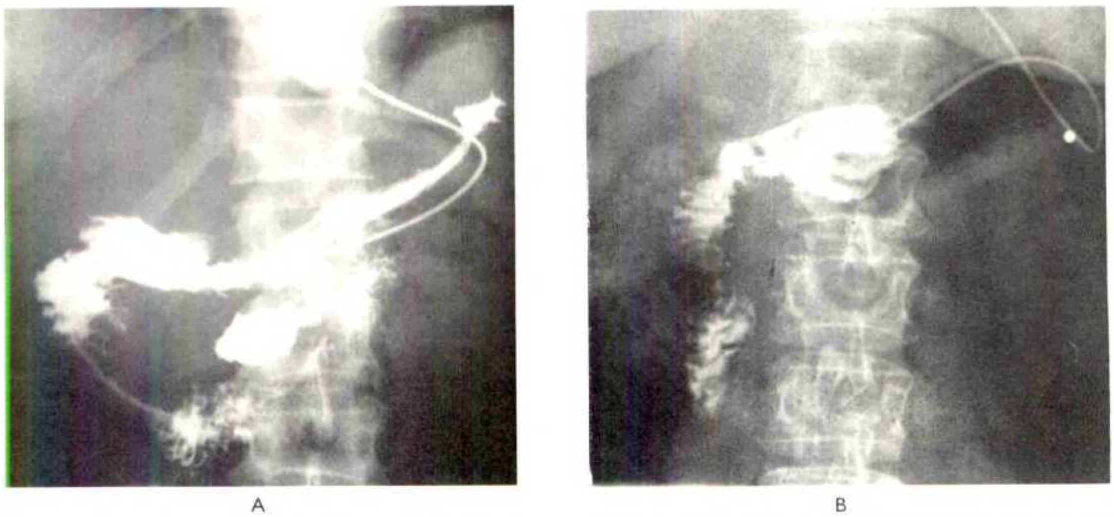
---

* Based on a communication to the Surgical Research Society in January, 1969.

4. Abdomen becomes blown-out so that the clothes have to be loosened.

Dyspepsia after meals

5. Burning discomfort in the epigastrium.
6. Burning discomfort in the chest ('heartburn').
7. Bitter fluid regurgitating into the mouth.



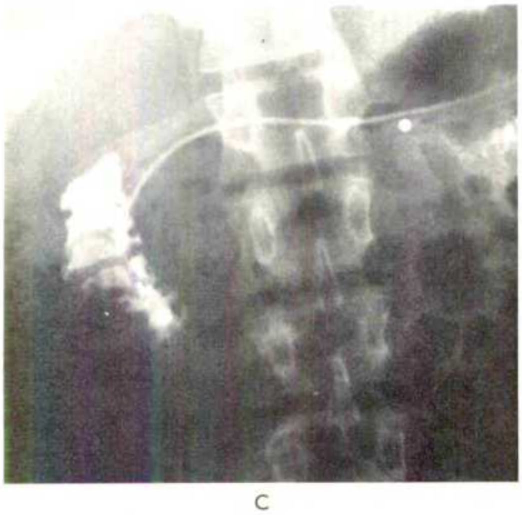


FIG. 1.—Radiographs showing (A) forceful regurgitation of barium into the stomach, (B) moderate regurgitation (note the radio-opaque gall-stones), and (C) no regurgitation.

8. Vomiting (? bile).
9. Nausea.

Some belching is normal. Inability to finish a normal-sized meal implies that the patient is hungry but feels full up soon after starting a meal and this must be distinguished from true anorexia. Heartburn is a symptom of oesophageal regurgitation and for this study it was only considered significant if accompanied by other symptoms. Vomiting is not a common part of the syndrome, but nausea and bloating may end in bilious vomiting.

Technique of the Test.—Capper's technique (Capper, Airth, and Kilby, 1966) was modified in several respects:—

1. A double-lumen plastic tube was used so that samples could be taken simultaneously from the stomach and duodenum, but the external diameter (3 mm.) of the tube passing through the pylorus was only a fraction larger than in Capper's technique.

2. The barium (Micropaque) which was in water was mixed with 0·9 per cent NaCl in the ratio 1 : 2 to produce a more physiological suspension (260 mosmol.). Ten ml. instead of 30 ml. were injected into the duodenum at any one time.

3. As the time that a patient should be screened radiologically is limited to a few minutes, the test was prolonged for $1-1\frac{1}{2}$ hours and evidence of regurgitation was detected biochemically. Duodenal and gastric samples were taken every 10 minutes (the stomach was emptied as completely as possible and 2 ml. of air were used to empty the tube after each sample) and each sample was analysed for *p*H, bilirubin concentration (method of Malloy and Evelyn, 1937), and tryptic activity (qualitatively and, in some patients, quantitatively by the method of Wiggins, 1967).

4. Because in many of these patients the symptoms are initiated or made worse by fatty foods, 7 ml. of arachis oil were put into the duodenum during the test in 25 of the patients.

5. The patient was always in the supine position with the gastric part of the tube in the body or fundus of the stomach, where any regurgitated fluid would collect, and well away from the pylorus. Capper and Airth (1970) found that posture affected the degree of regurgitation in patients with gastric ulcer but not in those with gall-stones.

The patients had not had anything to eat or drink for 4 hours before the test but they had not been starved overnight.

Method of Assessment of Regurgitation during the Test.—Regurgitation on a radiograph was classified as present (forceful, *Fig.* 1 A, or moderate, *Fig.* 1 B) or absent (*Fig.* 1 C), but only after at least four good contractions of the duodenal cap had been observed. The biochemical results were plotted on a graph. There are, therefore, in this test four ways of assessing regurgitation: (1) radiologically, (2) by the presence of barium in the gastric aspirate, or by the presence of (3) bilirubin, or (4) trypsin in the gastric samples (the *absence* of bilirubin or trypsin is only significant if their presence in the duodenal samples has been demonstrated).

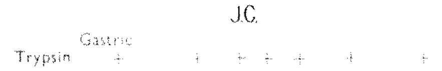


FIG. 2.—Graph of type-1 regurgitation. Note the presence of trypsin in the stomach throughout the test. Histograms represent the volume of the samples.

RESULTS

Positive evidence of regurgitation was of two types:—

Type 1: Where there was radiological (P.R.T. + ve) and biochemical evidence of pyloric regurgitation intermittently or continuously throughout the test; *Fig.* 2 shows the results of such a test in graph form. Trypsin is present in the gastric juice throughout.

Type 2: Where there was no radiological evidence of regurgitation (P.R.T. – ve), but regurgitation did occur after the duodenal bilirubin concentration had risen spontaneously (*Fig.* 3) or after arachis oil (*Fig.* 4).

Table I gives the results of the tests in each group of patients and shows the close correlation between a history of flatulent dyspepsia and the observation of pyloric regurgitation. When each group and its control are combined there is a highly significant statistical correlation ($P < 0{\cdot}001$). It should be noted that 2 patients with gall-stones (group A) and one with normal radiographs (group C) did not show any regurgitation despite a history of flatulent dyspepsia.

Table II shows each group subdivided by the type of regurgitation response observed and whether or not arachis oil was used. It could be argued that those who showed no regurgitation without the use of arachis oil might have shown regurgitation if it had been used. Even if it is assumed that all 7 subjects would have shown regurgitation the correlation between symptoms and regurgitation is still highly significant ($P < 0{\cdot}01$). When arachis oil was given to those already showing regurgitation (Type I) there was either an increase in the bilirubin concentration in the gastric juice (3 patients) or little change (6 patients).

Relationship between Pyloric Regurgitation and Flatulent Dyspepsia.—It is one thing to find a relationship between a *history* of flatulent dyspepsia and pyloric regurgitation in a test situation and quite another to say that the regurgitation causes the symptoms. However, of the 23 patients who showed regurgitation, 13 actually complained of their symptoms during the test at the time when regurgitation occurred. They said their symptoms were the same as those they had after meals and included sudden onset of belching as well as a bloated feeling, nausea, or burning epigastric discomfort. (These symptoms are included in the term 'nausea' in *Figs.* 3 and 4.) The first appearance of bile in the stomach just preceded the symptoms and in all cases they were immediately relieved by aspirating the gastric contents. Two out of 3 patients in whom a small quantity (5–10 ml.) of juice was aspirated from the

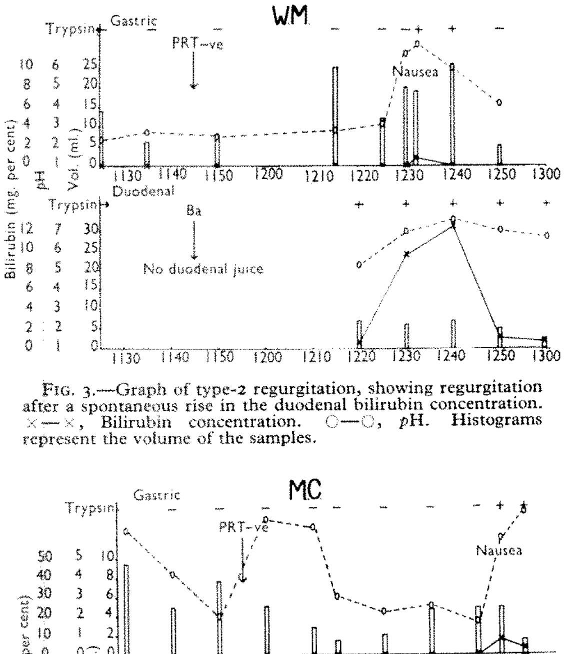


FIG. 3.—Graph of type-2 regurgitation, showing regurgitation after a spontaneous rise in the duodenal bilirubin concentration. ×—×, Bilirubin concentration. ○—○, *p*H. Histograms represent the volume of the samples.

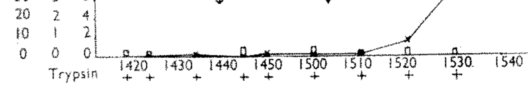


FIG. 4.—Graph of type-2 response, showing regurgitation after a rise in the duodenal bilirubin concentration following arachis oil.

duodenal tube and put down the gastric tube experienced their symptoms at this time. A similar observation was made by Toye and Williams (1965) in a patient with post-gastrectomy bilious vomiting.

A difference was observed in the rise of intragastric *p*H produced by the regurgitation between those who experienced their symptoms during the test and those who did not; 10 out of 13 in the first group showed a *p*H rise greater than 2, whereas only 2 out of 10 in the second group showed such a rise. (The initial *p*H levels did not differ significantly, but, *p*H being a logarithmic scale, the distributions were too far from normal for standard statistical tests to be applied.) This suggests that symptoms were produced by regurgitating duodenal juice if it was of sufficient quantity to change the gastric *p*H significantly, especially if this occurred suddenly.

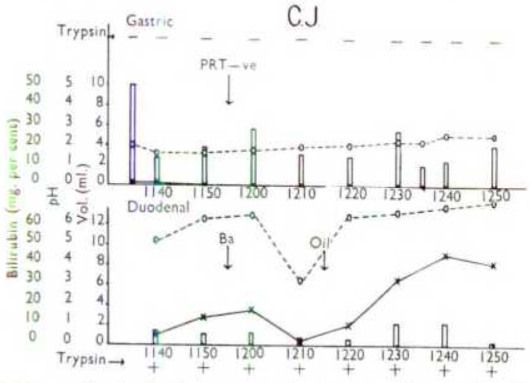


FIG. 5.—Graph showing no regurgitation even after arachis oil.

Table I.—CORRELATION BETWEEN A HISTORY OF FLATULENT DYSPEPSIA AND EVIDENCE OF PYLORIC REGURGITATION

GROUP	REGURGITATION OBSERVED	REGURGITATION NOT OBSERVED
A. Patients before cholecystectomy:—		
History of flatulent dyspepsia	12	2
No history of flatulent dyspepsia (controls)	0	6
B. Patients after cholecystectomy:—		
History of flatulent dyspepsia	3	0
No history of flatulent dyspepsia (controls)	0	6
C. Patients with normal radiographs:—		
History of flatulent dyspepsia	8	1
No history of flatulent dyspepsia (controls)	0	4
All patients:—		
History of flatulent dyspepsia	23	3
No history of flatulent dyspepsia (controls)	0	16

$\chi^2 = 33{\cdot}1$; $P < 0{\cdot}001$.

DISCUSSION

The Problem of 'Normal' Controls.—The selection of controls for a study such as this presents difficulties: to be sure that the control patient is 'normal' a cholecystogram and barium meal would have to be performed, as symptomless gall-stones and duodenal ulcers are not uncommon in this age-group. This is ethically unjustified in a symptomless person. The control patient, therefore, becomes one who is symptomless (*see Fig.* 5). It is for this reason that each group was compared with controls as similar as possible but without the symptoms under consideration. Capper and others (1966) found no regurgitation in 15 volunteer patients without any gastro-intestinal symptoms. Flint and Grech (1970) found regurgitation in 1 of 12 symptomless volunteers. We have studied 9 healthy young volunteers by the present technique (arachis oil being given in 3) and found slight radiological evidence of regurgitation in 1.

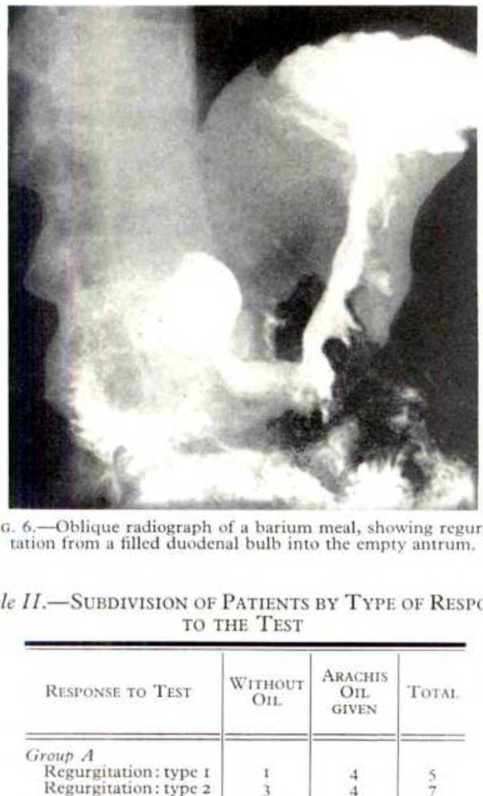


FIG. 6.—Oblique radiograph of a barium meal, showing regurgitation from a filled duodenal bulb into the empty antrum.

Table II.—SUBDIVISION OF PATIENTS BY TYPE OF RESPONSE TO THE TEST

RESPONSE TO TEST	WITHOUT OIL	ARACHIS OIL GIVEN	TOTAL
Group A			
Regurgitation: type 1	1	4	5
Regurgitation: type 2	3	4	7
No regurgitation	2	6	8
Group B			
Regurgitation: type 1	0	1	1
Regurgitation: type 2	0	2	2
No regurgitation	3	3	6
Group C			
Regurgitation: type 1	3	4	7
Regurgitation: type 2	0	1	1
No regurgitation	2	3	5

Criticism of the Test.—The obvious criticism of the technique of the test described in this paper is that the presence of the tube through the pylorus is itself responsible for the regurgitation. There are four answers to this criticism:—

1. Regurgitation did not occur in 19 out of the 42 patients tested, despite a tube being through the pylorus.

2. Regurgitation can be seen in about 50 per cent of routine barium meals if a careful technique is used (MacLean, 1969—*see Fig.* 6). This does not,

however, imply that regurgitation is a normal phenomenon as all the patients referred for barium meals have some gastric symptoms.

3. The duodenum can be filled with barium and then the tube carefully withdrawn into the stomach. This was done in 2 patients and subsequent regurgitation occurred in 1 and not in the other.

4. Regurgitation can be seen in some patients when the duodenum is filled via the common bile-duct at T-tube cholangiography (*Fig.* 7). This observation has recently been used as an argument that regurgitation is a physiological phenomenon as it was observed in one-third of 36 patients tested 10–14 days postoperatively (Beneventano and Schein, 1970). However, this is not a physiological situation and the present studies suggest that a proportion of patients will continue to show regurgitation after biliary operations. It is mentioned here to show that regurgitation does not occur only when a tube is across the pylorus.

The Timing of Pyloric Regurgitation.—Of particular interest are the patients who only show regurgitation after the duodenal bilirubin concentration rises (type 2), usually when the gall-bladder bile first appears in the duodenum but sometimes when there is an increase in bile-flow with a radiologically non-functioning gall-bladder or after cholecystectomy. Thomas and Baldwin (1969) found that duodenal motility is greatly affected by small quantities of bile or bile-salts in contact with the mucosa. Adlercreutz, Pettersson, Adlercreutz, Gribbe, and Wegelius (1960), while studying the effect of cholecystokinin on the duodenum, found an increase in tone and markedly accelerated contractions coinciding with the entrance of bile into the duodenum which failed to occur after cholecystectomy. These findings may provide a clue to the cause of duodenal juice regurgitation of type 2 and of those patients whose symptoms are cured by cholecystectomy. The effect of bile in the duodenum is not merely a result of an increase in volume, as the injection of a similar volume of barium saline is not accompanied by regurgitation. The regurgitation is also not solely due to inhibition of gastric motility by the arachis oil, as it occurs 25–30 minutes after the oil is given (*see Fig.* 4), whereas inhibition is complete within 4 minutes (Quigley, Werle, Ligon, Read, Radzow, and Meschan, 1941). The only clinical difference found between patients showing a type-1 and those showing a type-2 response was that type-1 patients tended to experience their symptoms at varying times after a meal whereas all except 1 of those with a type-2 response experienced their symptoms about half an hour after the meal. This is the time of maximum bile-flow and is the time after giving arachis oil that regurgitation occurred during the test (*Figs.* 3, 4).

Effects of Duodenal Juice in the Stomach.—If bile in the stomach is an aetiological factor in gastric ulceration, as has been suggested (Capper, 1967; Rhodes, Barnardo, Phillips, Rovelstad, and Hofman, 1969), then many of these patients with flatulent dyspepsia would be expected, sooner or later, to develop a gastric ulcer. It would need a long-term follow-up to demonstrate whether or not this occurs but other factors may be involved. For example, the length of time that the duodenal juice is in contact with the gastric mucosa may be important and a delay in gastric emptying may also be necessary for ulceration to occur.

CONCLUSIONS

1. There is a close correlation between a history of flatulent dyspepsia and radiological and biochemical evidence of regurgitation of duodenal juice into the stomach. This is true for patients before and after cholecystectomy and for those with a normal gall-bladder.

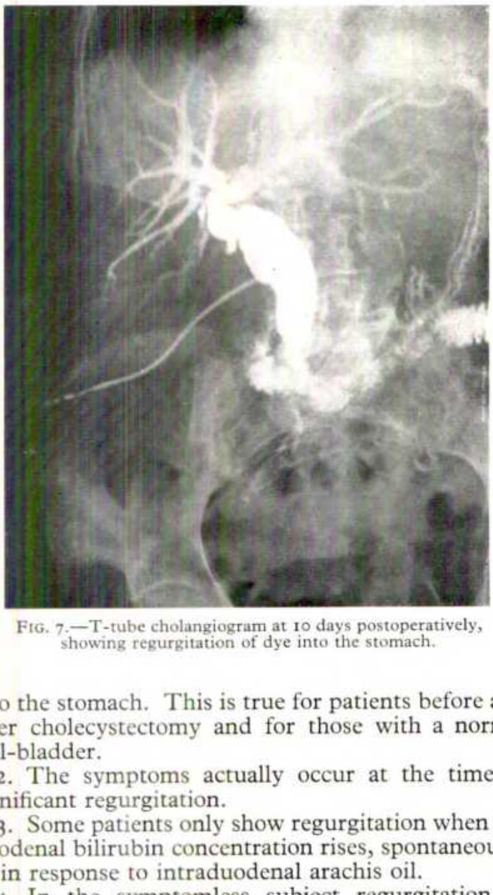


FIG. 7.—T-tube cholangiogram at 10 days postoperatively, showing regurgitation of dye into the stomach.

2. The symptoms actually occur at the time of significant regurgitation.

3. Some patients only show regurgitation when the duodenal bilirubin concentration rises, spontaneously or in response to intraduodenal arachis oil.

4. In the symptomless subject regurgitation of duodenal juice does not occur in the test situation.

The theory that regurgitation of duodenal juice is a significant factor in the production of the symptoms of flatulent dyspepsia provides a satisfactory explanation of the clinical findings. It explains why the same symptoms may occur in patients with a normal gall-bladder and in those with an abnormal gall-bladder, and why some patients have no symptoms of flatulent dyspepsia despite the presence of gall-stones. Those with a severely malfunctioning pylorus have symptoms which are little altered by cholecystectomy, but it is those whose pyloric malfunction is in some way related to their gall-stones who will be relieved by cholecystectomy; the mechanism of this relationship is the subject of further study.

Acknowledgements.—I am very grateful to Professor A. J. Harding Rains and Mr. H. L. Cochrane for allowing me to study patients under their care, and to Mr. R. C. Fuller for *Fig.* 7. I am also indebted to Dr. D. MacPherson and Miss

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A MODIFICATION OF THE FINNEY PYLOROPLASTY

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MANY different techniques have been used for the production of a pyloroplasty since Finney's original description in 1902. The one to be described here has been used in a personal series of 50 cases and is both simple and quick to perform. In none of the cases thus operated on has there been any complications attributable to the pyloroplasty.

THE TECHNIQUE

The second part of the duodenum is mobilized by dividing the peritoneum along its lateral border—the so-called 'Kocher manœuvre'. This results in exposure of the inferior vena cava and is not complete until the second part of the duodenum can be lifted forwards and to the left towards the midline.

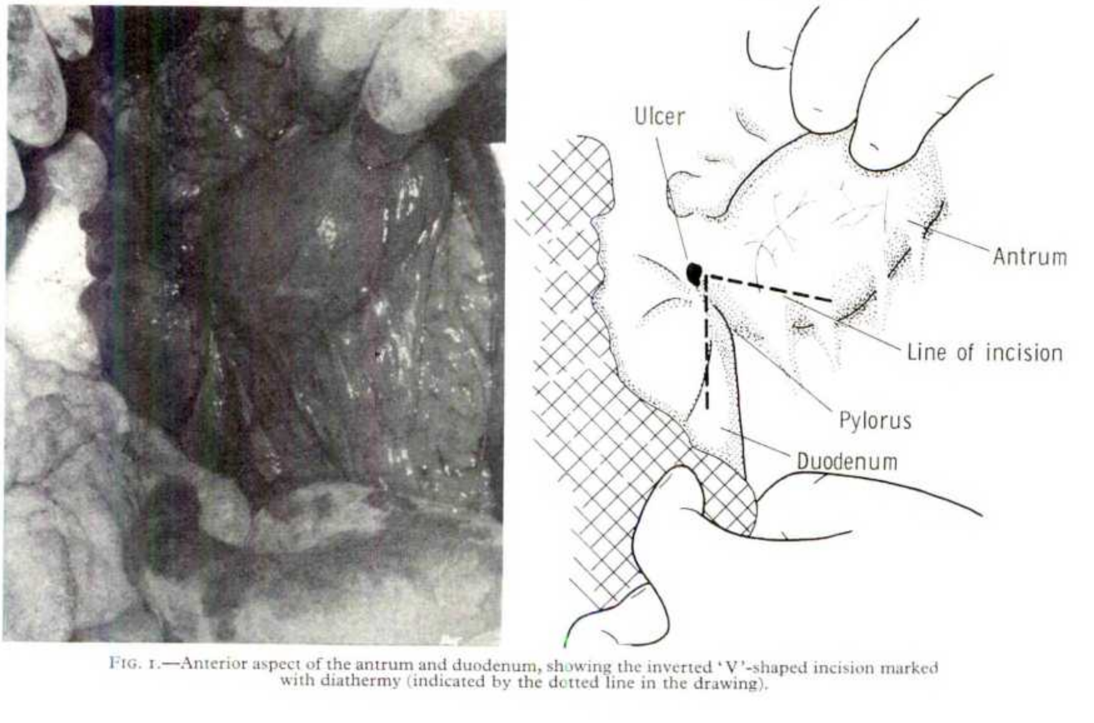
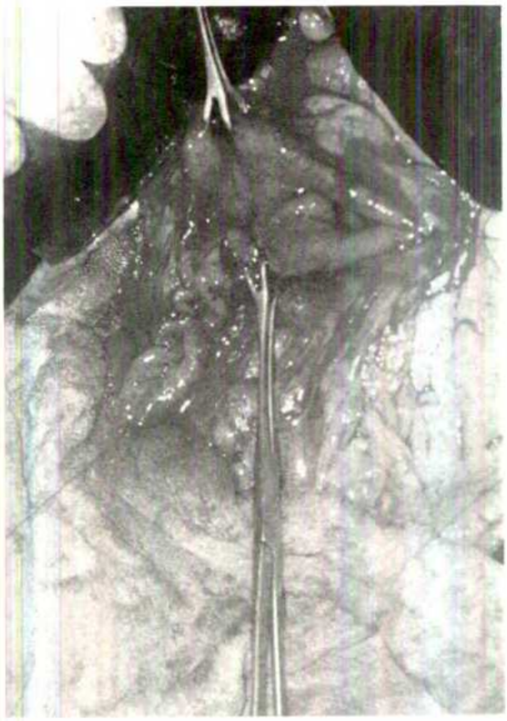


FIG. 1.—Anterior aspect of the antrum and duodenum, showing the inverted 'V'-shaped incision marked with diathermy (indicated by the dotted line in the drawing).

Fig. 1 shows the inverted 'V'-shaped incision, the apex being centred on the pylorus. Each limb of the 'V' is 5 cm. long, making the total length of the incision 10 cm. It has been found an advantage to measure this distance accurately with a ruler and a pair of callipers. The incision itself is made using the diathermy, and 00 chromic stay sutures are placed at either end. *Fig.* 2 shows the completed incision, the pyloric ring being marked by two Babcock forceps.



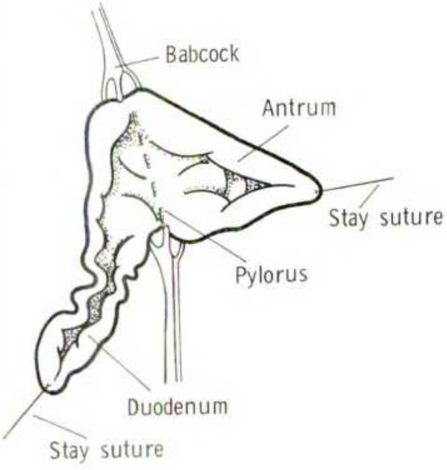
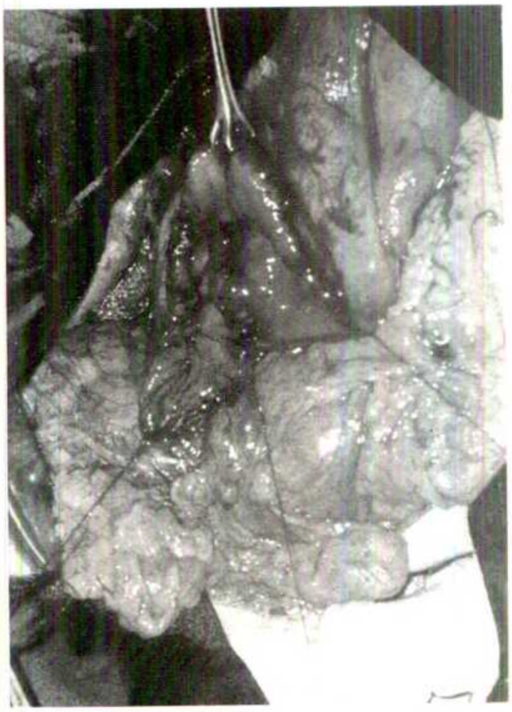


FIG. 2.—The incision has been made in the antrum, pylorus, and duodenum. The ends of the incision are being held apart by means of stay sutures and the pylorus by the two Babcock forceps.



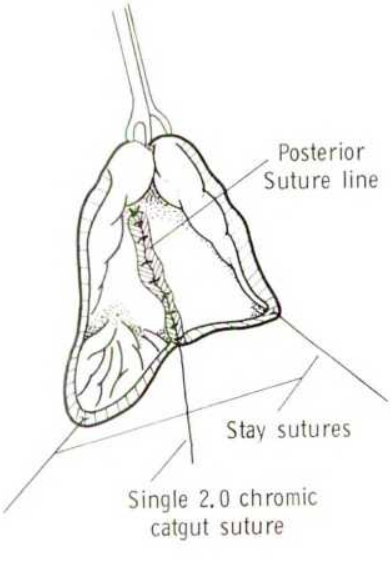
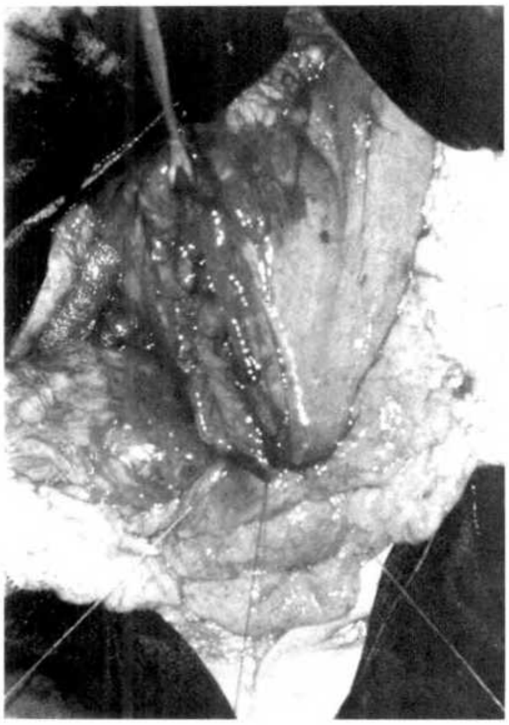


FIG. 3.—The posterior suture line is half completed.

The suture line for the pyloroplasty consists of one layer of 00 chromic catgut using a 30-mm. half-circle atraumatic needle. The suture line commences at the pylorus, at the point that it is being gripped by the lower Babcock forceps in *Fig.* 2. A simple all-coats stitch is used and the half-completed posterior wall of the pyloroplasty is illustrated in *Fig.* 3. *Fig.* 4 shows the nearly completed posterior line; the two stay sutures have almost been brought together. When the two stay sutures meet they are tied



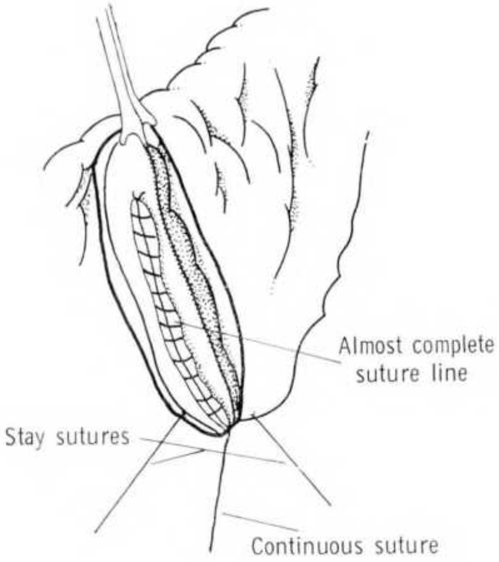
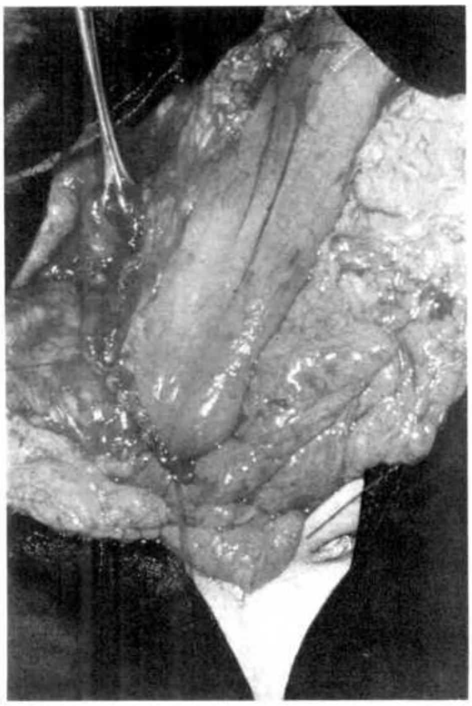


FIG. 4.—The posterior line is now nearly completed. The two stay sutures at either end of the incision are almost approximated.



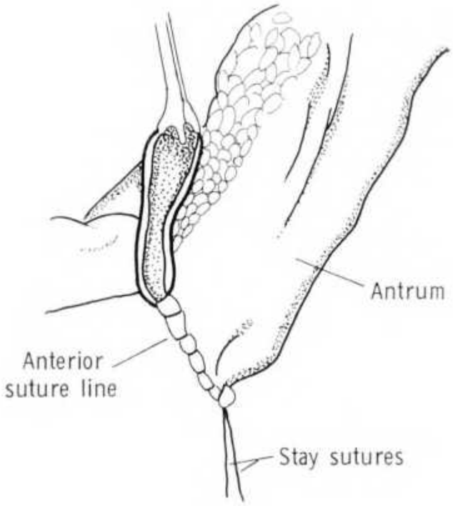
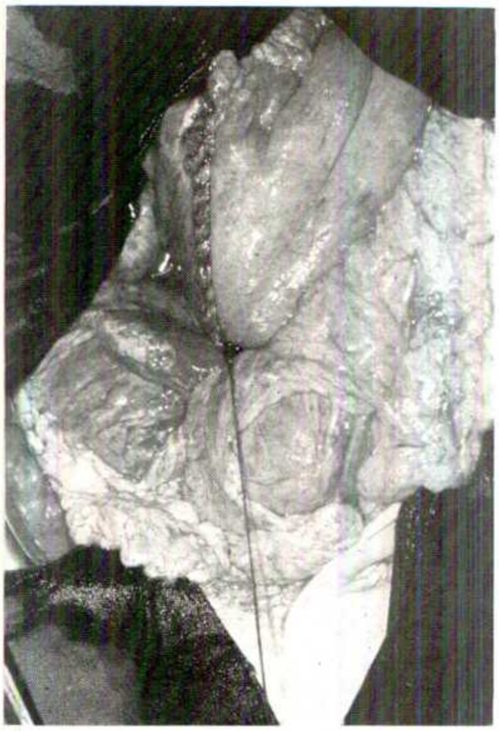


FIG. 5.—The stay sutures have been tied and the anterior suture line is half completed.

together and this point forms the inferior part of the pyloroplasty.

The continuous suture is now carried upwards on the anterior aspect, again using the simple over-and-over stitch, and *Fig.* 5 shows this anterior suture line half completed. The completed suture line is shown in *Fig.* 6.



The stoma between the antrum and the duodenum is the width of the tips of three fingers and is not seriously compromised by the inverted posterior suture line. The operation is completed by covering the anterior suture line with a layer of omentum lightly sutured in place.

DISCUSSION

The main feature of this modified Finney pyloroplasty is the closure of the incision with a single 00 chromic catgut suture. The advantage of this is twofold. First, a minimum of tissue is inverted and the reduction in the lumen is, therefore, slight. Secondly, it is quick to perform.

The strength of a suture line performed with a single suture is bound to be questioned. However, in the 50 cases operated on no leak has occurred in spite of the fact that no postoperative intragastric tube of any description was employed and patients were allowed 15 ml. of water per hour as soon as they had recovered from the anaesthetic. Naturally, if after the anastomosis has been finished it does not look satisfactory, then extra interrupted catgut sutures are introduced before the completed suture line is covered with omentum. Similarly, if in the first few postoperative days there is evidence of gastric retention, a nasogastric tube is introduced although none of the 50 cases reported here has required intubation.

We prefer to use catgut for these anastomoses because of the tendency of non-absorbable sutures to work their way into the lumen of the stomach and duodenum. Several cases in which non-absorbable sutures were used originally have been re-operated on and a piece of silk or thread has been found projecting from the suture line creating a 'foreign-body' anastomotic ulcer.

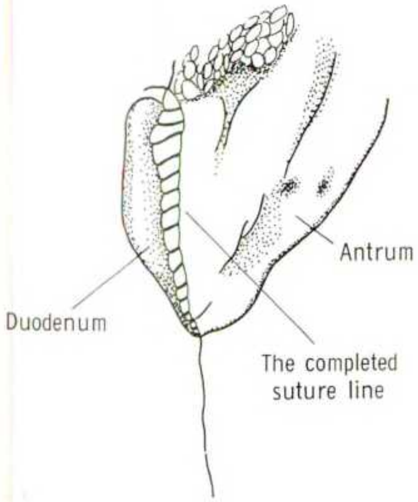


FIG. 6.—The completed anterior suture line.

The most common type of pyloroplasty used in this country is the Heineke–Mikulicz which suffers from two disadvantages. The first of these is that the centre of the suture line tends to be under some tension and the sutures may tear away from the duodenum. The second is that the stoma is not quite so large as that which results from a Finney pyloroplasty.

This modified Finney pyloroplasty can be used when there is considerable scarring of the first part of the duodenum. It therefore has the advantages of speed, reliability, and general applicability.

Acknowledgements.—My thanks are due to Dr. P. Hansell, Mr. D. Gibbons, and the Department of Medical Illustration for the line drawings and photographs, and also to Professor H. Ellis, Mr. D. Harland, Mr. R. Fidian, and Mr. E. Harper for referring some of the 50 cases.

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AORTO-ENTERIC FISTULAE: AN UNCOMMON COMPLICATION OF ABDOMINAL AORTIC ANEURYSMS

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SUMMARY

Three cases of aorto-enteric fistula which have been treated successfully by resection of the aortic aneurysm are described. Only 5 other successful cases have been reported. One hundred and thirty-one cases are reviewed and analysed, and though more than half of these survived for 24 hours or longer after the first gastro-intestinal haemorrhage, no untreated long-term survival has been recorded. We feel that urgent assessment and early corrective surgery is the only treatment which offers a reasonable chance of survival.

ABDOMINAL aortic aneurysms may remain asymptomatic for many years, but eventual intraperitoneal or retroperitoneal rupture is usual. Rupture into other structures is much less common. Rupture into the gastro-intestinal tract has been reported in 128 cases, 15 of which have been treated surgically with 5 survivors. Three cases have been seen at St. Bartholomew's Hospital since 1968 and have been successfully treated. These are described here and the condition is reviewed.

CASE REPORTS

Case 1.—T. B., a 63-year-old man, was transferred from his local hospital on 23 March, 1968, with a history of rectal bleeding and severe back and left loin pain for 1 day. Two and a quarter years previously an abdominal aortic aneurysm had been wrapped with three separate 1·2-cm. Teflon bands. Three hospital admissions for abdominal pain had subsequently been necessary, and a left superficial femoral artery occlusion had occurred 2 years after the operation.

Blood-pressure was 130/85 and pulse 84 per minute. A large expansile mass was palpable at the left costal margin and loin. The rectum contained dark blood.

At laparotomy a 12-cm. atheromatous infrarenal aneurysm was found to have become adherent to the small intestine between the Teflon bands and a 1-cm. aortojejunal fistula was present 30 cm. distal to the duodenojejunal junction. The aneurysm had also ruptured posteriorly into the left psoas muscle and the pelvis. The aneurysm was resected and replaced by a 19 × 9·5-mm. knitted Dacron bifurcation graft, while the jejunum was closed with 00 chromic catgut in two layers. Bilateral lumbar sympathectomy was performed, and following this the external iliac blood-flow was greater than 800 ml. per minute on each side. Reperitonealization of the graft was not possible.

Postoperative progress was satisfactory and the patient was well 4 years later.

Case 2.—G. Y., a 73-year-old woman, had been hypertensive for 10 years and an aortic aneurysm had been diagnosed at laparotomy 3 years earlier. On 4 Oct., 1968, she passed blood per rectum and was admitted to hospital. A similar massive bleed 1 month previously and haematemesis and melaena 3 months previously had been treated conservatively.

The patient was in moderate circulatory failure with a relatively low blood-pressure of 125/80. A moderate-sized abdominal mass was present, but there was no bruit. Haemoglobin was 7·1 g. per 100 ml., and P.C.V. was 22 per cent. A retrograde aortogram showed a saccular aortic aneurysm 3 cm. below the renal arteries, and a diagnosis of aorto-enteric fistula was made.

At laparotomy the duodenum was adherent to an atheromatous aneurysm and a 2·5-cm. defect was present in the anterior wall of the aneurysm with a 2-mm. fistula into the third part of the duodenum. In view of the potentially infected field a Dacron prosthesis was not used and an aortic aneurysmorrhaphy was performed. The aortic tube was reconstituted by an overlapping technique using two layers of 000 Mersilene and the duodenum was closed directly. Duodenal hold-up occurred for 2 weeks before adequate gastro-intestinal motility returned.

The patient was well 3½ years later and peripheral pulses were all present. She experiences occasional attacks of colicky abdominal pain.

Case 3.—F. S., a 60-year-old man, complained of 3 months' back pain. He was anxious and rather depressed with signs of chronic bronchitis. Radiographs of the chest and lumbar spine, routine blood chemistry, urine examination, and a pyelogram were all normal.

The pain persisted and the patient was admitted 2 months later on 17 May, 1969, when barium studies, a cholangiogram, a lymphangiogram, a bone-marrow biopsy, an inguinal lymph-node biopsy, and a lumbar puncture were unhelpful. There was no evidence of multiple myelomatosis or porphyria, and the Wassermann reaction was negative.

On 17 June haematemesis occurred, followed by the passage per rectum of about 700 ml. of bright-red blood. Laparotomy revealed a 7-cm. atheromatous aneurysm of the infrarenal aorta which had formed a 1-cm. fistula into the third part of a greatly distended and pulsating duodenum. The resected aneurysm was replaced by a 19 × 9·5-mm. knitted Dacron bifurcation graft, and the duodenal defect was closed with interrupted 00 chromic catgut sutures in two layers. Omentum mobilized on a gastro-epiploic pedicle was interposed between the graft and the duodenum.

The postoperative course was prolonged and stormy. The patient was ventilated and a tracheostomy was required on 21 June. Gram-negative septicaemia and peritonitis on 27 June necessitated a second laparotomy, and extensive ischaemic necrosis of the colonic wall with perforation of the sigmoid was found and was treated with a Hartmann's resection and colostomy.

Cephaloridine and streptomycin were changed to cephaloridine and chloramphenicol. Right-lung collapse occurred on two occasions, leading to cardiac arrest and requiring bronchoscopy and further intermittent positive-pressure ventilation until 16 July. Further chest infections with *Pseudomonas* and *Proteus* organisms, another lung collapse and consolidation, and two more cardiorespiratory arrests delayed progress. Progressive anaemia required repeated transfusion, and a period of acute renal failure followed a major transfusion reaction. Drainage of a pneumothorax was necessary following an attempt to tap a subphrenic abscess. Polymyxin parenterally and by inhalation was followed by gentamicin, and infection was finally controlled.

Three months after operation and after 8 weeks' ventilation the patient was discharged, his weight having increased from 40·6 to 53·6 kg. At 24 months' follow-up the patient was well, with a functioning colostomy, and the alimentary, respiratory, and peripheral vascular systems were otherwise normal. Closure of the colostomy has been postponed on account of his chronic bronchitis.

Table I.—AETIOLOGY, SEX, AND AGE AT PRESENTATION IN 118 PATIENTS WITH PRIMARY AORTO-ENTERIC FISTULA*

AETIOLOGY	NO. OF CASES		AVERAGE AGE			PERCENTAGE OF TOTAL CASES		
	Male	Female	Male	Female	Both	Male	Female	Both
Atherosclerosis	54	18	67	66	67	59	67	61
Syphilis	8	1	42	32	41	9	4	8
Tuberculosis	8	2	57	58	57	9	7	8
Mycotic	6	1	46	20	42	7	4	6
Unknown	15	5	53	56	54	16	18	17
Total	91	27	60	60	60			

* Insufficient information was available in a further 13 reported cases.

Table II.—PRESENTING SYMPTOMS IN 118 PATIENTS WITH PRIMARY AORTO-ENTERIC FISTULA*

Presenting Symptom	*Percentage of Patients*
Haematemesis	40
Melaena	40
Abdominal pain	48
Lumbar or back pain	22
Previously known abdominal mass (diagnosed or probable aneurysm)	20

* Insufficient information was available in 13 other patients.

DISCUSSION AND REVIEW OF LITERATURE

Sir Astley Cooper first described a case of aorto-enteric fistula in 1829 (7),* and the condition was mentioned by Chamel and Dalmas in 1833 (5). Successful surgical treatment was reported in 1961 by Maclean and Couves (31), the patient being well 30 months afterwards. One hundred and twenty-eight cases have been found in the literature (1–4, 6, 8, 10–26, 28–45), to which we have added 3 cases, making 131 in all. Sex, age, and aetiology are summarized in *Table I*. Seventy-seven per cent of the cases occurred in males and the average age for both sexes was 60 years. Atherosclerosis was the commonest cause, being reported in 61 per cent of the cases. The average age of these patients was 67 years. Intra-abdominal sepsis complicated 3 cases in the atherosclerotic group. Twenty-two per cent of cases were syphilitic, tuberculous, or mycotic and these tended to occur in younger patients.

The commonest presenting symptoms were gastro-intestinal bleeding and abdominal and back pain (*Table II*). Sixty-five per cent of the patients had haematemesis and 54 per cent melaena, but bleeding was not manifest until after admission in some patients. In 56 per cent of the patients an abdominal mass was felt on admission, three-quarters of these being pulsatile. In only 20 per cent had a mass been known to be present beforehand.

The most common site for the fistula was the third part of the duodenum (72 out of 125 fistulae) and this is probably due to the relative fixity of the duodenum compared with the rest of the bowel, and the close relationship of the third part of the duodenum to the aorta. Aorto-enteric fistulae have, however, been reported affecting all parts of the gut from the stomach to the rectum (*Table III*).

Table III.—SITES OF RUPTURE INTO THE BOWEL IN 123 PATIENTS WITH PRIMARY AORTO-ENTERIC FISTULA*

Site	*Number*	*Percentage*
Stomach	6	4·8
Duodenum		
First part	1	0·8
Second part	5	4·0
Third part	72	57·6
Fourth part	6	4·8
Unspecified	18	14·4
Total	102	81·6
Small bowel		
Jejunum	7	5·6
Ileum	2	1·6
Unspecified	1	0·8
Total	10	8·0
Large bowel		
Caecum	1	0·8
Ascending colon	1	0·8
Sigmoid colon	4	3·2
Rectum	1	0·8
Total	7	5·6

* Insufficient information was available in 8 other patients.

Two cases ruptured into two sites, and both sites are included. Two cases with fistulation into the bowel ruptured in addition into the vena cava and into the left ureter.

Table IV.—LENGTH OF TIME FROM FIRST GASTRO-INTESTINAL HAEMORRHAGE TO DEATH OR SURGICAL INTERVENTION IN 115 PATIENTS WITH PRIMARY AORTO-ENTERIC FISTULA*

Length of Time	*No. of Patients*
Less than 6 hours	30
From 6 to 24 hours	17
From 1 to 7 days	31
More than 1 week	37

* Insufficient information was available in 16 other patients.

The interval between the first gastro-intestinal bleed and diagnosis is of importance in allowing time for treatment (*Table IV*). Some patients have had several episodes of bleeding extending over several months, and 68 of 115 patients for whom information is available survived for 24 hours or longer after the first haemorrhage. Adequate time is therefore available for surgery to be attempted in the majority of cases.

SURGICAL TREATMENT

Details are given in the literature of 15 patients who were treated surgically (2, 6, 10–13, 17–19, 30, 31, 33, 44), of whom 5 (33 per cent) survived. The

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* Throughout figures in parentheses relate to the reference numbers.

3 cases reported in this paper all recovered and bring the survival to 8 out of 18 cases (44 per cent). All of the known surviving cases had ruptured into the small intestine (7 into the duodenum). Seven of the 8 survivors were treated with prosthetic grafts, the exception being *Case* 2 in the present series in whom aortic aneurysmorrhaphy was possible.

Of the 18 patients who were treated surgically, 10 had serious postoperative complications and only 1 of these survived (*Case* 3 in the present series). Septicaemia or intra-abdominal sepsis occurred in 7, with ischaemic colitis and peritonitis requiring partial colonic resection in 2. In 5 patients there was graft leakage, with further gastro-intestinal haemorrhage in 3, while 3 patients developed renal failure.

Although the mortality following surgery is formidable (56 per cent in the cases reviewed here), we have not found any reports of survival for more than a few months in patients with an untreated aorto-enteric fistula. Early surgery holds the only hope of long-term survival for these patients. Our experience of survival in all of 3 patients suggests that prompt diagnosis and operation may lead to improvement in the present overall figures. The diagnosis should be considered in all patients with gastro-intestinal bleeding and an abdominal mass, especially if it is pulsatile. An increased incidence of peptic ulceration, however, is associated with abdominal aortic aneurysms in a necropsy population (27). In 44 per cent of patients no abdominal mass was reported. In such cases the diagnosis is likely to be made at laparotomy for persistent gastro-intestinal haemorrhage, and the outcome then depends largely on the facilities and skills available to the surgeon. Once surgery has been performed and the patient has recovered, it seems likely that the prognosis will be similar to that following resection of aortic aneurysms which have not developed fistulae. DeBakey, Crawford, Cooley, Morris, Royster, and Abbott (9) have shown that long-term survival after resection of aortic aneurysms is only slightly less than that for a normal population matched for age and sex, unless hypertension or ischaemic heart disease was present before surgery.

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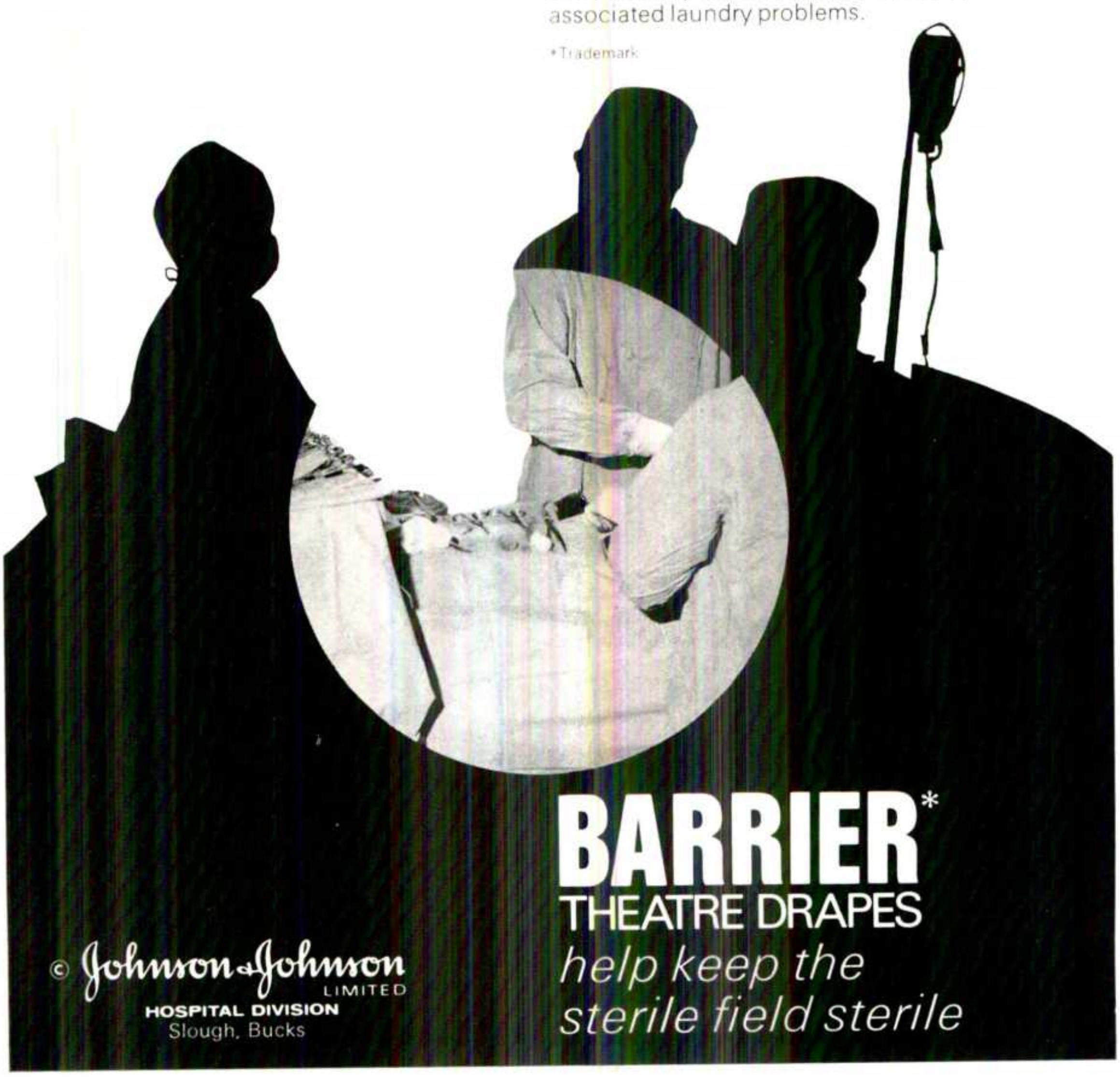

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AORTO-CAVAL FISTULAE: AN UNCOMMON COMPLICATION OF ABDOMINAL AORTIC ANEURYSMS

By J. P. D. RECKLESS, I. McCOLL, and G. W. TAYLOR
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SUMMARY

Two cases of successfully treated aorto-caval fistula are described, bringing the total number of reported cases to 71. Forty-one cases which were treated surgically are reviewed. The aetiology of the leg oedema is discussed.

THE natural history of abdominal aortic aneurysms is usually of enlargement and eventual rupture. This is commonly intra- or retroperitoneal, but may occur into other structures such as the gut (26)* or the inferior vena cava.

Three cases of aorto-caval fistula have been seen at St. Bartholomew's Hospital and have been successfully treated. One of these has been reported elsewhere (28), and the other 2 are described below. The literature is briefly reviewed.

CASE REPORTS

Case 1.—A. H., a 59-year-old man, was admitted on 9 Aug., 1968, complaining of backache, nausea, vomiting, and malaise of 2 months' duration. Six weeks before admission considerable oedema of the legs and scrotum had suddenly developed and had been treated with digitalis and diuretics.

There was mild dyspnoea at rest and bilateral basal crepitations, and the jugular venous pressure was raised 8 cm. The pulse was 72 per minute and collapsing, the blood-pressure was 160/40, and a Corrigan sign was present. The liver was palpable 5 cm. below the costal margin, and a large pulsatile epigastric mass with a harsh continuous bruit was present. An abdominal radiograph showed calcification in an aortic aneurysm. The Wassermann reaction was positive, but was thought to be nonspecific as full serology was otherwise negative. The cardiac failure was thought to be due to an aorto-caval fistula.

On 14 Aug. an aneurysm, 22 × 15 cm., was excised and a 3·5-cm. defect in the inferior vena cava was closed with 000 Mersilene. Aorto-femoral continuity was restored by a 22 × 11-mm. knitted Dacron bifurcation graft across which omentum was sutured. The central venous pressure dropped from 27 cm. to 10 cm. as the fistula was controlled, and a marked diuresis and a 10-kg. weight-loss were noted in the next 10 days.

Histology showed atheromatous change without evidence of luetic aortitis. Hypertension (260/125) was controlled by methyldopa, and the patient was symptom free and had all the pedal pulses present 3½ years postoperatively.

Case 2.—H. B., a 62-year-old man, was admitted on 23 Feb., 1970. Over 24 hours, following sudden pain in the left iliac fossa and groin, marked left leg oedema had developed. The patient had been obese and hypertensive for some years, and was taking guanethidine and a diuretic.

The blood-pressure was 105/50 and the pulse was 70 per minute and collapsing. There was a hyperdynamic cardiac impulse and an aortic systolic ejection murmur, but no evidence of left or right heart failure. In the left iliac fossa an expansile mass was present with a thrill and a machinery murmur. The left leg was markedly oedematous, blue, and with dilated pulsating veins draining upwards over the lower abdomen. The circumference of the thigh was 3 cm. greater on the left side, and that of the calf was 8·5 cm. greater.

A diagnosis of an aorto-iliac aneurysm with a left iliac arteriovenous fistula led to laparotomy on the same day. An aortic aneurysm, 8 × 12 cm., extended into a left common iliac artery aneurysm, 10 × 10 cm. Arterial pulsation was present in the inferior vena cava. The aorta and iliac vessels were controlled and the iliac aneurysm was opened. Venous bleeding was stopped by clamping the external and common iliac veins and by occluding the internal iliac vein lumen through the 2·5-cm. fistula by using a Fogarty embolectomy catheter balloon. The defect was closed and the aneurysm resected, leaving the posterior wall of the aortic aneurysm in situ. A 22 × 11-mm. knitted Dacron bifurcation graft was used to restore aorto-iliac continuity.

Apart from a deep venous thrombosis of the left leg and a possible pulmonary embolus, progress was uneventful. Follow-up at 24 months was satisfactory.

DISCUSSION

Arteriovenous fistulae of the large intra-abdominal vessels are known to be a possible complication of surgery to the intervertebral disks, but the cases reported here and a number of others in the literature occurred as primary events of ruptured abdominal aneurysms. The first such case of aorto-caval fistula was reported in 1831 by Syme (34) in a 22-year-old man in whom the aetiology was probably syphilitic. Slow deterioration occurred till death 3½ months later.

Twenty-six cases were found by Boffi (2) in 1955, and 28 further cases were reviewed in 1968 by Nennhaus and Javid (25). The present review (3, 13, 15, 17, 20–22, 27, 30, 32, 33, 37, 38) brings the total number of reported cases to 71. Forty-one cases have been surgically treated (1, 3, 7, 8, 18, 19, 21, 25, 27–33, 35–38). The average age of these cases was 61 years, and all except 3 were male. The aetiology was atherosclerotic in the majority of the cases, but 2 were syphilitic (18, 33), 1 was probably mycotic (25), 1 was due to Ehlers-Danlos syndrome (20), and a further patient had Marfan's syndrome (12).

Abdominal or back pain, a palpable aneurysm, and a continuous abdominal bruit were each present in over four-fifths of the patients, while a high output cardiac state and a widened pulse pressure were present in over half (*Table I*).

While cardiac failure is common, the abdominal and lower limb oedema is partly the result of venous hypertension and partly due to inferior vena cava compression by the aneurysm. *Case* 2 had a high output cardiac state without failure, and the gross oedema on the side of the fistula only confirms the importance of these local factors. Venous hypertension may be the cause of haematuria and rectal bleeding in some patients, and may contribute to the incidence of anorexia, nausea, and vomiting. Renal function is also impaired in some patients where a raised urea is reported.

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* Throughout figures in parentheses relate to the reference numbers.

Table I.—Symptoms and Signs in 41 Surgically Treated Patients presenting with Primary Aorto-caval Fistula

Symptoms and Signs	*Occurrence* (per cent)
Abdominal or back pain	88
Palpable aneurysm	90
Abdominal bruit	83
High output cardiac state	54
Congestive cardiac failure	37
Wide pulse pressure and reduced diastolic pressure	61
Lower-limb oedema	56
Haematuria	17
Rectal bleeding	5
Anorexia, nausea, and vomiting	24
Lethargy, impaired cerebration	20

Surgery was undertaken at about 16 days after fistulation (range, 6 hours to 2 months). Not until surgical control of the fistula is achieved does the patient's condition usually improve, with the central venous pressure falling from 20–30 cm. to normal.

Thirty of the 41 patients survived surgery, but 4 are known to have died of later complications. Three developed secondary aorto-enteric fistulae (9, 10, 35), whilst the fourth, in whom a post-mortem examination was not performed, suffered a terminal haematemesis (25). Such secondary fistulae are well recognized and occur more frequently than the primary fistulae discussed in this article. They occur early after surgery (accompanied by infection, or by graft and suture-line disruption with false aneurysm formation), or late (with graft and suture material failure, or with adherence of the bowel to the prosthesis). Care in the choice of the graft and suture material, and separation of the prosthesis and bowel by peritoneum or omentum will reduce these complications.

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NON-GANGRENOUS ISCHAEMIC COLITIS

A REVIEW OF 17 CASES

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SUMMARY

Ischaemic lesions of the colon can be divided into gangrenous and non-gangrenous groups.

In this paper 17 patients with non-gangrenous ischaemic colitis are reported; 16 of these occurred spontaneously and 1 followed an anterior resection of the rectum.

The clinical and radiological findings are described.

The lesions varied in extent and severity from a short segment of transient mucosal damage to a long permanent stricture.

An early barium-enema examination is essential for the initial diagnosis. Repeat barium enemas are necessary to ascertain the final outcome. The radiological changes are at least partially reversible and even extensive strictures may show a marked improvement over a period of months.

In this group five lesions were resected but none of the resections was performed during the acute phase. It is concluded that non-gangrenous lesions can usually be managed conservatively. The indications for surgical intervention are discussed.

ISCHAEMIC colitis is a non-specific inflammatory disease of the colon. It has been reported as a complication of abdominal aortic surgery (Birnbaum, Rudy, and Wylie, 1964), as a terminal event in patients with cardiac disease (McGovern and Goulston, 1965), and as a spontaneous occurrence in otherwise well patients (Marston, Pheils, Thomas, and Morson, 1966).

Marston and others (1966) classified the lesions according to the severity of the damage into (1) gangrenous, (2) stricturing, and (3) transient groups. However, experience with the present cases and with other reported cases (Boley, Schwartz, Lash, and Sternhill, 1963; de Dombal, Fletcher, and Harris, 1969) suggests that the most useful classification distinguishes only gangrenous and non-gangrenous lesions.

Gangrenous ischaemic colitis is often fatal and usually follows aortic surgery (Barnes, Ellis, Kirklin, and Edwards, 1958; Young, Britton, de Wolfe, and Humphries, 1962; Miller and Knox, 1966; Bicks, Bale, Howard, and McBurney, 1968). Spontaneously occurring gangrenous lesions are rare (Demos, 1963).

More than 120 cases of non-gangrenous ischaemic colitis have been reported. A few of these have followed aortic surgery (Movius, 1955; Bernatz, 1960; Smith and Szilagyi, 1960; Birnbaum and others, 1964; Goodman, 1964; Bicks and others, 1968; Miller and Bennet, 1968), but most have occurred spontaneously (Boley, Schwartz, Kreiger, Schultz, Siew, and Allen, 1965; Irwin, 1965; Marshak, Maklansky, and Calem, 1965; Payan, Levine, Bronstein, and King, 1965; Roberts, 1965; Shippey and Acker, 1965; Varga and Currie, 1965; Dunbar, 1966; Farman, 1966; Marston and others, 1966; Bentlif and Eichhorn, 1967; Coligado and Fleshler, 1967; Shea, 1967; Byrd, Sawyers, Bomar, and Klatte, 1968; Calem, Gaudiano-Ruiz, Pochaczevsky, and Papadakis, 1968; Dickson, 1968; Kilpatrick, Farman, Yesner, and Spiro, 1968; Sturdy, 1968; Thomas, 1968; Bentlif, 1969; de Dombal and others, 1969; Gross, 1969, Pheils, 1969; Rowe-Jones, 1969; Williams, Bosniak, Wittenberg, Manuel, Grimes, and Byrne, 1969; Balslev, Jensen, Norgaard, and Poll, 1970).

CLINICAL MATERIAL AND OBSERVATIONS

Seventeen patients suffering from non-gangrenous ischaemic colitis are reported. Sixteen of the lesions occurred spontaneously, and 1 followed an anterior resection of the rectum.

The group comprises 10 women and 7 men. Their ages ranged from 36 to 88 years with a median age of 64 years (*Table I*).

Clinical Features.—One patient (*Case* 4) had had a single episode of painless rectal bleeding 6 months earlier. None of the other patients had had a previous bowel disorder.

Fourteen patients presented with rapidly developing and usually continuous pain in the left or lower abdomen. Eleven of them required urgent admission to hospital. The pain was accompanied by vomiting in 7 patients.

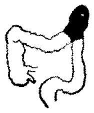
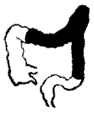
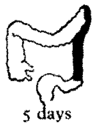
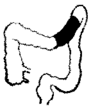
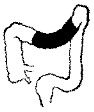
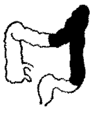
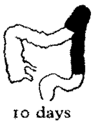
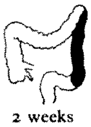
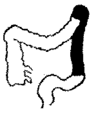
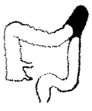
Three patients had no pain, *Cases* 9 and 12 presented with recurrent episodes of blood-stained diarrhoea, and *Case* 14 had no symptoms attributable to the ischaemia.

Sixteen patients had diarrhoea, sometimes preceded by tenesmus.

Thirteen patients had rectal bleeding. This occurred either as blood-stained diarrhoea or as frank rectal bleeding after an initial bout of diarrhoea. In some cases the bleeding persisted for several days, but it was never sufficient to require transfusion. Two other patients (*Cases* 4 and 17) were found to have occult blood in their stools, and both became anaemic.

In contrast to the severity of the symptoms the physical signs were usually mild. Localized abdominal tenderness was noted in 8 patients. A diagnosis of intestinal obstruction was made in 3 patients (*Cases* 5, 6, and 7), and some abdominal distension was noted in others. *Case* 2 developed a pyrexia and a tachycardia with abdominal distension and tenderness and was diagnosed as having acute ulcerative

Table I.—DETAILS OF T

CASE	AGE AND SEX	CLINICAL FEATURES	DURATION OF ILLNESS	EXTENT OF LESION ON INITIAL BARIUM ENEMA, AND TIME BETWEEN ONSET AND RADIOGRAPH	INITIAL DIAGNOSIS MANAGEMENT OF L
1	64 F.	Pain, diarrhoea, bleeding	4 days	 3 weeks	Carcinoma of colon. Ir section
2	65 M.	Pain, tenesmus, diarrhoea, bleeding. Toxicity, fever, distension, tenderness	12 days	(*Fig.* 1)  3 weeks	Acute ulcerative colitis resection
3	64 M.	Pain, tenderness, diarrhoea, bleeding. Mild pyrexia, tenderness	4 days	(*Fig.* 2 A)  5 days	Segmental ulcerative c Conservative manage
4	73 F.	Pain, vomiting, diarrhoea, occult bleeding. Distension, tenderness	3 days	(*Fig.* 3 A)  6 days	Carcinoma of colon. I section
5	40 F.	Pain, vomiting, diarrhoea, bleeding. Mild pyrexia, distension, tenderness. Fluid levels on radiograph	1 day	 12 days	Strangulating intestinal tion. Emergency la Conservation of colon
6	88 F.	Pain, vomiting, diarrhoea, bleeding. Mild pyrexia, distension, tenderness. Fluid levels on radiograph	3 days	 2 weeks	Strangulating intestina tion. Emergency la Conservation of colon
7	63 F.	Pain, vomiting, diarrhoea, bleeding. Distension, tenderness. Fluid levels on radiograph	3 days	 10 days	Intestinal obstruction. hernia explored. Con management
8	79 M.	Pain, diarrhoea, bleeding	3 days	 2 weeks	Ischaemic colitis. Con management
9	43 M.	Recurrent attacks of diarrhoea and bleeding	6 weeks (intermittently)	 7 weeks	Ulcerative colitis. Con management
10	36 F.	Pain, vomiting, diarrhoea, bleeding. Tenderness	3 days	(*Fig.* 4 A)  2 days	Ischaemic colitis. Co management

RESENT SERIES

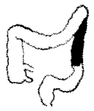
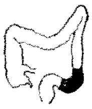
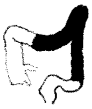
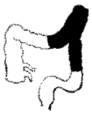
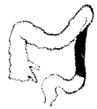
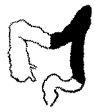
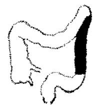
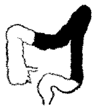
EDICAL IONS	BASIS FOR DIAGNOSIS OF ISCHAEMIC COLITIS	EXTENT OF LESION ON REPEAT BARIUM ENEMA, AND TIME BETWEEN RADIOGRAPHS	CLINICAL PROGRESS	COMMENTS
sion	Histology of resected colon	—	Normal bowel function for 5 years	Patient first seen 2 weeks after illness. Clinical and radiological features suggestive of ischaemic colitis in retrospect
lerosis hyper-	Histology of biopsy and resected colon	—	Died 4 years later (myocardial infarction). Normal bowel function for 4 years	Extensive involvement with severe symptoms, but resolved in 2 weeks. Patient apparently well at time of resection
	Clinical features and radiological changes	(*Fig.* 2 B)  8 months	Mild constipation for 3 years	Diagnosed in retrospect after reviewing history and radiographs. Symptoms not severe but colonic damage permanent
asthma hysema	Histology of resected colon	—	Died in postoperative period (respiratory complications)	Frequently used adrenaline nebulizer for asthma—possibly contributing to ischaemia. Episode of painless rectal bleeding 6 months previously
	Clinical features, radiological changes, and operative findings (in retrospect)	Normal colon. 1 month	Normal bowel function for 3 years	Diagnosed in retrospect despite age. Not taking the 'pill'. Symptoms severe but radiographic changes transient
lerosis emen-	Clinical features, radiological changes, and operative findings (in retrospect)	Not done	Died 2 months later (pneumonia). Reported to have normal bowel function prior to last illness	Senile dementia made assessment difficult. Laparotomy performed after 3 days of apparently severe symptoms. Patient died in psychiatric institution. No autopsy
erten-	Clinical features and radiological changes (in retrospect)	Not done	Normal bowel function for 2 years	Femoral hernia found to contain only omentum. No laparotomy performed. Failed to attend follow-up but replied to questionnaire
plegia re-	Clinical features and radiological changes	Normal colon. 3 months	Normal bowel function for 2 years	Patient first seen 1 week after illness. Symptoms mild and radiographic changes transient
	Radiological changes	Normal colon. 15 months	Normal bowel function for 2 years	Clinical features regarded as atypical. Normal rectum at sigmoidoscopy. Radiological changes definite but transient
	Clinical features and radiological changes	(*Fig.* 4 B). Normal colon. 5 months	Normal bowel function for 18 months	Diagnosis suspected clinically despite age. Radiological changes confirmatory. Symptoms severe but transient radiographic changes

Table I —DETAILS OF T

CASE	AGE AND SEX	CLINICAL FEATURES	DURATION OF ILLNESS	EXTENT OF LESION ON INITIAL BARIUM ENEMA, AND TIME BETWEEN ONSET AND RADIOGRAPH	INITIAL DIAGNOSIS MANAGEMENT OF L
11	77 M.	Pain, vomiting, diarrhoea, bleeding. Tenderness	2 days	 10 days	Ischaemic colitis. Con management
12	76 F.	Recurrent attacks of diarrhoea and bleeding (subsequent obstruction by diverticular mass)	3 months (intermittently)	 3 months	Crohn's disease plus di disease. Interval rese
13	58 F.	Pain, diarrhoea, bleeding. Tenderness	2 days	(*Fig.* 5 A)  4 days	Ischaemic colitis. Con management
14	72 M.	No symptoms (iatrogenic) (defunctioning colostomy present)	—	(*Fig.* 6)  3 weeks	Ischaemic colitis. Int section
15	64 F.	Pain, vomiting, diarrhoea, bleeding. Distension, tenderness	3 days	(*Fig.* 7 A)  2 days	Ischaemic colitis. Cons management
16	55 M.	Pain, tenesmus, diarrhoea	3 days	 5 days	Ischaemic colitis. Con management
17	51 F.	Pain, diarrhoea, occult bleeding. Tenderness. Persistent pyrexia (for 4 weeks)	1 week (apart from pyrexia)	(*Fig.* 8 A)  2 weeks	Crohn's disease or colitis. Conservative ment

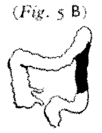
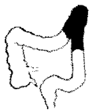
colitis. Four other patients (*Cases* 3, 5, 6, and 17) were noted to have a mild pyrexia and in *Case* 17 this persisted for 4 weeks.

Sigmoidoscopy.—Thirteen patients had a sigmoidoscopy when first seen. Although several of them had blood in the rectum, only 3 (*Cases* 2, 11, and 12) had mucosal changes. In these 3 patients the rectal mucosa was normal, but the mucosa of the rectosigmoid was oedematous. In *Case* 2 it was possible to manipulate the sigmoidoscope into the sigmoid colon; the mucosa here was reddened and superficial ulcers with areas of submucosal haemorrhage were noted. A biopsy from this region showed infarcted mucosa. A repeat examination a few days later revealed several shallow granulating ulcers with areas of normal mucosa between.

Radiology.—Plain radiographs of the abdomen were taken of all the patients who were seen during their acute illness. These showed dilated loops of small intestine with fluid levels in the 3 patients who were diagnosed as having intestinal obstruction.

All of the patients had one or more barium enemas performed. In those patients in whom the first examination was performed early the demonstration of 'thumb printing' and tubular narrowing was considered to be diagnostic (*Figs.* 2 A, 4 A, 5 A, and 7 A). *Cases* 2, 12, and 17 were thought to have stricturing from ulcerative colitis or Crohn's disease

PRESENT SERIES—(*continued*)

MEDICAL ITIONS	BASIS FOR DIAGNOSIS OF ISCHAEMIC COLITIS	EXTENT OF LESION ON REPEAT BARIUM ENEMA, AND TIME BETWEEN RADIOGRAPHS	CLINICAL PROGRESS	COMMENTS
—	Clinical features and radiological changes	Not done	Normal bowel function for 1 year	Clinical features and radiological findings considered diagnostic. Patient declined repeat barium enema
—	Histology of resected colon	—	Normal bowel function for 9 months	Initial diagnosis of Crohn's disease. Resection 12 months later for obstruction by diverticular mass. Histology showed ischaemic colitis plus diverticulitis
perten-	Clinical features and radiological changes	(*Fig.* 5 B)  4 months	Normal bowel function for 9 months	Symptoms mild and resolved rapidly in spite of extensive colonic involvement with permanent radiographic changes
—	Radiological changes and histology of colon	—	Normal bowel function for 6 months	Marginal artery probably ligated inadvertently with bleeding point in region of splenic flexure during anterior resection of rectum
—	Clinical features and radiological changes	(*Fig.* 7 B). Normal colon. 7 weeks	Normal bowel function for 6 months	Symptoms severe and initial involvement of colon extensive, but radiographic changes transient
—	Clinical features and radiological changes	Normal colon. 7 weeks	Normal bowel function for 6 months	Patient first seen 1 week after illness. No bleeding noticed by patient
pro- haemor- at same	Radiological changes and clinical course	(*Fig.* 8 B)  8 months	Normal bowel function for 8 months	Diagnosis of Crohn's disease favoured initially because of pyrexia, but subsequent clinical course and radiological changes favour ischaemic colitis

(*Figs.* 1 and 8 A). *Cases* 1 and 4, with short segments of colon involved, were each thought to have a carcinoma (*Fig.* 3 A).

Nine patients had a repeat barium enema later. In 3 there was permanent colonic damage in the form of stricturing, sometimes with 'sacculation' of the colonic wall (*Figs.* 2 B, 5 B, and 8 B). In the other 6 the colon had returned to normal (*Figs.* 4 B and 7 B).

Management.—Twelve patients were in hospital during their acute illness, but in some of the patients the correct diagnosis was not made until later. *Cases* 5 and 6 both had an emergency laparotomy performed for suspected intestinal obstruction, and *Case* 7 had a femoral hernia explored for the same reason. *Case* 2 was treated as acute ulcerative colitis with systemic and local steroids. *Case* 17 was given ampicillin for an intercurrent infection. The treatment of the other patients was symptomatic: several were given intravenous fluids, and some required narcotic analgesics. All of the patients except *Cases* 2 and 17 were symptom-free within 5 days.

Five lesions were resected. In *Cases* 1 and 4 the radiological appearances were suggestive of carcinoma, and a resection was performed because of the uncertain nature of the lesion found. *Case* 12 required a resection because of complications arising in coexistent diverticular disease. Only 2 patients (*Cases* 2 and 14) required resections because of the extent of the colonic damage (*Figs.* 2 and 6). All of the resections were done after the acute episode had subsided.

Operative Findings.—In the patients who had an emergency laparotomy the affected segments of the colon were pale and contracted. In both cases the colonic wall felt thickened and oedematous and became plum-coloured with handling. The transition to normal colon was abrupt at both ends of the affected segments. The nature of the lesion was not appreciated at the time, and the state of the mesenteric circulation was not noted in either case. The lesions were not resected.

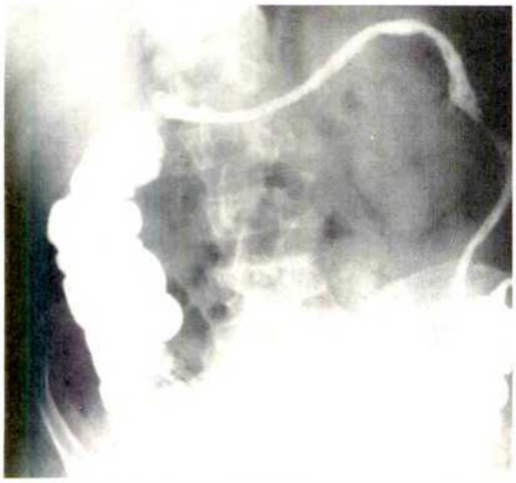
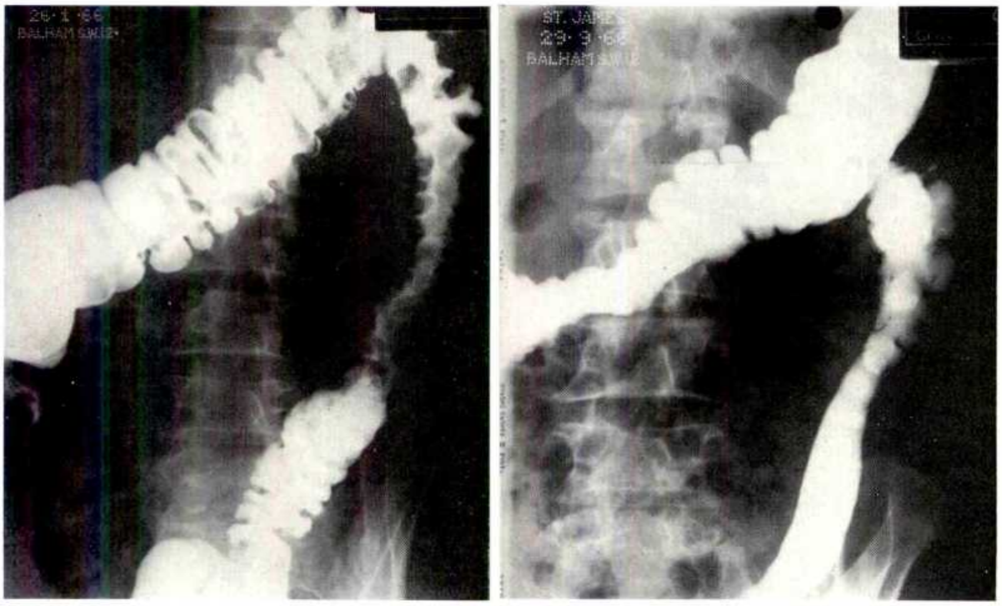


FIG. 1.—*Case* 2. Long ischaemic stricture involving the transverse and descending colon. Demonstrated 3 weeks after onset of symptoms.



A B

FIG. 2.—*Case* 3. A, Tubular narrowing and 'thumb printing' involving the splenic flexure and the descending colon. Demonstrated 5 days after onset of symptoms. B, Permanent stricturing with 'sacculation' of the antimesenteric side of the descending colon. Demonstrated 8 months later.

In the patients who had resections the appearances of the lesions at operation were similar, but they felt fibrotic rather than oedematous and small dilated veins were evident on the serosal surfaces. Omental and peritoneal adhesions were noted. The condition of their mesenteric vessels was not recorded.

Pathology.—All of the resected specimens had similar macroscopic appearances: superficial mucosal ulceration with narrowing of the lumen and rigid thickening of the colonic wall mainly due to widening of the submucosal layer (*Fig.* 3 B).

Microscopically the submucosal layer, and to a lesser extent the subserosal layer, were infiltrated with fibrous tissue containing inflammatory cells. A few haemosiderin-containing macrophages were noted after staining of the sections with Prussian blue. In two specimens some endarteritis was noted in the intramural arteries and arterioles. There were no granulomas visible in the sections. No colonies of *Clostridium welchii* were seen.

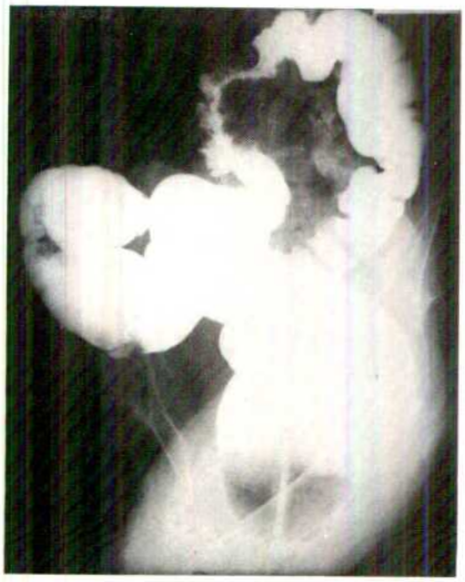
Progress.—None of these patients has had a recurrence of the ischaemia. At least 3 patients have permanent colonic damage, but they have remained well, with normal bowel function, for up to 3 years.

DISCUSSION

Non-gangrenous ischaemic colitis is diagnosed on the basis of both clinical and radiological findings. Histological confirmation is obtained only when the lesion can be reached sigmoidoscopically for biopsy, or a resection becomes necessary. In the present group such cases constituted a minority.

Clinically the most notable features are (1) the acute onset; (2) the severity of the abdominal pain; (3) diarrhoea, which may be preceded by tenesmus and which commences soon after the onset of the pain; (4) the passage of blood per rectum; (5) the mild systemic disturbance; (6) the paucity of physical signs; and (7) the self-limiting nature of the condition. A few patients have signs of intestinal obstruction during the acute illness, and a few develop incomplete large-bowel obstruction later if severe stricturing occurs. Occasionally a patient presents an atypical picture with little or no pain and with a chronic rather than an acute illness. Such a presentation is still compatible with reversible changes in the colon. When the local and systemic signs are pronounced the possibility of a gangrenous lesion must be considered.

The differentiation of this condition from, for example, acute ulcerative colitis, Crohn's disease, diverticular disease, carcinoma, or intussusception of a polyp is made radiologically. The most notable radiological features are (1) the presence of 'thumb printing' in the acute stage (Boley and others, 1963); (2) tubular narrowing of the affected segment, which is usually clearly demarcated but which sometimes has 'funnelled' ends (Thomas, 1968); (3) the quite



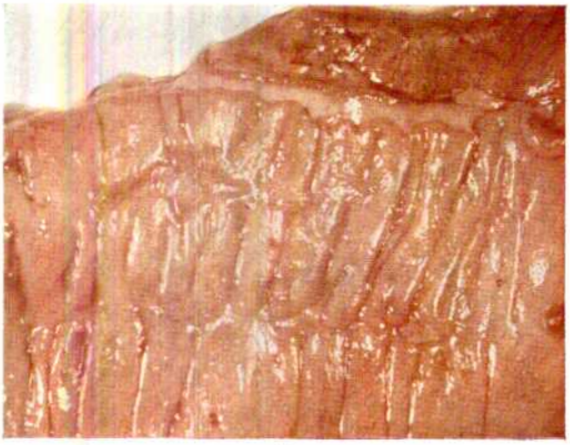


FIG. 3.—*Case* 4. A, Ischaemic lesion in the transverse colon mistaken for carcinoma. Demonstrated 6 days after onset of symptoms. B, Specimen showing marked widening of the submucosal layer, granulating ulcers, and normal mucosa. Resected 2 weeks after onset of symptoms.

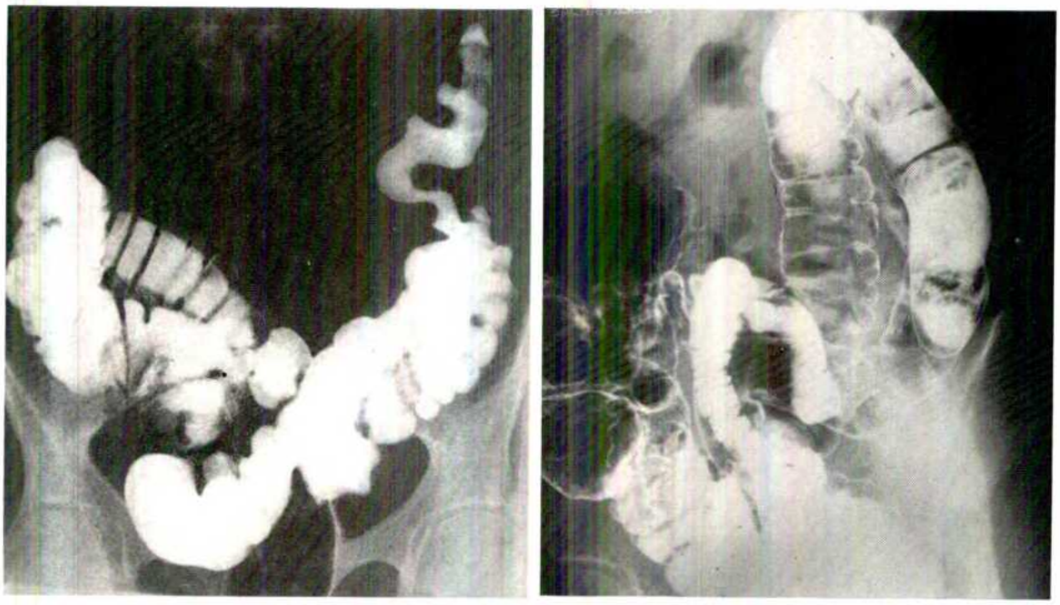


FIG. 4.—*Case* 10. A, Tubular narrowing with 'thumb printing' in the splenic flexure region. Demonstrated 2 days after onset of symptoms. B, The colon has returned to normal. Demonstrated 5 months later.

rapid changes in appearance resulting either in a return to normal or in segmental stricturing, sometimes with 'sacculation' of the wall (Marston and others, 1966); (4) the tendency for the affected segment of colon to shorten, even after stricturing has occurred; and (5) the tendency for the lesions to occur in the splenic flexure region (Marston and others, 1966). However, these features are non-specific and other conditions may have similar appearances. For example, polyposis, pseudopolyposis, lipomatosis, pneumatosis, and some malignant tumours can produce appearances similar to 'thumb printing'. Crohn's disease, ulcerative colitis, tuberculosis, and linitis plastica of the colon can produce similar segmental stricturing. Nevertheless, when the radiographic findings are considered in conjunction with the clinical picture the distinction between these lesions and ischaemic lesions usually can be made.

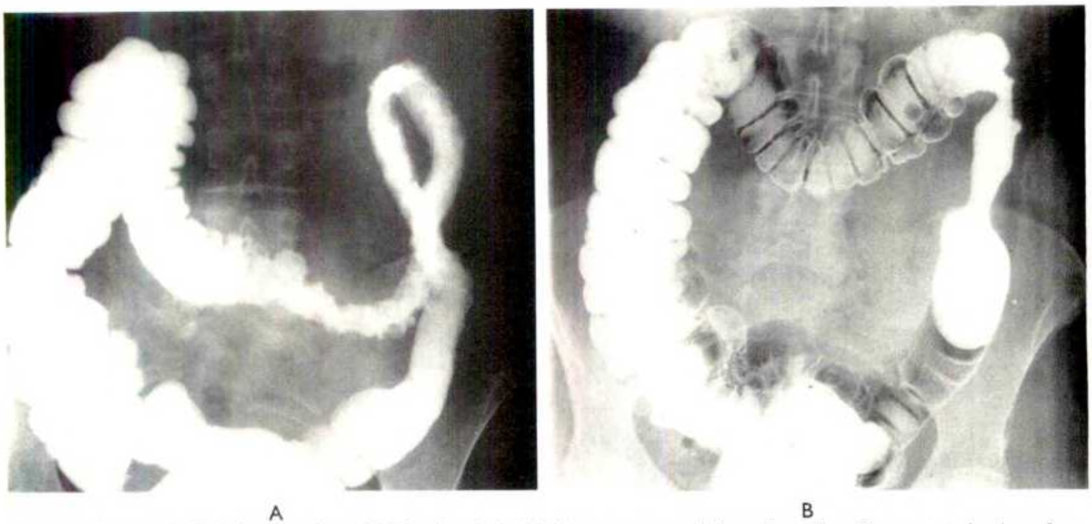


FIG. 5.—*Case* 13. A, Tubular narrowing with 'thumb printing' in the transverse and descending colon. Demonstrated 4 days after onset of symptoms. B, Permanent long stricture with 'funnelling' of ends. Demonstrated 2 months later.

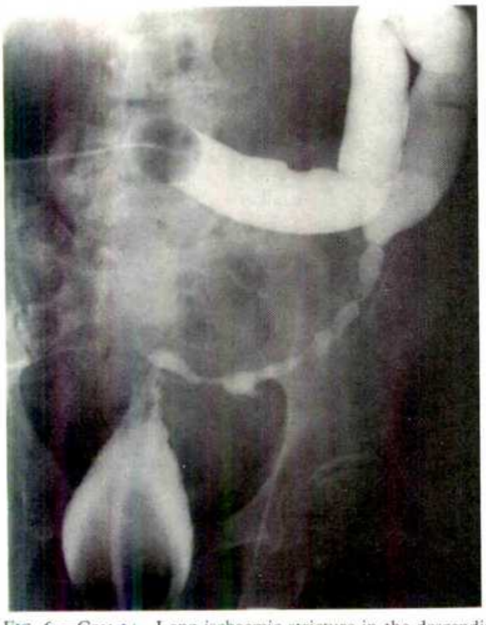


FIG. 6.—*Case* 14. Long ischaemic stricture in the descending colon after anterior resection of rectum (barium introduced per rectum and via the colostomy).

It is notable that the severity of the symptoms often bears no relation to the severity or the extent of the colonic damage as shown on the radiographs. For example, a patient with quite severe symptoms may sustain transient damage (*Fig*. 7), while a patient with relatively mild symptoms may have extensive permanent damage (*Fig*. 5).

The tendency for the radiological changes to be reversible emphasizes the need for an early barium enema when an ischaemic lesion is suspected, and the examination can be performed while symptoms are still present.

When diagnostic doubt exists after the first barium enema, serial barium enemas should be performed to demonstrate the evolutional changes which distinguish ischaemic lesions from other lesions. Serial barium studies also make it possible to determine whether the colonic damage is permanent and how extensive it is. In some patients the initial colonic involvement proves to be largely permanent (*Fig*. 2), while in others even the presence of marked stricturing (*Fig*. 8 A) does not prevent considerable recovery (*Fig*. 8 B). It is probable that such shortening of the strictured area is not entirely the result of recovery, for contracture of the affected segment may also contribute to it (Rowe Jones, 1969; Brown, 1972).

In the acute stage the duration of the symptoms is more useful than the severity of the symptoms as a guide to the extent of the colonic damage. *Cases* 2 and 17 each had an acute illness lasting longer than 5 days and both sustained extensive damage with marked stricturing (*Figs*. 1 and 8 A), yet *Case* 2 had severe symptoms, while *Case* 17 had relatively mild ones.

Thus in some patients the changes in the colon are temporary while in others they are permanent, although their modes of presentation are similar. At the time of their acute illness it is not possible clinically, or radiologically, to determine which patients have sustained permanent colonic damage and which have not. This unpredictable variation in the end-result of the ischaemic episode restricts the applicability of the classification of ischaemic lesions proposed by Marston and others (1966). The distinction between 'stricturing' and 'transient' lesions can only be made several weeks after the acute illness, and it is better therefore to regard non-gangrenous ischaemic colitis as a condition with lesions ranging in severity from extensive permanent stricturing at one extreme to transient ischaemic damage at the other.

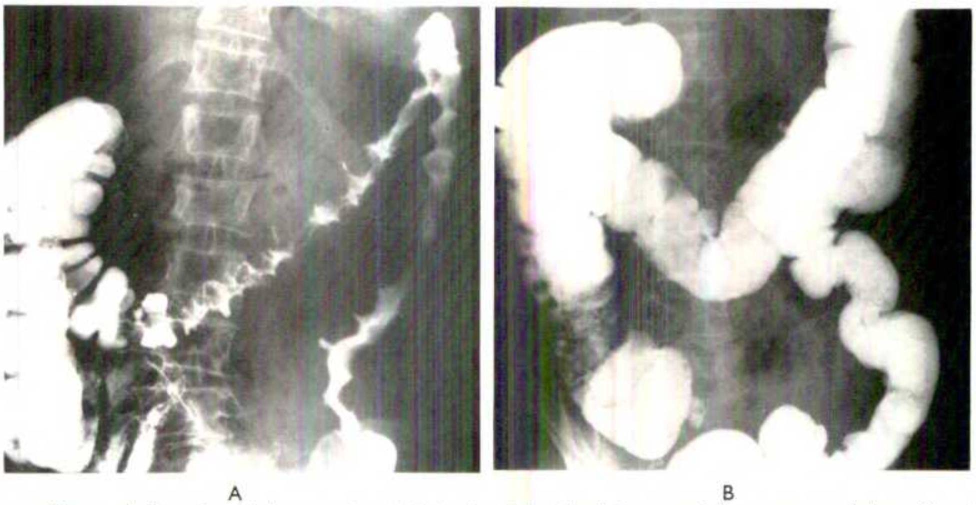


FIG. 7.—*Case* 15. A, Extensive tubular narrowing with 'thumb printing' involving most of the transverse and descending colon. Demonstrated 2 days after onset of symptoms. B, The colon has returned to normal. Demonstrated 7 weeks later.

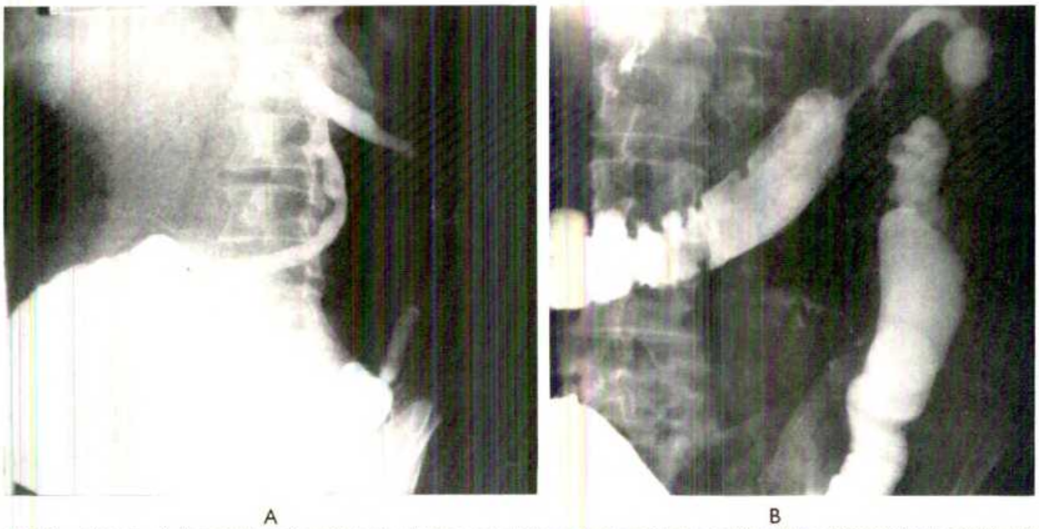


FIG. 8.—*Case* 17. A, Long ischaemic stricture involving most of the transverse and descending colon. Demonstrated 2 weeks after onset of symptoms. B, Marked reduction in the length of the stricture with the appearance of 'sacculation' of the colonic wall. Demonstrated 8 months later.

Management.—The management of ischaemic colitis in the acute phase is determined by the presence or absence of colonic gangrene. Clinically, the paucity of physical signs, the mild systemic disturbance, and the self-limiting course of the non-gangrenous condition are sufficient to distinguish it from the highly lethal gangrenous one, in which signs of peritonitis with shock predominate.

With spontaneously occurring lesions progression from a non-gangrenous to a gangrenous state is unlikely (Marston, 1968), and if there are signs of intestinal obstruction they will resolve with conservative management. Operation should be reserved for those patients in whom there is doubt about the viability of the colon.

After abdominal aortic surgery the development of gangrene may be insidious (Miller and Knox, 1966) and more caution seems necessary, but vigilance during the original procedure should reduce the chances of intestinal ischaemia developing (Rob and Snyder, 1966).

Established lesions sometimes require operation because there is doubt about the diagnosis, but resection is necessary only when there is partial obstruction due to severe segmental stricturing. Marston (1969) advocates resection of all permanently strictured lesions, but several of the patients described here have maintained normal bowel function in the presence of quite marked stricturing. This is a benign condition mainly affecting older patients, and it is desirable therefore to avoid a colonic resection when possible. There is no evidence that the lesions subsequently extend, and a symptomless benign stricture can be retained without hazard.

When an established lesion is resected the extent of involvement is usually well defined and is less than had appeared in the acute phase. Provided the viability of the remaining colon is not in doubt a one-stage resection is then a safe procedure.

In the present group, although no specific therapy was given either for the ischaemia or for the colonic damage, the persistence of ischaemic damage in some of the patients emphasizes the need for non-operative therapeutic measures.

Experimental studies have shown a number of measures to be beneficial in the management of ischaemic bowel. However, the natural tendency for the colon to recover makes the efficacy of such measures difficult to assess, and clinical experience of them is small.

Low-molecular-weight dextran to prevent sludging of the blood has proved useful experimentally (D'Angelo, Ameriso, and Tredway, 1963) and would be safer than anticoagulation since the lesions are usually haemorrhagic.

Adrenergic alpha-receptors which are prominently represented in the arterioles of the bowel (Green and Kepschar, 1959) may be significant in the production of non-occlusive ischaemia. Williams, Anastasia, Hasiotis, Bosniak, and Byrne (1968) have shown that phenoxybenzamine (an alpha-receptor-blocking agent) prevents necrosis of the intestine in experimental non-occlusive ischaemia, but the place of this substance in clinical practice has yet to be defined.

A fuller understanding of the pathogenesis of the colonic lesions should lead to more effective measures to minimize the permanent damage. Marston (1967) has described these lesions as infected infarcts because bacterial invasion of the colonic wall is to be expected following damage to the mucosa, but what part bacteria play in the pathogenesis of the resulting lesions is uncertain. Experimentally, antibiotics reduce the severity of ischaemic damage to the bowel (Cohn and Atik, 1961). Prophylactic non-absorbable antibiotics are sometimes used routinely in aortic surgery, but ischaemic lesions of the colon still occur (Bicks and others, 1968). Nevertheless, a combination of systemic broad-spectrum antibiotics and non-absorbable intestinal antibiotics could be beneficial in the management of lesions that occur spontaneously.

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AN ASSESSMENT OF THE VALUE OF MEASURING UNCOLLECTED GASTRIC SECRETION DURING ROUTINE SECRETION STUDIES IN MAN*

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SUMMARY

A simple 'wash-out' collection technique employing phenol red as a marker has been used during routine gastric secretion studies and its value has been assessed. Studies repeated on a single individual showed good reproducibility. When measured this way loss was not affected greatly by the volume secreted.

With this technique the repeatability of pentagastrin tests has been assessed at intervals of 6 weeks. This demonstrated that both acid and pepsin outputs could vary considerably, with a mean variation in acid of over 26 per cent.

The effects of histamine, pentagastrin, and insulin upon loss have been studied.

Loss has been found to vary considerably from one study to another and from one patient to another and may on occasions be considerable, particularly after previous surgery.

These findings suggest that a method of measuring loss should be adopted by any centre which wishes to use secretion studies to analyse the effects of treatment.

THE value of secretion studies in clinical practice depends upon the accuracy with which they are performed. One possible source of inaccuracy is the failure to collect all the secretion produced, giving a falsely low calculated secretion. Surprisingly few workers have attempted to measure such losses so that the value of estimating the amount of secretion escaping collection has not been assessed fully.

The present study was designed to establish a simple method of collection. Sophisticated techniques (such as the use of a radioactive marker) have been avoided and the method described relies upon changes in the concentration of phenol red (a non-absorbable marker) between the time of instillation and withdrawal from the stomach.

MATERIALS AND METHODS

Technique.—Prior to a test all medications were withheld for 24 hours and the subject was fasted for 12 hours.

A double-lumen tube of special construction was used (*Fig.* 1). One lumen ended 15 cm. proximal to the other and had two holes drilled near its end to produce a fine spray when phenol red was infused through it. Infusion was controlled by a peristaltic pump (Watson-Marlowe) at a rate between 10 and 15 ml. per minute. Phenol red was made up before a test by adding 20 ml. of stock solution (1·5 g. per litre) to 2 litres of distilled water. The second lumen was connected to suction (5 mm. Hg) via a three-way tap that allowed air to be injected if the tube became blocked.

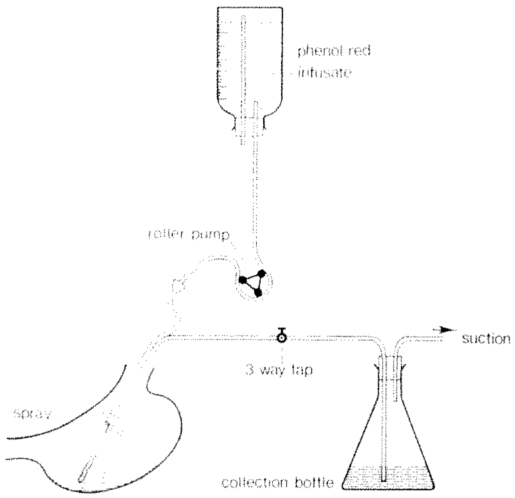

FIG. 1.—Diagrammatic representation of the collection technique.

Tests were performed by passing the tube into the stomach and adjusting its position until phenol red injected down the infusion limb was recovered easily up the other limb. This technique proved as good as radiographic screening, confirming the findings of Hassan and Hobsley (1970). After positioning 'wash-out' was commenced. It was found necessary to have a preliminary period of 'wash-out' to remove residual overnight secretion and to allow equilibration of phenol red to occur otherwise the concentration of phenol red recovered was low, giving a false measurement of loss of secretion. Usually 15 minutes were sufficient unless gastric retention was present, when preliminary 'wash-out' was continued until the recovered fluid was clear.

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* Based on a paper delivered to the Surgical Research Society in January, 1969.

Basal secretion was collected for 15 minutes and pentagastrin (6·0 µg. per kg. i.m.) or histamine (40 µg. per kg. s.c.) was given and the stimulated secretion was collected over the next 60 minutes. In some studies insulin (0·2 U. per kg.) was given intravenously at the end of this period and secretion was collected for a further 75 minutes.

Measurements.—The volume of each collection was recorded and samples were analysed for acid, pepsin, and phenol red.

Acid.—Total titratable acidity was measured to *p*H 7 using an automatic titrimeter.

Pepsin.—This was measured as total peptic activity at *p*H 2·1 using a modified Hunt (1948) technique. The modification was the use of bovine serum albumin (fraction) as substrate; this gave a similar activity curve for gastric juice and purified pepsin (Sigma 1 : 60,000). Results are expressed as equivalent to the amount of Sigma pepsin having the same activity (1 Hunt unit = 4·2 µg.).

Table I.—RESULTS OF FOUR PENTAGASTRIN AND FOUR HISTAMINE TESTS PERFORMED ON A SINGLE HEALTHY MALE OVER A 12-MONTH PERIOD IN ORDER TO TEST REPRODUCIBILITY

TEST	BASAL HOUR				STIMULATED HOUR						LOSS	
	Acid (mEq. per hr.)		*Pepsin* (mg. per hr.)		*Acid* (mEq. per hr.)		*Pepsin* (mg. per hr.)		*Volume* (ml. per hr.)			
	Mean ± S.E.	Coefficient of Variation (per cent)	Mean ± S.E.	Coefficient of Variation (per cent)	Mean ± S.E.	Coefficient of Variation (per cent)	Mean ± S.E.	Coefficient of Variation (per cent)	Mean ± S.E.	Coefficient of Variation (per cent)	Mean ± S.E.	Coefficient of Variation (per cent)
Histamine	1·4 ± 0·4	32	60·1 ± 25·9	43	18·7 ± 2·3	12	210·5 ± 11·8	6	302·0 ± 23·0	7	22·1 ± 6·7	30
Pentagastrin	1·4 ± 0·7	50	59·8 ± 34·8	58	16·6 ± 2·7	16	163·6 ± 30·6	19	302·0 ± 30·9	10	12·7 ± 4·1	33

Phenol Red.—After filtration 5 ml. of the collected secretion were added to 10 ml. of sodium phosphate solution (2·75 g. per 100 ml.) and the optical density (O.D.) was read at 545 mµ using a blank of 5 ml. of distilled water in phosphate solution. Biliary contamination could produce erroneous results; to correct this each sample was re-read at 670 mµ against a blank of the original infusate in phosphate solution. If a reading was obtained this was subtracted from that at 545 mµ to give the corrected optical density. The validity for this correction was established in *in vitro* studies.

Calculation of Loss.—This was calculated from the following formulae:—

$$\text{Total volume } (T)\ (\text{secretion} + \text{phenol red}) = \frac{\text{O.D. infusate}}{\text{O.D. sample}} \times \text{volume infused } (V_1),$$

$$\text{Secretion volume} = T - V_1,$$

$$\text{Loss } (L) = T - \text{volume recovered},$$

$$\text{Percentage loss} = (L/T) \times 100.$$

Plan of Investigations.—Three hundred and fifty-four patients and volunteers were investigated. Most were patients with suspected peptic ulcer disease and all had the procedure explained and their co-operation was obtained. The studies performed were as follows:—

1. *Reproducibility.*—Four pentagastrin and four histamine tests were performed upon a single healthy male subject over a 12-month period.

2. *Effect of 'Wash-out' upon Pentagastrin-stimulated Secretion.*—

a. 'Wash-out' versus 'non-wash-out': Twelve patients had a 'wash-out' and a 'non-wash-out' pentagastrin test at intervals from a few days to 3 months.

b. 'Wash-out' versus 'wash-out': Twenty-one duodenal ulcer patients had repeat 'wash-out' pentagastrin studies performed at 6-week intervals.

3. *Effect of Volume secreted upon Loss.*—This was assessed by comparing the percentage losses during pentagastrin studies in 150 patients who had not been subjected to surgery. These were drawn at random from over 1000 studies performed with this collection technique over a 3-year period. The patients were divided into five groups depending upon the volume secreted in the hour after stimulation, the first 30 patients drawn in each group being used for the comparison.

4. *Effect of Different Stimuli upon Loss.*—

a. Histamine versus pentagastrin: Twelve patients had a pentagastrin and histamine test performed using the 'wash-out' collection technique. The tests were all performed within a few days of one another.

b. Pentagastrin versus insulin: Fifty-nine duodenal ulcer patients had a combined pentagastrin/insulin test prior to surgery.

5. *Effects of Different Surgical Procedures upon Loss.*—

a. Vagotomy and pyloroplasty: Fifty-nine patients had pentagastrin/insulin tests before and 6 weeks after this operation.

b. Various gastric operations: Losses in the hour following pentagastrin were compared in the following groups of patients studied more than 18 months after surgery: Billroth-I gastrectomy (15); Polya gastrectomy (21); vagotomy and gastro-enterostomy (28); vagotomy and pyloroplasty (34).

RESULTS

1. Reproducibility (*Table I*).—Basal secretion showed marked variation from one study to another, but the mean outputs of acid and pepsin during the

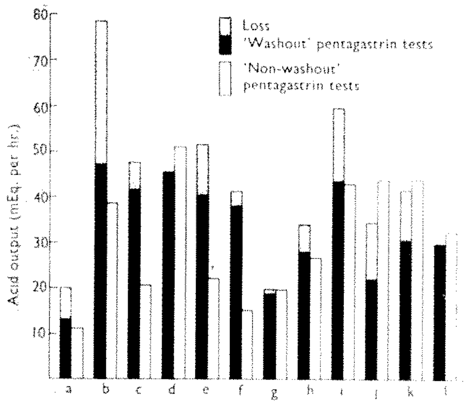

FIG. 2.—Individual acid outputs in response to pentagastrin stimulation in 12 patients studied by 'wash-out' and 'non-wash-out' collection techniques. (Recovery was complete during the 'wash-out' studies on d and l.)

Table II.—COMPARISON OF MEAN ACID OUTPUTS WITH AND WITHOUT CORRECTION FOR LOSS DURING 'WASH-OUT' AND 'NON-WASH-OUT' STUDIES ON 12 SUBJECTS

TEST	ACID OUTPUT (mEq per hr.)			
	Basal Secretion		*Pentagastrin-stimulated Secretion*	
	Corrected for Loss	Uncorrected for Loss	Corrected for Loss	Uncorrected for Loss
'Wash-out'	27·9 ± 14·0	16·1 ± 15·6	42·0 ± 16·7	33·2 ± 11·2
'Non-wash-out'	—	7·0 ± 4·3	—	30·6 ± 13·3

Table III.—COMPARISON OF THE LOSSES FOUND AND VARIATION IN ACID, PEPSIN, AND UNCOLLECTED SECRETION IN REPEAT 'WASH-OUT' STUDIES ON 22 DUODENAL ULCER PATIENTS

	LOSS (per cent)		VARIATION BETWEEN TWO TESTS (per cent)		
	Test 1	Test 2	Acid	Pepsin	Loss
Corrected for loss	23·5 ± 17·0	21·3 ± 19·1	26·7 ± 18·9	33·9 ± 23·0	16·9 ± 16·1
Uncorrected for loss	— —	— —	25·1 ± 20·7	30·3 ± 23·2	— —

histamine and pentagastrin studies were remarkably similar. Following stimulation the coefficient of variation was lower after histamine (acid 12 per cent; pepsin, 6 per cent) than after pentagastrin (acid, 16 per cent; pepsin, 19 per cent), but both were lower than the variation in loss, suggesting that had this not been measured the variability would have been larger. Pepsin output following pentagastrin was significantly lower than after histamine ($P < 0·05$) but acid output was not.

2. Effect of 'Wash-out' upon Pentagastrin-stimulated Secretion (*Table II*).—

a. 'Wash-out' versus 'Non-wash-out'.—Basal secretion was significantly higher during the 'wash-out' studies than during the 'non-wash-out' tests even when no allowance for loss was made ($P < 0·05$). On the other hand, 'wash-out' did not affect the response to pentagastrin, as the mean acid output was not significantly different ($P > 0·30$) when loss was not measured. An interesting finding was that 5 patients showed considerable differences (*Fig.* 2) in their acid outputs on the two occasions and the mean difference between the response obtained on the two occasions was 26·1 per cent (S.D. ± 22·6).

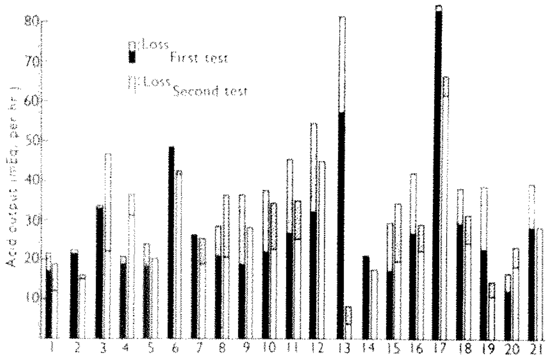

FIG. 3.—Acid outputs in 21 patients studied by 'wash-out' on two occasions.

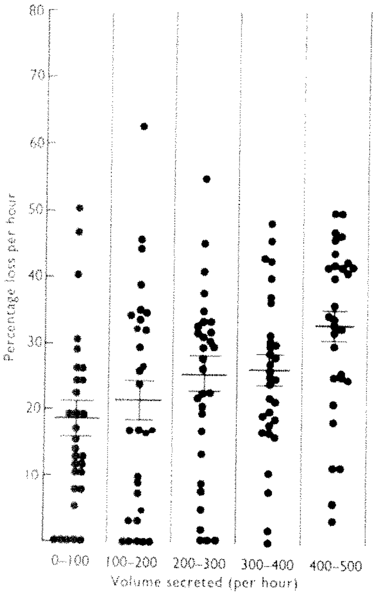

FIG. 4.—Measured percentage loss during pentagastrin studies on 150 patients secreting at various rates.

b. 'Wash-out' versus 'Wash-out'.—There was no difference in the mean acid and pepsin outputs in the two studies but, as in (*a*), individual patients showed considerable differences in the responses obtained (*Fig.* 3). Four had acid outputs and 9 had pepsin outputs that differed between the two studies by more than 30 per cent. These differences could not be attributed to errors in measuring loss as they still occurred when this was not calculated, and the variation in loss between the two studies (16·9 ± 16·1 per cent) was less than the variation in either acid or pepsin outputs (*Table III*).

3. Effect of the Volume secreted upon Loss.—Hobsley and Silen (1969) noted that the measured loss in their studies varied with the rate of secretion, being largest when the volume secreted was small. The present study differed from theirs in the use of a high flow-rate (10–15 ml. per minute compared with 0·05 ml. per minute) and it was necessary to investigate whether similar results would be obtained with this technique. *Fig.* 4 illustrates the percentage losses found in 150 patients investigated before surgery in whom the volume secreted after pentagastrin varied from less than 100 ml. per hour to 500 ml. per hour. It was found that the lowest losses occurred when the volume secreted was small and highest when the volume secreted was large, although the mean losses in each group were not significantly different from one another until the volume secreted was greater than 400 ml. per hour.

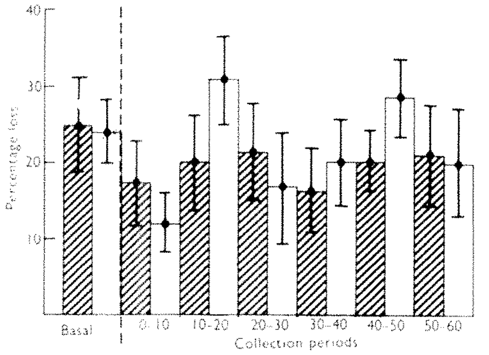

FIG. 5.—Mean percentage losses in individual collection periods following histamine and pentagastrin stimulation in 12 individuals.

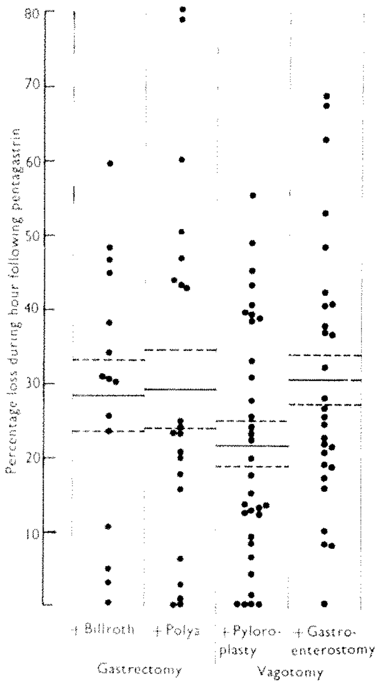

FIG. 7.—Measured losses during the hour after pentagastrin stimulation in 98 patients studied more than 18 months after various gastric operations.

4. Effect of Different Stimuli upon Loss.—

a. Histamine versus Pentagastrin (*Fig.* 5).—For these studies secretion was collected at 10-minute intervals and loss was calculated both for each collection period and for the hour after stimulation. There was no difference in the mean loss for the whole hour after histamine (19·9 ± 19·0 per cent) or after pentagastrin (20·4 ± 16·1 per cent), but during individual collection periods differences were seen. Histamine was associated with an almost constant loss of around 20 per cent, whilst pentagastrin produced two peak periods of loss during the 10–20-minute and 40–50-minute periods. The first peak was associated with the peak in acid secretion.

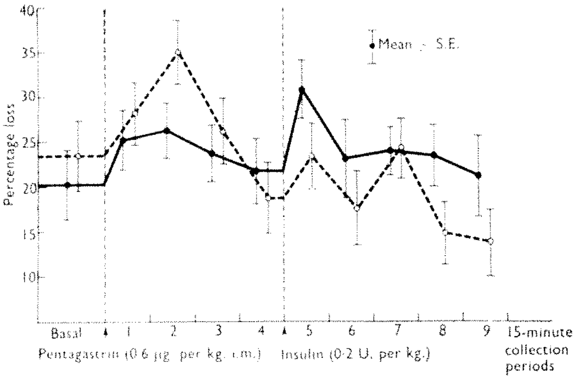

FIG. 6.—The effects of vagotomy and pyloroplasty upon the percentage loss during comparable collection periods in repeat pentagastrin/insulin studies before (——) and 6 weeks (– – –) after operation.

b. Pentagastrin versus Insulin (*Fig.* 6).—These were compared by assessing loss during the peak periods of secretion (15–45 minutes after pentagastrin and 30–60 minutes after insulin) following each substance. The stimuli were given consecutively in a combined test prior to surgery. Loss did not differ significantly following pentagastrin and insulin when investigated in this way, the mean loss after pentagastrin being 24·9 per cent (S.D. ± 22·9) and that after insulin being 23·7 per cent (S.D. ± 23·6) before surgery.

5. Effects of Different Surgical Procedures upon Loss.—

a. Vagotomy and Pyloroplasty.—During repeat pentagastrin/insulin tests performed before and 6 weeks after surgery loss was calculated for each collection period (*Fig.* 6). It was found that after operation there was an increase in loss during the basal period and the first three collection periods after pentagastrin, but thereafter loss was less in the postoperative study. The only periods when these differences achieved statistical significance were the 15–30-minute period after pentagastrin and the 0–15-minute and 45–60-minute periods after insulin.

b. Various Gastric Operations.—The effect of different gastric operations upon loss was assessed by calculating the amount of uncollected secretion during pentagastrin studies performed more than 18 months after operation. There was a considerable variation (*Fig.* 7) in the amount lost in different patients, the largest occurring when the stomach had been anastomosed to the jejunum. The vagotomy and pyloroplasty group had a lower mean loss (21·9 per cent) than any of the other groups (Billroth-I, 28·4 per cent; Polya, 29·2 per cent; vagotomy and gastro-enterostomy, 30·7 per cent), but this difference was only significant when compared with the vagotomy and gastro-enterostomy group ($P < 0.05$).

DISCUSSION

Royle and Catchpole (1967) showed that significant losses could occur during gastric secretion tests, and Hobsley and Silen (1969) confirmed their findings. The importance of such losses during routine studies has not been investigated in detail. A collection technique was required that would be readily applicable to any investigation and would give an estimate of loss. Stephens and Kyle (1963) tried to prevent losses by means of a 'blocker' in the pylorus but this technique is too difficult for routine studies. Phenol red was chosen for the present investigation because it is not absorbed by the stomach (Hollander, Penner, and Saltzman, 1937; Hunt, 1949) and it appears to be a good 'marker' in recovery studies in the dog (Bloom, Jacobson, and Grossman, 1967). Other workers have used phenol red but most have instilled and withdrawn it over a fixed time interval (Brooks, Erskine, Gephart, Swaim, and Moore, 1950; Hunt and Spurrell, 1951; Sen and Roy, 1963; Aylett and Tonkin, 1964), which is unsuitable for following the pattern of a response. In the present studies the marker was infused continuously throughout the test, a technique similar to that described by Scobie and Rovelstad (1965) using phenolphthalein and by Hobsley and Silen (1966). The major difference in the present study was in the use of a high flow-rate. This made the collection of secretion easier as the volume infused was nearly always greater than the volume secreted, thus producing a physical 'wash-out' effect. This overcame the increased loss at low secretion rates noted by Hobsley and Silen (1969) when a low flow-rate was used. The method proved to be simple to perform, requiring little additional equipment. Most of the studies reported in this paper were performed by a trained nurse with minimal medical supervision. Reproducibility was found to be acceptable and appeared to be improved compared with studies where loss was not measured. The only disadvantages were that basal secretion was increased and that the calculation of acid concentrations could be inaccurate when the volume secreted was small. This latter disadvantage only became important if Hollander's (1951) criteria for incomplete vagotomy were used during insulin studies. Why was basal secretion increased (a finding reported by others using marker techniques)? The most likely explanation is that dilution of gastric juice prior to its entering the duodenum removed some of its inhibitory effects.

Having established the method it was then used to investigate several aspects of loss. The first was whether its use would improve the repeatability of secretion studies, and this did not occur. It was interesting to find how much the response to pentagastrin could vary from one study to another, whether loss was measured or not. This appeared to be a true variation in response and has not been reported before, presumably because most repeat studies have been performed within a day or so and not at 6-week intervals as was done here. It is obviously important to recognize that this can occur as repeat studies may be used to assess treatment.

Investigation of the effect of various standard stimuli (histamine, pentagastrin, and insulin) upon loss was examined. Insulin and pentagastrin were found to be similar in their effects, producing fluctuations in loss with peak losses during the period of peak gastric secretory activity. This suggests that these agents may have an effect upon motility as well as upon secretion. Histamine, on the other hand, did not appear to affect emptying directly.

The amount lost during pentagastrin stimulation was increased by vagotomy and pyloroplasty. The greatest loss occurred at the time of peak acid secretion, so that if this is not measured a falsely high reduction in acid output would be calculated. Other operative procedures were associated with considerable losses in some individuals, particularly where the stomach had been anastomosed to the jejunum.

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TWO UNUSUAL LEG ULCERS

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SUMMARY

Two unusual leg 'ulcers' are reported. The first represents an uncommon site for a basal-cell epithelioma, the atypicality of which is emphasized by its lymph-borne metastasis. The second, a fibrosarcoma, is an example of a rare type of malignant transformation occurring in a long-standing varicose ulcer.

ULCERATION of the leg is commonly associated with varicose veins or is a sequel of deep-vein thrombosis. Other causes are burns, syphilis, lupus vulgaris, scrofuloderma, and pyoderma gangrenosum. In this paper two unusual ulcers of the leg are described.

CASE REPORT

Case 1.—Mrs. F. G. was first seen in 1965 at the age of 73 years. For 8 years she had noticed a progressively enlarging ulcer below and medial to the left knee. In 1961 she had attended another hospital where the lesion had been excised and the defect covered with a skin-graft. Histology had shown the lesion to be a basal-cell epithelioma. Satisfactory healing had occurred, but by 1964 the ulcer had recurred and the patient had been given a course of radiotherapy (5000 rad over 7 days). This had failed to produce any regression of the tumour and she was admitted in August, 1965, for further surgery. At that time the ulcer measured 6·5 × 5 cm. and the proximal edge, which was 7·5 cm. distal to the knee-joint, had indurated edges and a raw, bleeding base. Inguinal lymph-nodes were not palpable. A biopsy confirmed the diagnosis of basal-cell epithelioma and a further excision was performed, including part of the periosteum over the tibia, and the defect was covered satisfactorily with a skin-graft.

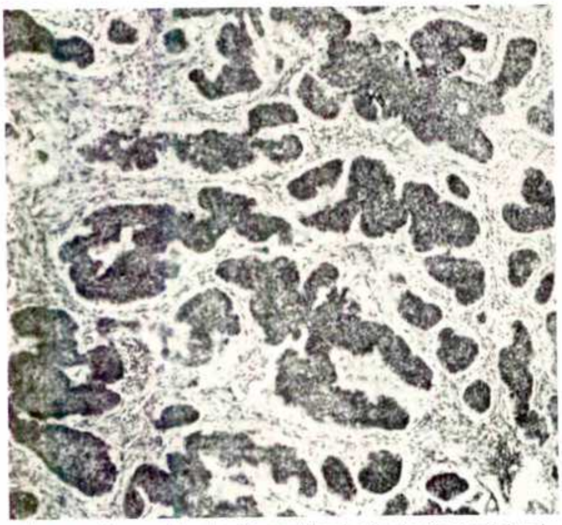

FIG. 1.—*Case* 1. Islands of typical basal cells showing peripheral palisading. H. and E. (× 32.)

By April, 1966, the tumour had recurred and was again excised. Histology again showed the lesion to be a basal-cell epithelioma and suggested that excision had been incomplete. By October, 1967, a nodule 1·5 cm. in diameter was present in the scar and this was excised, giving a 2-cm. clearance around the nodule, but again histological examination suggested that the excision was incomplete. Subsequent traumatic ulceration of the grafted area was successfully treated by bed-rest, and in April, 1968, a wide excision of the upper part of the grafted area was performed in an attempt to eradicate any remaining tumour, but malignant cells were not seen in the excised specimen.

In June, 1969, the patient was found to have developed an enlarged lymph-node in the left groin with some tethering to the overlying skin, but this appeared to progress only slowly until September, 1970, when she developed a small ulcer in the groin. Biopsy of this ulcer showed the presence of basal-cell epithelioma and she was given a course of irradiation to the inguinal gland fields (4500 rad in 17 treatments over 25 days). This produced a slight improvement in the ulcer but failed to heal it.

HISTOLOGY.—The histological features of the four positive biopsy specimens taken between 1965 and 1968 were essentially similar and were typically those of a basal-cell epithelioma. The tissue forming the ulcer base consisted of irregular islands of pale basal cells which extended deeply into the underlying dermis (*Fig.* 1). There was a moderate degree of nuclear pleomorphism and mitotic figures were fairly frequent. In addition, several small foci containing parakeratotic cells and horn cysts were seen, particularly in the first specimen (*Fig.* 2). In all the specimens peripheral palisading was present in some degree, but deeper areas of the sections revealed a tendency for the basal-cell islands to break up and disperse widely as narrow strands through the fibrotic stroma. In the most attenuated areas these were represented by columns of single cells which often anastomosed with neighbouring strands (*Fig.* 3). Tumour tissue extended up to the resection margins in all three biopsies taken before the grafted area was widely excised in 1968,

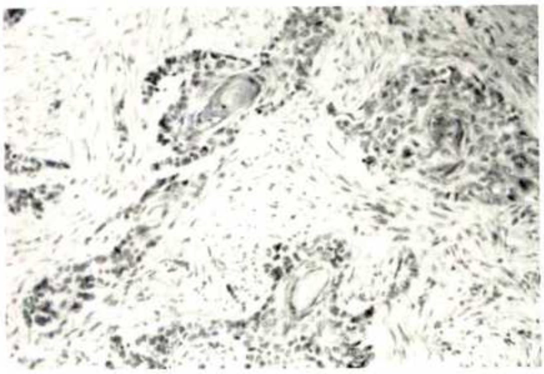

FIG. 2.—*Case* 1. Foci of keratinization with basal-cell nests. H. and E. (× 57.)

and infiltration of the subcutaneous fat was noted. Although in none of the sections was there any evidence of lymphatic invasion the biopsy in 1966 showed a small dermal blood-vessel partially surrounded by tumour cells, with a breach of continuity of the wall in one area (*Fig.* 4). The histological pattern of the tumour seen in the biopsy of the inguinal gland was similar to that of the original ulcer, except that the foci of parakeratosis with horn cysts were absent.

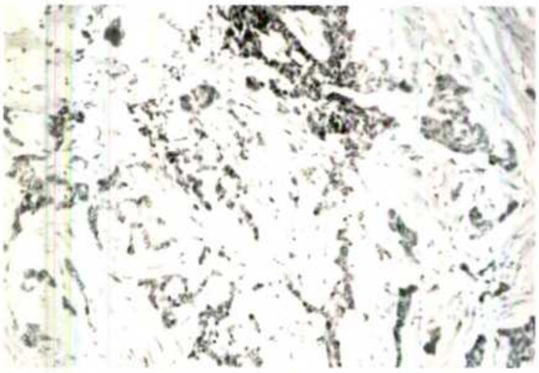

FIG. 3.—*Case* 1. Strands and columns of basal cells showing infiltrating characteristics with stromal fibrosis. H. and E. (× 57.)

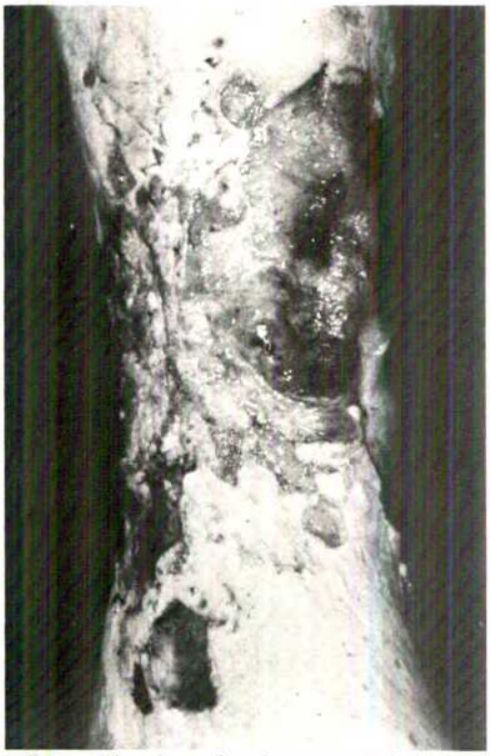

FIG. 5.—The primary ulcerating tumour on the left leg.

Lattes and Kessler (1951) laid down four criteria for accepting the diagnosis of metastasizing basal-cell epithelioma: first, that the primary tumour or metastasis is not of squamous-cell type; secondly, that the metastasis is not a new primary tumour or a direct extension of the primary; thirdly, that the primary tumour arises from the skin; and fourthly, that the histological appearance is typical of basal-cell epithelioma. If these criteria are adhered to, proven

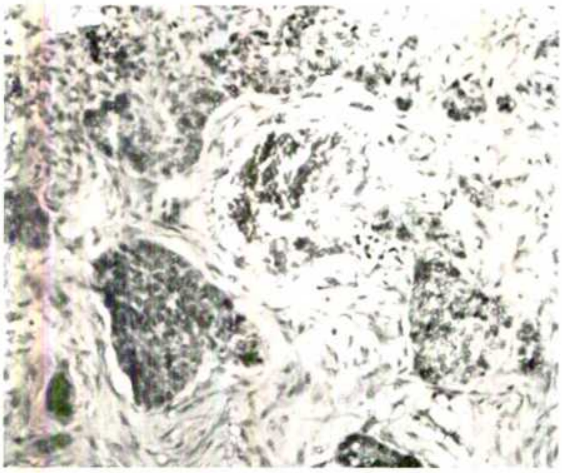

FIG. 4.—*Case* 1. Small arteriole surrounded by basal-cell epithelioma and showing a breach in the continuity of the wall below and to the right. H. and E. (× 75.)

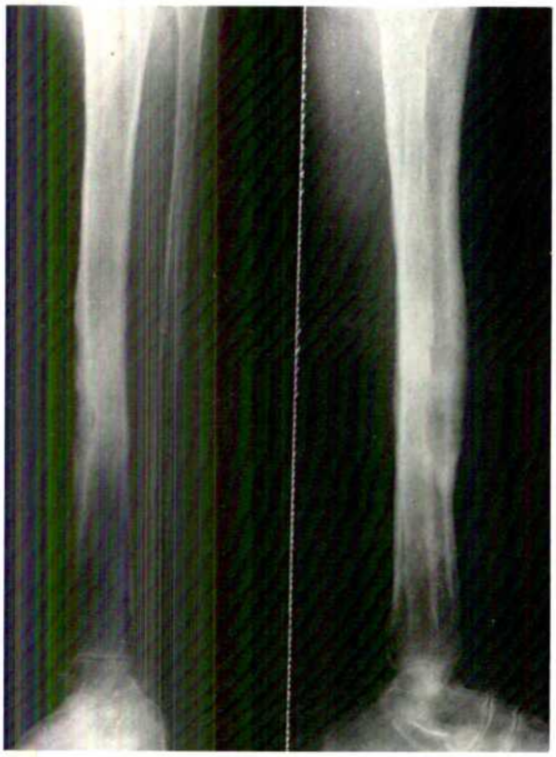

FIG. 6.—Radiograph of the left lower limb, showing marked periosteal reaction.

cases of metastasizing basal-cell epithelioma are uncommon. Cotran (1961) reviewing 9050 cases of basal-cell tumour could find only 9 with definite evidence of metastasis, an incidence of 0·1 per cent. Earlier, Cade (1940) described 1 such case in 183 epitheliomas, an incidence of 0·54 per cent. The site of the primary tumour in the present case is also unusual. Only 1 of Cotran's (1961) cases had a primary tumour not on the face or scalp, this being on the back, as was the single case reported by Urbach and Alkek (1969). Coletta, Haentze, and Thomas (1968) reported a case of basal-cell epithelioma of the left leg with multiple metastases, including involvement of the inguinal lymph-nodes. The sites of the primary tumour in other case reports include the scapular region (Binkley and Rauschkolb, 1962), the scalp (Crawford and Joslin, 1964), the face (Singer, 1944; Pickren and Katz, 1958), and the forehead (DeNavasquez, 1941). In many of the cases referred to metastases were widespread and included not only the regional lymph-nodes but also the lungs (the most frequent site of extension beyond the regional nodes), bone-marrow, and the viscera. Both vascular and lymphatic routes of spread are quoted and DeNavasquez (1941), Cotran (1961), and Crawford and Joslin (1964) report blood-vessel invasion in their material. Although vascular invasion was noticed in our case in 1966 there is, to date, no clinical evidence of widespread metastasis.

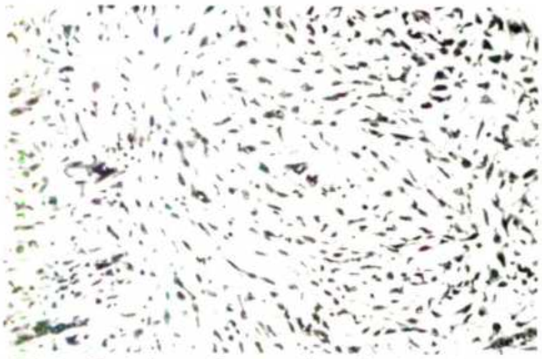

FIG. 7.—Typical area of tumour, illustrating both plump and spindle-cell elements of fibrosarcoma. H. and E. (× 57.)

In 2 of the cases with lung involvement (Pickren and Katz, 1958) widespread metastasis developed as a direct result of invasion of the oral mucosa by an ulcerating basal-cell epithelioma of the face and the aspiration of viable tumour cells.

The interval of 10 years between the appearance of the primary and secondary tumours gives a good indication of the usual time sequence, 7–43 years being quoted by Cotran (1961), and contrasts strongly with a 3-year period for most metastasizing squamous-cell carcinomas (Katz, Urbach, and Lilienfield, 1957). In spite of this a mortality rate of 50 per cent has been calculated (Binkley and Rauschkolb, 1962).

Attempts have been made to correlate the histological appearances with metastatic tendencies, and whilst Cotran (1961) could find no consistent differential features, 4 of his cases showed central foci of keratinization in typical basal-cell masses. Two other cases showed a tendency to form central cell whorls. The areas of keratinization do not resemble those seen in well-differentiated squamous-cell carcinoma since there is absence of an evolution through the prickle-cell phase. These features, seen in our case, were also commented upon by DeNavasquez (1941), Binkley and Rauschkolb (1962), and Crawford and Joslin (1964). Lever (1967), however, considers that these features are frequently seen in typical non-metastasizing basal-cell epitheliomas. Urbach and Alkek (1969) suggested that basal-cell epitheliomas with so-called basi-squamous or metatypical features are more likely to metastasize. These include prominent pleomorphism, malignant dyskeratosis, and abnormal mitotic figures, all of which were seen in the present case. Not seen, however, were the larger, acidophilic cells with loss of peripheral palisading described in the case of Thomas (1968).

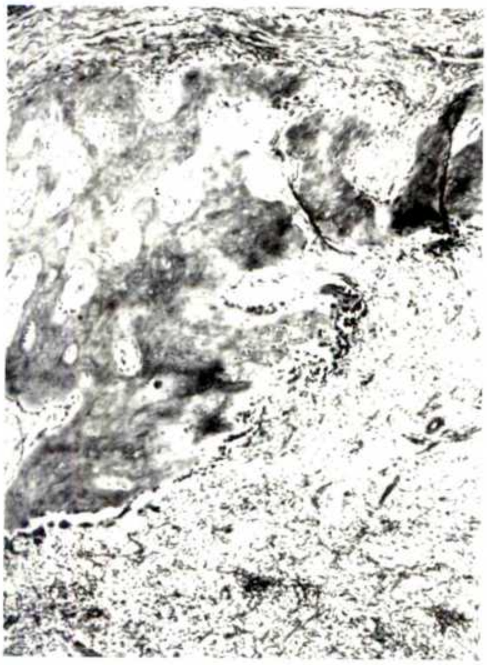

FIG. 8.—Bone trabeculae infiltrated by fibrosarcoma. H. and E. (× 30.)

Case 2.—Mrs. F. M., aged 68 years, reattended at the Out-patients' Clinic in January, 1971. She had previously been seen in 1961 and at that time she had given a 38-year history of varicose veins and a 25-year history of recurrent ulceration of the left lower leg to which skin-grafts had been applied on 6 occasions. At that time the lower two-thirds of the left leg had been grossly indurated and multiple ulcers had been present. The patient had been markedly overweight (88·3 kg., 164 cm.). She had therefore been advised to lose weight and in 1 year she had lost 25 kg. and the ulcers had healed completely. She had been admitted to hospital in November, 1962, and a Trendelenburg operation had been performed on the left leg and the long saphenous vein stripped out. The wounds in the lower leg had healed rather slowly and the patient had been lost to follow-up in July, 1963. When she attended in January, 1971, the patient maintained that her ulcers had remained completely healed for several years until she had knocked her leg 6 weeks before her out-patient visit. Two weeks later she had noticed a lump in the area and this had rapidly been followed by ulceration (*Fig.* 5). In addition a large node was palpable in the left groin.

A chest radiograph was normal, but a radiograph of the left lower leg showed extensive periosteal reaction extending down the shafts of the lower halves of both the tibia and fibula (*Fig.* 6). A small area of bone rarefaction was noted and the appearances were thought to be due to a chronic inflammatory condition rather than neoplastic invasion. The lesion was biopsied on two occasions and a left Gritti-Strokes amputation was subsequently performed.

HISTOLOGY.—A number of sections were prepared from the original biopsy material and later from the operative specimen. In addition to routine haematoxylin and eosin preparations special stains used included Beilschowsky-Maresch's stain for reticulin, periodic acid-Schiff, and Masson's trichrome.

The epithelium at the ulcer margins showed a marked downward prolongation of the stratum Malpighii but no evidence of either pseudo-epitheliomatous hyperplasia or overt carcinomatous change. The main tumour mass consisted of interlacing bundles of both plump and spindle-celled elements with much metachromatic mucopolysaccharide material in the less compact areas (*Fig.* 7). In the ulcer floor there were large areas of pale, eosinophilic, necrotic tissue with many thin-walled capillaries and a dense, acute inflammatory cell infiltrate which in places resembled active granulation tissue. Towards the periosteum the inflammatory infiltrate was less obvious and the vascular component diminished. In addition to considerable nuclear pleomorphism mitotic figures were frequent and in many cases abnormal. Throughout the tumour there was an absence of well-marked intercellular collagen bundles and taken together with the other features a diagnosis of fibrosarcoma was made. Sections made to include periosteum and bone showed evidence of wide infiltration by tumour tissue which in areas occupied the interstices of the marrow cavity (*Fig.* 8). Although a careful search of the serial sections failed to reveal unequivocal lymphatic or blood-vessel involvement, the invasive characteristics of the tumour make this virtually certain.

In any area of long-standing skin ulceration abnormalities in the adjacent tissues may become evident. Most commonly these are reactive changes in the epidermis bordering the ulcer and are seen as downward prolongations of the prickle-cell layer. This was clearly seen in one area in the present case. A slightly more alarming picture is presented by the changes of pseudo-epitheliomatous hyperplasia which nevertheless is benign. A malignant change occurring in chronically ulcerated skin is usually carcinomatous in type and the development of sarcoma is uncommon. Glasser (1939) could find reports of only 2 cases of sarcoma arising in varicose ulcers. More recently, Cruickshank, McConnell, and Miller (1963), reviewing 44 cases of malignancy occurring in scars, chronic ulcers, and sinuses, described 3 sarcomas, 2 arising in a varicose ulcer. The average duration of varicose ulceration before the development of a carcinoma was 21 years, whilst the single sarcoma developed in an ulcer of less than 5 years' duration with a fatal outcome 6 months later. This relatively short time interval contrasts with the present case in which ulceration had been present for 35 years. Difficulties in the histological diagnosis occur in cases of epidermoid epitheliomas simulating sarcoma, and this has been reported particularly in connexion with chronic radiodermatitis (Sims and Kirsch, 1948). The absence of prickle-cells or keratin is a point against an epitheliomatous origin. Although the features of the present case are typically fibrosarcomatous, other sarcomas reported have been myxomatous growths with so many blood-vessels that their appearance strongly suggested granulation tissue (Cruickshank and others, 1963). The single case of Dawson and McIntosh (1970) contained a malignant haemangiomatous element sufficient to warrant a diagnosis of 'granulation tissue sarcoma'.

As in all cases of malignant transformation the question of pathogenesis has been discussed at length. Menkin (1960) suggested that a growth-promotion factor, which he believed to be present in inflammatory exudate, acts in conjunction with scar tissue to produce excessive growth and finally the features of malignancy. In this respect a varicose ulcer lies midway between a healed scar and an osteomyelitic sinus in malignant potential. Peterkin (1955) also discussed an additional factor in the erythema ab igne commonly seen in women.

Acknowledgements.—Our thanks are due to Mr. D. H. Randall for allowing us to publish details of these 2 patients who were under his care, and to Mrs. Marion Row, Department of Pathology, University of Sheffield, for the preparation of the photomicrographs.

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ROUTINE OPERATIVE ARTERIOGRAPHY IN ARTERIAL EMBOLECTOMY

BY G. E. MAVOR, M. G. WALKER, AND D. P. DHALL
ABERDEEN ROYAL INFIRMARY

THE results of surgical treatment of peripheral arterial embolism have been greatly improved by the use of balloon catheters, which were first introduced for this purpose by Fogarty, Cranley, Krause, Strasser, and Hafner (1963). It is now recognized that surgery is the treatment of choice in peripheral embolism in both the upper and lower limbs and is probably contra-indicated only in the presence of established limb gangrene or, when following myocardial ischaemia and failure, embolism is a near terminal event.

The aim of treatment is no longer mere limb survival but the restoration of patency of the affected arterial tree in its whole length. Only by arteriography can complete arterial patency be guaranteed. Our experience with embolectomy under routine operative arteriographic control confirms that clearance of the arterial tree in its whole length is greatly facilitated and results thereby improved.

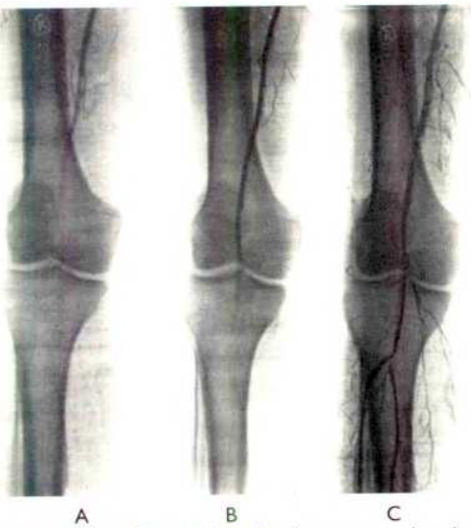
A B C

FIG. 1.—Operative arteriography shows progressive clearing of the popliteal artery (A, B). In the final arteriogram (C) some thrombus may remain at the popliteal bifurcation area.

MATERIALS AND METHODS

The present series covers the last 71 arterial embolectomies carried out at the Aberdeen Royal Infirmary. Sixty of the embolectomies were performed on the lower limb (*Table I*). In all instances embolectomy was carried out from the common femoral artery for the lower limb and from the axillary artery for the upper limb. In all instances except 9 operative arteriography was used. After routine passage of the balloon catheter distally, either once or twice with removal of thrombus, operative arteriography was undertaken. The technique consisted of the passage of a 30-cm. Portex nylon intravenous cannula via the arteriotomy distally into the femoral or brachial arteries. About 10 ml. of Angiografin 3 per cent were injected distally and an arteriogram was taken, attention being directed particularly to the popliteal and brachial bifurcation areas. Occasionally two or three arteriograms were required before adequate clearance was demonstrated. When operative arteriography was satisfactory results were good (*Table II*). In 13 cases arteriography was unsatisfactory in so far as proper visualization of the popliteal or brachial bifurcation and the distal arterial tree was not obtained, owing mainly to technical inexperience or difficulty. All the cases with peripheral arterial embolism were subjected to embolectomy except when gangrene was established. In some,

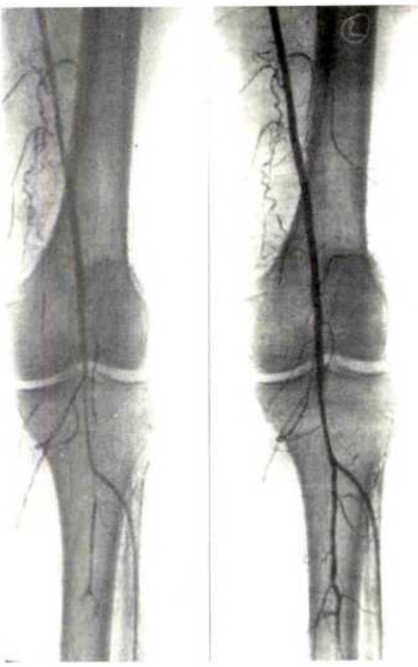
A B

FIG. 2.—On the left side the second operative arteriogram (B) shows that posterior tibial artery clearance is adequate, where previously (A) it was unsatisfactory.

Table I.—POSITION OF ARTERIAL EMBOLECTOMY CARRIED OUT IN 56 PATIENTS

Position	*No. of Embolectomies*
Leg	60
Arm	11
Total	71

delay was considerable (*Table III*). There were 14 early deaths in the series (*Table IV*).

CASE REPORTS

Case 1.—A man aged 61 years presented complaining of the sudden onset of coldness pallor in both legs. A left femoroprofunda embolus had been removed 3 years previously. The common femoral arteries were exposed and bilateral embolectomies were carried out under operative arteriographic control. On the right side two operative arteriograms showed that clearance was inadequate despite removal of much thrombus (*Fig.* 1 A, B). Further passage of the balloon catheter to the ankle and the removal of more thrombus were then followed by a third and finally adequate operative arteriogram (*Fig.* 1 C). On the left side operative arteriography showed that clearance of the posterior tibial artery was initially inadequate (*Fig.* 2 A). Postoperative recovery on both sides was satisfactory (*Fig.* 2 A, B).

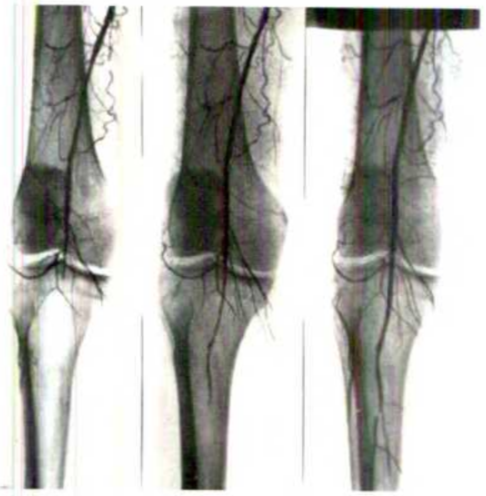

FIG. 3.—The first operative arteriogram (A) shows persistent distal popliteal occlusion. Progressive clearance is demonstrated in (B) and (C).

Table II.—RESULTS OF ARTERIAL EMBOLECTOMY

	ARTERIOGRAPHY SATISFACTORY	ARTERIOGRAPHY UNSATISFACTORY (13)/NOT DONE (9)
No. of embolectomies	49	22
Patent arterial tree and normal leg (clinically)	47	13
Persistent ischaemia	2*	8†
No. of deaths	4	10

* One case was due to persistent posterior tibial occlusion and the other to peroneal artery damage and arteriovenous fistula formation. There was 1 amputation in this group.

† There were 5 amputations in this group.

Table III.—TIME BETWEEN ONSET OF OCCLUSION AND SURGERY

Time	*No. of Embolectomies*
0–6 hours	21
6–12 hours	13
12–24 hours	4
72 hours	11
No information	22
Total	71

Case 2.—A woman aged 52 years was admitted with an obvious arterial embolus lodged in the right common femoral artery. She had had a myocardial infarction about 1 year previously, and was in atrial fibrillation when seen at the present time. The right common femoral artery was exposed and considerable thrombus was removed from the distal arterial tree, the balloon catheter being passed easily to the ankle twice. A subsequent operative arteriogram centred on the distal popliteal area showed that distal popliteal occlusion persisted (*Fig.* 3 A). More thrombus was removed, and although the operative arteriogram showed improvement it was not yet satisfactory (*Fig.* 3 B). Further thrombus was removed and further arteriography revealed adequate clearance (*Fig.* 3 C). The postoperative result was satisfactory.

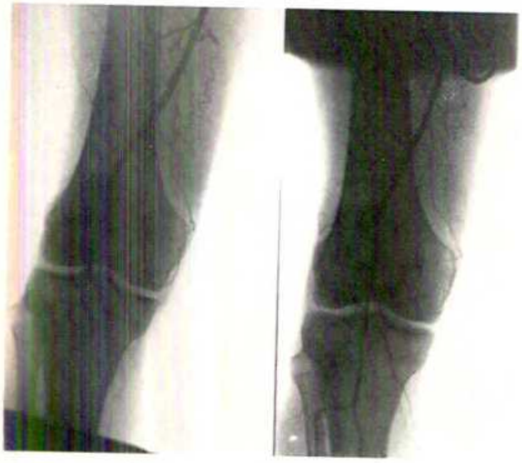

FIG. 4.—The first operative arteriogram (A) shows persistent distal popliteal occlusion despite previous removal of much thrombus. The final film (B) is satisfactory.

Table IV.—CAUSES OF DEATHS OCCURRING WITHIN 7 DAYS AFTER EMBOLECTOMY

Cause of Death	*No. of Deaths*
Myocardial infarction/failure	6
Cerebral embolism	2
Mesenteric embolism	1
Carcinoma	1
Amputation	2
Unknown	2
Total	14

Case 3.—A woman aged 42 years complained of coldness and numbness of the right foot 10 hours after undergoing mitral valvotomy for rheumatic heart disease. A diagnosis of right common femoral embolism was made, and at operation a femoroprofunda embolus was removed, the balloon catheter being passed easily to the ankle. Routine operative arteriography then showed that the distal popliteal artery was still occluded (*Fig.* 4 A). The balloon catheter was passed to the ankle, further thrombus was removed, and a second arteriogram visualized the distal popliteal and anterior and posterior tibial arteries (*Fig.* 4 B). The patient's subsequent postoperative course was satisfactory.

DISCUSSION

The improved results in arterial embolectomy with the Fogarty balloon catheter are largely due to the feasibility of treating the whole length of the arterial tree, removing both the embolus and its fragments and any propagated thrombus. The operation is carried out from the common femoral artery for the lower limb and from the axillary artery for the upper, irrespective of the supposed site of impaction of the embolus. It has been our experience, however, that despite careful manipulation of the catheter and its frequent passage and the establishment of free 'back-bleeding', complete patency of the arterial tree in its whole length is not always achieved. In such instances residual clot in the main artery, particularly at its bifurcation area, can readily be demonstrated by postoperative arteriography, usually dictated by a poor or unsatisfactory recovery of the peripheral circulation.

As the aim of embolectomy is to restore patency of the arterial tree, arteriography is clearly a technical facility which should be used. As the present case reports illustrate, without arteriography arterial clearance would not have been adequate in some instances despite the repeated passage of the Fogarty catheter. Without the objective evidence of clearance which arteriography produces the surgeon must therefore remain uncertain of the outcome of his operation. Alternatively, in some instances operative arteriography will also demonstrate that clearance is not possible, or in rarer instances that damage, usually to the peroneal artery, has resulted (Mavor, Walker, Dhall, and Pegg, 1972).

As reported, operative arteriography has improved our results, particularly where there has been some delay before operation. It is safe, simple, and causes little delay, and in our opinion should become an essential and routine part of the operation of arterial embolectomy.

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CARCINOMA OF COLON SIMULATING CROHN'S DISEASE

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SUMMARY

1. Three cases are described where carcinomatous involvement of the colon was mistaken for Crohn's disease of the large bowel.

2. The need to obtain histological proof is emphasized.

3. Ascitic fluid should be examined histologically in a patient diagnosed as having Crohn's disease.

4. Selective mesenteric angiography was used and is considered a valuable tool in diagnosis.

THREE patients are described who were initially diagnosed as having Crohn's disease. Subsequent investigations proved the diagnosis to be that of carcinoma in each case. The diagnosis of Crohn's disease of the colon based solely on the evidence of barium-enema examinations may be erroneous and should be confirmed by additional techniques whenever possible.

CASE REPORTS

Case 1.—A 45-year-old Greek woman was referred to St. Mark's Hospital with a 2-year history of pain in the right iliac fossa and a low backache. In 1964 for 3 months the patient had had diarrhoea, up to twenty motions daily, with occasional slight bleeding. The diarrhoea had been relieved a little by Dexamethasone given by her own physician. She had lost nearly 8 kg. in weight. There was no history of previous illness.

Examination showed an obese woman with some tenderness over a vague mass in the right iliac fossa. On rectal examination there was a stricture palpable at 6–8 cm. from the anal verge. On sigmoidoscopy the mucosa was oedematous below the stricture but was normal above it to 20 cm. A biopsy of the stricture was reported as showing non-specific, chronic, inflammatory changes only.

Barium-enema examination (*Fig.* 1) confirmed the rectal stricture; irregular strictures in the sigmoid, transverse, and ascending colon were also observed, together with 'rose-thorn' spiculations in the transverse colon and a 'cobblestone' appearance of the lateral wall of the ascending colon. Between these 'skip' areas the colon was normal. These radiological appearances were thought to be typical of Crohn's disease. A barium-meal and follow-through examination was normal. The erythrocyte sedimentation rate was 49 mm. per hour Westergren.

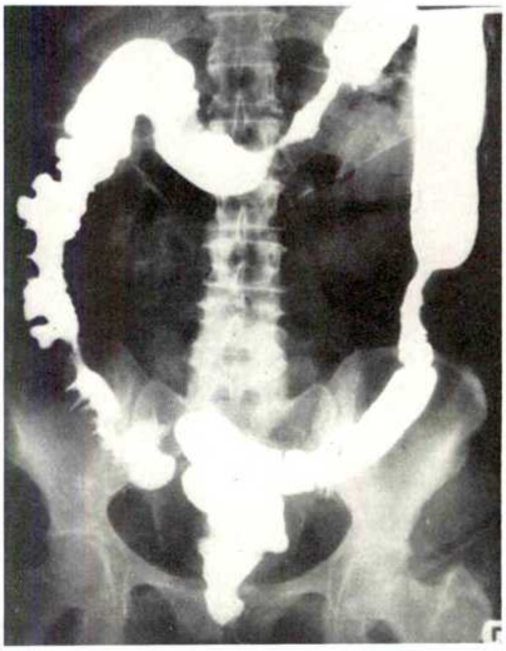

FIG. 1.—*Case* 1. Barium-enema film showing appearances typical of Crohn's disease.

A diagnosis of Crohn's disease was made.

On 3 March, 1964, a colectomy with an ileosigmoid anastomosis was carried out, the rectal stricture being dilated at the same time. It was noted that most of the colon felt rubbery. The remainder of the intra-abdominal organs, including the stomach and small intestine, appeared normal. There was no operative finding inconsistent with the diagnosis of colonic Crohn's disease.

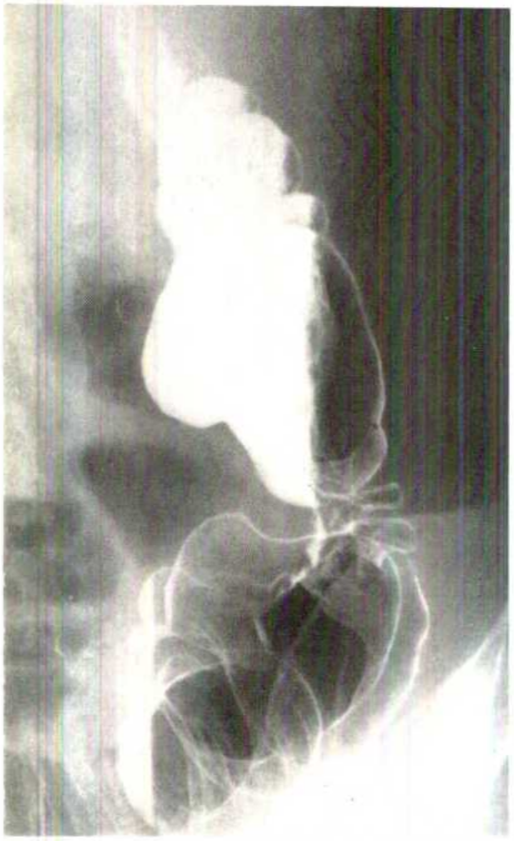

FIG. 2.—*Case* 3. Barium-enema film showing the descending colon with an asymmetrical 'purse-string' stricture.

The pathological report on the operative specimen was of multiple strictures caused by a widespread infiltration of the bowel wall by a high-grade anaplastic carcinoma with occasional signet-ring-type cells. The mucosa was not ulcerated. The stomach was suggested as the site of the primary neoplasm.

Apart from the regular use of Hegar's dilators for the stricture no further treatment was advised.

In May, 1967, a barium meal showed a small prepyloric ulcer. This slowly progressed to form a pyloric stenosis.

In April, 1968, a laparotomy was done to relieve a pyloric obstruction, which was found to be due to a carcinoma. There was no obvious tumour in the liver, but there were multiple plaques of growth throughout the abdominal cavity. A gastrojejunostomy was performed. The patient returned to Greece later in the year and no further information as to her survival has been received.

Case 2.—A 22-year-old English woman presented at another hospital with a 14-month history of low backache. For 3 months she had had lower abdominal discomfort with left-sided pain. The patient complained of colic preceding defaecation and also of intermittent constipation and diarrhoea, with the passing of some blood and mucus occasionally.

Examination of the abdomen at that time was normal, but an extrarectal mass was felt high anteriorly on rectal examination. Sigmoidoscopy showed mucosal oedema. A biopsy of the rectal mucosa adjacent to the mass showed only oedema.

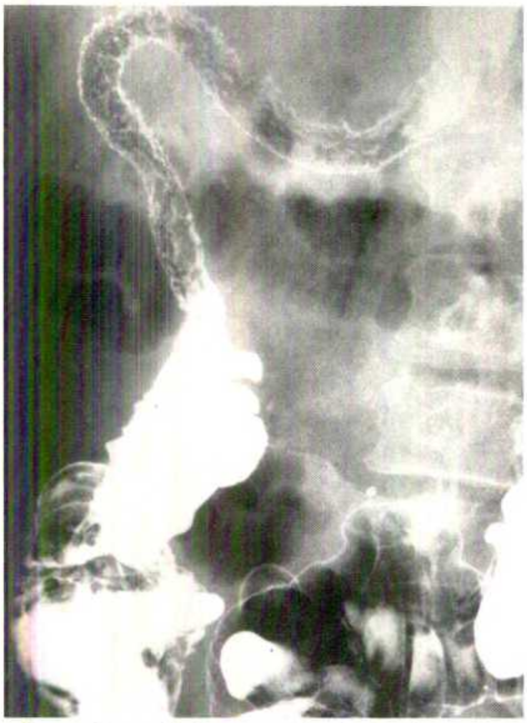

FIG. 3.—*Case* 3. Barium-enema film showing the ascending colon and part of the transverse colon with 'cobblestoning', fissure formation, and a sharp stricture.

Barium-enema examination disclosed a stricture in the sigmoid colon, 10 cm. in length, with marked fissuring consistent with Crohn's disease. The erythrocyte sedimentation rate was 28 mm. per hour Westergren.

A diagnosis of Crohn's disease was made and treatment with Salazopyrin, 0·5 g. four times a day, was commenced, but the symptoms worsened and the patient lost 10 kg. in weight. At this stage she was referred to St. Mark's Hospital.

The abdomen was slightly distended and the colon was loaded with faeces. A mass was present in the rectovaginal pouch. The rectal mucosa appeared oedematous and there was much mucus in the lumen.

Treatment with prednisolone enemata was commenced, but obstructive symptoms were developing and these necessitated a transverse colostomy on 4 Sept., 1970. Some ascitic fluid was noted and examination of the pelvis showed a circumferential stricture of the upper half of the rectum above 10 cm. The posterior fornix of the vagina was indented. Biopsies taken from the mucosa of the rectum and from the transverse colon showed no evidence of Crohn's disease. At a further examination under anaesthesia on 15 Sept. the mass was found to have extended down the rectovaginal septum, and large para-aortic lymph-nodes were palpable. Deep biopsies from the rectovaginal septum and the posterior wall of the rectum each showed infiltration by anaplastic, mucus-secreting, signet-ring cells of high-grade malignancy.

A course of 5-fluoro-uracil, 750 mg. daily intravenously for 5 days, was given prior to further surgery.

On 8 Oct. a laparotomy showed ascites and gross thickening of the sigmoid colon and rectum which were fixed in the pelvis. Many tumour masses were found; all the peritoneal surfaces were studded with mucus-secreting adenocarcinomatous nodules (a frozen-section report). The liver contained no metastases. An intraperitoneal dose of 1 g. of 5-fluoro-uracil was instilled; a further intravenous course had to be stopped after 3 days because of nausea.

The patient died 4 months after the last operation.

Case 3.—A 49-year-old English man was referred to St. Mark's Hospital with a 3-year history of postprandial, retrosternal pain with increasing anorexia and a loss of weight of 7 kg. He complained of increasing attacks of loose stools, with up to five or six motions per day.

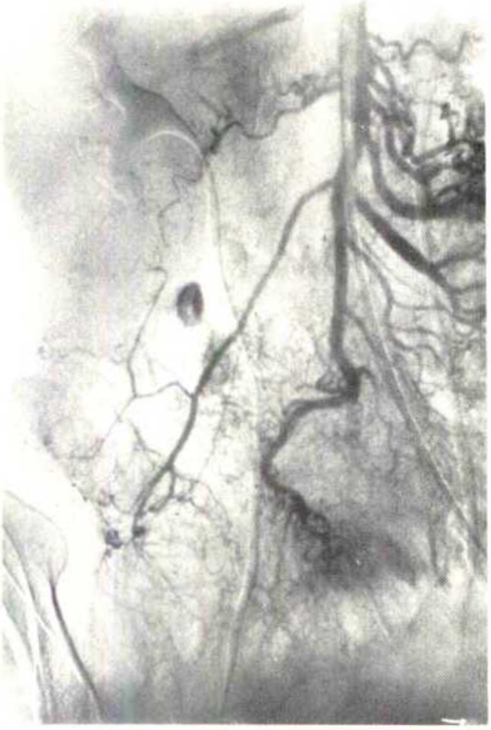

FIG. 4.—*Case* 3. Selective angiogram showing the interruption in the marginal artery supply to the ascending colon, near the lower pole of the kidney.

Examination revealed an ill man with a hard mass in the right iliac fossa. Sigmoidoscopy at that time was normal to 20 cm. A rectal biopsy was normal.

Barium-enema examination showed an asymmetrical stricture in the descending colon with a 'purse-string' appearance (*Fig.* 2). There was a second stricture in the transverse colon having both 'cobblestone' and fissure formations, and a third, very sharp stricture in the ascending colon (*Fig.* 3). These appearances were reported as being almost pathognomonic of Crohn's disease, a diagnosis of carcinomatosis having been considered and rejected as being most unlikely. The erythrocyte sedimentation rate was 25 mm. per hour Westergren. Admission was arranged with a view to resecting the colon.

In the period before admission a barium-meal and follow-through examination was done. This showed a prepyloric filling defect.

On admission an impassable stricture was found to have developed in the rectum at 14 cm. A deep biopsy of this stricture showed an intact mucosa with infiltration of the submucosa by a high-grade carcinoma, consistent with a primary in the stomach.

Laparotomy on 17 Sept., 1970, confirmed the presence of ascites with widespread intraperitoneal tumour deposits, especially in the upper abdomen and transverse mesocolon. The whole colon felt thickened.

Selective angiography was carried out, for reasons discussed later. This showed interruptions in the marginal artery supply to the colon (*Fig.* 4) such as would be expected in carcinomatosis and not with Crohn's disease.

The patient died 2 months later.

DISCUSSION

The radiological features of Crohn's disease of the colon are held to be transverse fissures, longitudinal and deep, ragged, mural ulcerations, pseudodiverticula, strictures, pseudopolypoid changes, eccentric involvement of the bowel, 'skip' lesions, and internal fistula and sinus tracks (Marshak and Lindner, 1970). There is often involvement of the terminal ileum in addition to these findings.

In each of the 3 cases described here the barium-enema appearances were consistent with a diagnosis of Crohn's disease of the colon and rectum, having many of the characteristics listed above. In addition, all 3 patients were comparatively young.

In *Cases* 2 and 3 biopsies of the rectal strictures altered the diagnosis from Crohn's disease to that of carcinoma. In *Case* 1, however, the diagnosis was made only when the colectomy specimen was examined histologically. The value of *deep* biopsies of any rectal stricture of uncertain origin is emphasized, the stricture not necessarily being of intrinsic origin.

Where no stricture is present and a rectal mucosal biopsy is either negative or inconclusive, selective angiography of the superior and inferior mesenteric arteries may prove helpful. In *Case* 3 marginal artery interruptions were easily demonstrable. These are not found in Crohn's disease and are usually due to tumour invasion. A further benefit of this examination is that it may demonstrate the presence of a tumour circulation, which is of value when considering the use of antimitotic agents.

Although cytological studies of peritoneal fluid were not carried out in any of these cases it is recommended that, when ascites is present in a patient who is considered to have Crohn's disease, paracentesis should be done and the deposit examined for malignant cells.

Acknowledgements.—Thanks are expressed to Dr. H. Herlinger for the angiograms, to Mr. H. E. Lockhart-Mummery and Mr. P. R. Hawley for permission to publish *Cases* 1 and 2 respectively, and to Mr. N. Mackie who kindly prepared the photographs.

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PROSTATECTOMY AND DEEP-VEIN THROMBOSIS

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SUMMARY

In a study of 50 patients who had undergone prostatectomy the incidence of deep-vein thrombosis was measured, using the ^{125}I-fibrinogen test. Of these, 12 (24 per cent) developed deep-vein thrombosis. This preliminary study showed that in patients who had had a transurethral resection the incidence of deep-vein thrombosis was 6·8 per cent, while in patients who had had a retropubic prostatectomy it was 47·6 per cent.

RECENT venographic studies have suggested that the incidence of deep-vein thrombosis is high after prostatectomy (Becker, Borgström, and Saltzman, 1970), and it has been reported that pulmonary embolism is the commonest cause of death after this operation (Antila, Markkula, and Iisalo, 1966). These studies have prompted the present investigation, in which an attempt has been made to determine not only the incidence of deep-vein thrombosis but also the time and site of formation of thrombi and whether any group of patients is particularly at risk.

The true incidence of deep-vein thrombosis cannot be estimated clinically because signs are unreliable in diagnosing the condition (Flanc, Kakkar, and Clarke, 1968; Negus, Pinto, Le Quesne, Brown, and Chapman, 1968). The ^{125}I-fibrinogen test, however, is an accurate method of detecting thrombosis at the earliest stage (Atkins and Hawkins, 1965; Flanc and others, 1968; Negus and others, 1968). There is no doubt that effective attempts to treat deep-vein thrombosis and to prevent pulmonary embolism are more successful when carried out early (Kakkar, Howe, Flanc, and Clarke, 1969). By using a ratemeter (Kakkar, Nicolaides, Renney, Friend, and Clarke, 1970) the technique is rapid and simple and can be used as a routine screening procedure in a large number of patients. This technique was adopted in the present study.

MATERIALS AND METHODS

Selection of Patients.—Fifty consecutive patients admitted for routine prostatectomy were studied. Their ages ranged between 55 and 92 years. Patients with clinical signs or a history of recent deep-vein thrombosis were excluded.

Transurethral resection was performed in patients with obstructive symptoms due to prostates which were small and fibrous, in those with benign glands which were estimated to weigh less than 30 g., and in those with glands which were thought to be malignant. Retropubic prostatectomy was reserved for large benign glands. All the patients had an indwelling catheter for approximately 4–5 days after operation.

Diagnosis of Deep-vein Thrombosis.—All the patients were screened by the ^{125}I-fibrinogen test, using the Pitman 235 isotope localization monitor (Kakkar, Nicolaides, and others, 1970). Human fibrinogen was obtained in the form of Antihaemophilic Factor Concentrate (Kabi). Carrier-free ^{125}I in sodium hydroxide solution with a specific activity of 120 m.c. per ml. was obtained from the Radiochemical Centre, Amersham, England. The fibrinogen was iodinated, using the 'jet iodination' method of McFarlane (1963). Each patient was given 100 μc. of ^{125}I fibrinogen intravenously the day before operation, after blocking the thyroid gland with sodium iodide. The legs were scanned 2 hours after the injection of ^{125}I fibrinogen, immediately after operation, on the day following operation, and then on alternate days. All the patients were examined daily for local tenderness in the calf or thigh and for pitting oedema at the ankle. If the radioactivity increased or if clinical signs of thrombosis developed the legs were scanned daily. On average, the legs were scanned for 9 days. Using the Pitman monitor, the radioactivity of the various positions in the legs was expressed as a direct percentage of the heart-count. Patients were considered to have deep-vein thrombosis when an increase of 20 was observed in the percentage value of radioactivity at the same place on two different days or between two adjacent sites, provided that this increase persisted for more than 24 hours (Kakkar, Nicolaides, and others, 1970).

Table I.—INCIDENCE OF DEEP-VEIN THROMBOSIS

OPERATION	NO. OF PATIENTS		
	No Deep-vein Thrombosis	Deep-vein Thrombosis	Total
Retropubic prostatectomy	11	10 (47·6 per cent)	21
Transurethral resection	27	2 (6·8 per cent)	29

Fisher's exact test: $P = 0{\cdot}0012$.

RESULTS

Twelve of the 50 patients studied developed deep-vein thrombosis, giving an overall incidence of 24 per cent. Twenty-one patients had a retropubic prostatectomy, and 10 (47·6 per cent) of these developed deep-vein thrombosis. Twenty-nine patients had a transurethral resection of the prostate but only 2 (6·8 per cent) of these developed deep-vein thrombosis (*Table I*). The difference between the two groups was significant (Fisher's exact test: $P = 0{\cdot}0012$). The distribution of various factors known to predispose to deep-vein thrombosis (Kakkar, Howe, Nicolaides, Renney, and Clarke, 1970) in the patients studied is such that these two groups are comparable (*Table II*).

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There was no significant difference between the mean age of the patients. Obese patients and patients who had a history of deep-vein thrombosis were equally distributed in the two groups. The presence of malignancy, according to previous studies (Kakkar, Howe, and others, 1970), would, if anything, predispose to thrombosis. However, none of the patients with carcinoma of the prostate developed deep-vein thrombosis after transurethral resection.

In all the 12 patients who developed deep-vein thrombosis the thrombi started in the calf. In 3 of these, thrombi were bilateral. Thrombi were detected in 9 limbs during the first 48 hours after operation, in 1 limb on the third day, in 1 limb on the fourth day, in 3 limbs on the fifth day, and in 1 limb on the seventh day after operation.

Table II.—DISTRIBUTION OF FACTORS FAVOURING DEEP-VEIN THROMBOSIS

OPERATION	MEAN AGE (years; ± S.D.)	NO. OF PATIENTS				
		Obesity	History of Deep-vein Thrombosis	History of Pulmonary Embolism	Varicose Veins	Presence of Malignancy
Retropubic prostatectomy	69·6 ± 11·7	4	1	0	0	0
Transurethral resection	64·3 ± 9·4	5	1	0	0	7

In 1 patient the thrombus extended into the popliteal vein, but in the remaining patients the thrombi were confined to the calf. In none of the patients did the thrombi extend into the femoral vein and none had overt clinical evidence of pulmonary embolism.

DISCUSSION

The findings of this preliminary study support the high incidence of deep-vein thrombosis recently reported in patients undergoing prostatectomy (Becker and others, 1970). Above all, however, they demonstrate that patients who have a retropubic prostatectomy are far more likely to develop deep-vein thrombosis (47·6 per cent).

It has already been shown that the incidence of deep-vein thrombosis is related to the severity of the operation (Kakkar, Howe, and others, 1970). Furthermore, stasis, which is believed to be an important factor in the aetiology of venous thrombosis, is less during a transurethral resection because the legs are elevated (Nicolaides, Kakkar, and Renney, 1971). In addition, the absence of pain after transurethral resection allows the patients to be more active during the early postoperative period. The facts that 60 per cent of the thrombi are first detected during the first 48 hours after operation and that they all start in the calf may be useful guides in the future for planning prevention. In the meantime the high risk of deep-vein thrombosis in patients undergoing open prostatectomy should be another factor to be borne in mind when deciding the type of operation to be performed.

Experience in the management of postoperative patients in general surgery (Murray, 1971) may well serve as a guide in the management of deep-vein thrombosis. In practice, the thrombi first develop in the calf (Flanc and others, 1968), and particularly in the soleal veins (Nicolaides, Kakkar, Field, and Renney, 1971). In only 20 per cent of these patients does the process extend more proximally into the popliteal, femoral, or iliac veins. If the thrombus is limited to the calf the risk of pulmonary embolism is, for all practical purposes, negligible, but if the popliteal and more proximal veins are thrombosed the risk of pulmonary embolism rapidly increases to about 50 per cent (Kakkar and others, 1969).

It would thus appear that, when considering the threat to life, it is those patients with a thrombus above the popliteal vein who are most at risk, and it is for these patients that early therapy is particularly important. Extension of the thrombus can be easily detected with the Pitman isotope localization monitor and treatment can then be instituted at the proper time. In the absence of an effective method of prophylaxis this screening test, combined with prompt treatment when necessary, offers the best chance of preventing pulmonary embolism. The details and results of treatment have been described elsewhere (Murray, 1971).

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SHORT NOTES OF RARE OR OBSCURE CASES

HYDATID DISEASE OF THE SPLEEN

REPORT OF AN UNUSUAL CASE

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SUMMARY

A case of an unusually large hydatid cyst of the spleen measuring 53 cm. in diameter and containing 21 litres of fluid and scolices is reported in a 40-year-old farmer. He had a brief history of nausea, intermittent vomiting, and shortness of breath.

Surgical removal of the spleen with the cyst was followed by complete recovery.

ECHINOCOCCOSIS (Batsch, 1786) is a well-known disease and it is endemic in some sheep-raising countries. The incidence in peons in Uruguay is thought to be as high as 50 per cent (Manson-Bahr, 1966). In Iceland 16·6–33 per cent of humans are infected and 28 per cent of dogs harbour the adult worms (Dungal, 1946).

The disease is common in Iran, and in some south-western areas about 4·3 per cent of sheep carcasses are infected (Khalili, 1962). At the university hospitals in Teheran an average of 120–130 cases are operated on each year (Azizi, 1966). This constitutes about 2 per cent of all the minor and major surgical operations.

Hydatid disease of the spleen is relatively rare and comprises approximately 4 per cent of the cases of hydatid disease presenting to the Pahlavi Medical Centre, University of Teheran. Jidejian (1953) reports an incidence of 3·6 per cent, while Dévé (1933) mentions 2·7 per cent.

The symptoms of these cysts in the spleen are vague. The cyst sometimes reaches an enormous size before giving rise to any complaints. Occasionally the patient has a sensation of a swelling or heaviness in the left side of the abdomen; in some other cases nausea, anorexia, and intermittent vomiting are reported.

Since January, 1966, 19 cases of echinococcosis of the spleen have been seen in the Pahlavi Medical Centre, University of Teheran. Left upper abdominal pain associated with heaviness and a sensation of swelling in this area were present in 10 cases. In 1 case, a 24-year-old housewife, the only symptom was gastric bleeding. This was found to be due to splenic vein thrombosis leading to portal hypertension and extensive varices of the short gastric veins. Two cases were discovered during other abdominal operations and the remaining patients presented with a history of nausea, anorexia, and loss of weight. One of these patients complained of constant diarrhoea. Hydatid cysts are usually slow growing. In some organs, especially in the spleen, they can reach an enormous size and be asymptomatic. It was therefore thought worth while to present a case which demonstrates how large a hydatid cyst can become before giving rise to symptoms.

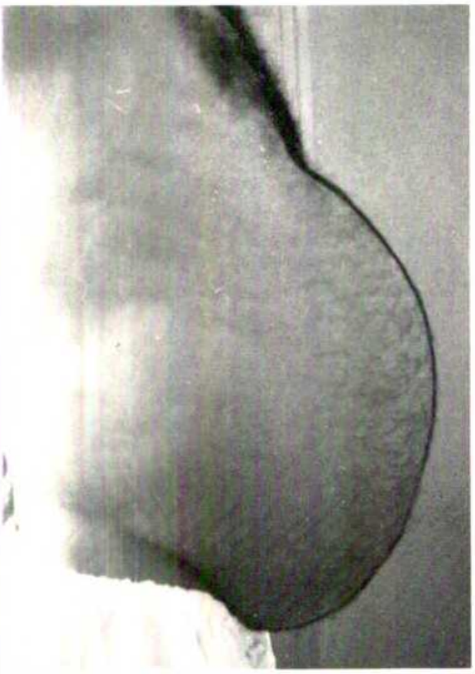

FIG. 1.—The patient before operation with an abdominal circumference of 118 cm.

CASE REPORT

A 40-year-old farmer was referred to the Surgical Unit of the Pahlavi Medical Centre for the diagnosis and treatment of a large abdominal mass. He had had no symptoms until 3 months previously. Since that time he had experienced left upper abdominal pain associated with nausea and intermittent vomiting. In the past 2 months he had noticed progressive abdominal distension and had had episodes of dyspnoea on exertion.

INVESTIGATIONS.—The patient was in a very poor general condition. His weight on admission was 96 kg., his height, 172 cm., and his abdominal circumference, 118 cm. (*Fig.* 1). His blood-pressure was 110/70, and his pulse-rate was 96. There was no clinical abnormality of the heart, lungs, or nervous system. An electrocardiogram was normal. A postero-anterior radiograph of the chest showed elevation and limited movement of both diaphragms.

The haemoglobin was 14·7 g. per 100 ml. and the peripheral white-cell count was 4600 per c.mm. (neutrophils, 70 per cent; lymphocytes, 12 per cent; eosinophils, 8 per cent; monocytes, 10 per cent). The erythrocyte sedimentation rate was 55 mm. in the first hour; the blood-urea and electrolytes were normal. An intradermal (Casoni) test was negative.

OPERATION (15 Sept., 1970).—The operation was carried out through a midline incision from the xiphoid process to the symphysis pubis. A large cyst measuring 53 cm. in diameter (*Fig.* 2) was found arising in and largely displacing the spleen. The liver showed no abnormality; the stomach, transverse colon, and jejunum were displaced and adherent to the posterior surface of the cyst. The surface of the cyst was pale, smooth, and, in some parts, calcified. Two other daughter cysts measuring 5 and 7 cm. in diameter were found attached to the omentum and were removed (*Fig.* 3).

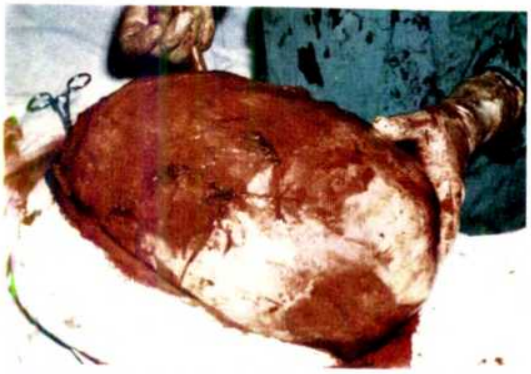

FIG. 2.—Operative view of the hydatid cyst of the spleen. White areas at the lower pole correspond to calcified portions of the cyst wall.

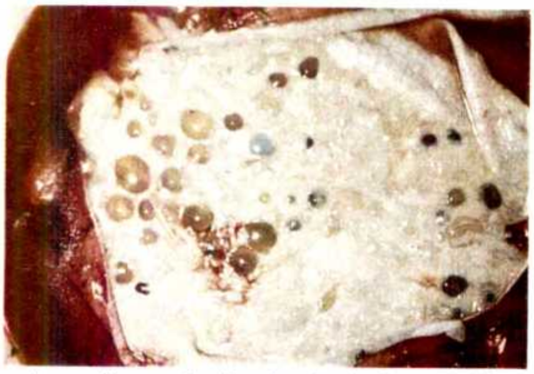

FIG. 4.—The cyst after dissection, showing the germinal layer and scolices.

An attempt to reach the splenic pedicle was soon given up. The fluid contents were then aspirated and 21 litres of a clear watery fluid containing thousands of scolices were removed (*Fig.* 4). After treating the cavity with 1 per cent formalin it was possible to remove the cyst completely with the spleen. The empty cyst weighed 9 kg.

Immediately after operation the patient developed signs of hypovolaemic shock. This was treated with transfusions of several units of blood. Subsequent recovery was uneventful and the patient was discharged from hospital 14 days after operation. His weight on discharge was 63 kg.

DISCUSSION

The hydatid cyst is the only parasitic cyst of the spleen and it is said to be twice as common as the non-parasitic variety (Fowler, 1953). Hydatid cyst of the spleen may be primary or secondary to ruptured liver cysts. It is found in about 2–4 per cent of patients with *Echinococcus* infections (Dévé, 1933; Jidejian, 1953).

In the case of a solitary large cyst or multiple cysts an enlarged spleen may be found. In other cases a mass attached to the spleen may be palpated and confused with pancreatic or omental cysts.

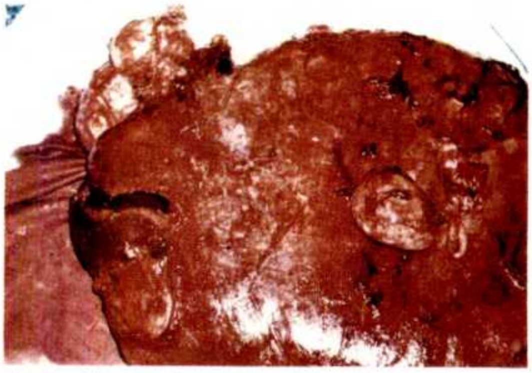

FIG. 3.—The operative specimen. Splenic tissue is seen at the lower pole and the daughter cysts at the left upper pole.

Calcification of the cyst wall which sometimes occurs may help in making a preoperative diagnosis (Neubauer and Wiandt, 1967). As in the present case, exogenous daughter cysts in the omentum are secondary. They are caused by herniation or rupture of both the germinal and laminated layers through weakened parts of the adventitia owing to intracystic pressure (Manson-Bahr, 1966).

Rupture of a splenic hydatid cyst can occur spontaneously caused by intracystic pressure or trauma. This can lead to severe shock, which is probably anaphylactic, and dissemination throughout the peritoneal cavity.

Symptoms vary with the size of the cyst. Small or uncomplicated hydatid cysts may be silent, while large cysts produce pressure on the neighbouring organs, leading to abdominal discomfort, a dull ache in the left upper quadrant, nausea, vomiting, and sometimes diarrhoea or obstipation.

The intradermal (Casoni) test is a valuable diagnostic procedure. It is positive in 90 per cent of hydatid infections (Dew, 1928); a positive reaction half an hour after intradermal injection is said to indicate a young cyst, whereas a reaction after 48 hours is often found in an older or biologically inactive cyst (Neubauer and Wiandt, 1967).

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SUBCUTANEOUS RUPTURE OF THE BREAST: A SEAT-BELT INJURY

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SUMMARY

Subcutaneous rupture of the breast caused by a car seat belt is reported. The patient was 7 months pregnant, and there was difficulty in suppressing lactation; the management of this problem is discussed.

CASE REPORT

THE patient, aged 33 years, was a front-seat car passenger, wearing a lap-diagonal seat belt, when the car in which she was travelling was involved in a collision at moderately high speed. She sustained minor lacerations of the legs, a dislocation of the left first metacarpophalangeal joint, and abrasions and bruising of the chest and right breast owing to pressure of the diagonal strap of the seat belt; the line of the strap shows clearly in *Fig.* 1.

Twenty-four hours after the accident the patient miscarried; a 7-day course of stilboestrol (10 mg. t.d.s.) was given to suppress lactation. Engorgement of the left breast subsided satisfactorily, but the damaged right breast remained tense and tender; it was aspirated on the fifth day postpartum and a mixture of blood and milk was obtained. Aspiration was repeated on the eleventh day (500 ml.) and on the fifteenth day. Because of continued reaccumulation of milk a Zimmer suction drain was inserted on the twenty-first day; the daily aspirate was 300–500 ml. until the drain was removed on the thirtieth day. Milk continued to collect between the two halves of the breast and to drain from the stab incision. A further 5-day course of stilboestrol was given, and the effect of magnesium sulphate and of water deprivation was tried. Infection occurred and a mixture of milk and pus was evacuated on the forty-sixth day; milk continued to be secreted, as much as 250 ml. being expressed at one time.

At operation 7 weeks after the injury the breast was explored through a 5-cm. incision in the submammary groove. The breast tissue was found to be completely split in two and about four-fifths of the ducts were avulsed from the back of the nipple. The two halves of the breast were coapted by through-and-through nylon sutures held by aluminium stops, and a corrugated drain was left in place; firm bandaging and strapping were applied. The sutures were tightened on two occasions as the breast became less swollen, and pressure was maintained by Elastoplast strapping over adhesive sponge. The sutures were removed on the tenth postoperative day, by which time the drainage of milk was much reduced. Discharge ceased on the eighteenth postoperative day, 11 weeks after the original injury.

The breast continued to involute satisfactorily although it remained moderately grooved. A simple tension cyst 1½ cm. in diameter was removed from the peripheral part of the upper portion of the breast 8 months after the injury. Further surgery to improve the appearance of the breast is under consideration.

DISCUSSION

The common measures used to suppress lactation—stilboestrol, water deprivation, and firm bandaging—were not effective in this patient's damaged breast. Stilboestrol is not an effective agent for stopping lactation, failure of suppression or subsequent reinitiation of lactation not uncommonly following its use. The main effect of stilboestrol is in the reduction of pain and turgidity of the breast when suckling is discontinued, and there is evidence that it will even promote lactation if the flow of milk from the breast is encouraged. The splitting of the breast tissue and its avulsion from the ducts prevented the build-up of intragland pressure, and simple bandaging was ineffective as the two halves were merely held apart by it. The aspiration of the cavity between them is a measure which could be expected to encourage continued secretion. The situation is analogous to the production of witch's milk by squeezing the breasts in an infant, or paralactation induced by sucking in adult males or females outside the influence of pregnancy; with repeated emptying of the breasts full lactation can be

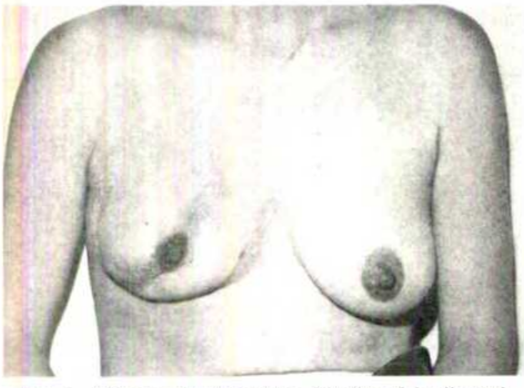

FIG. 1.—Eleven weeks after injury. The line of the diagonal strap of the seat belt can be clearly seen.

established (Bonser, Dossett, and Jull, 1960; Dossett, 1960).

Although it cannot be claimed that the drawing together of the two halves of the breast with sutures and the constant application of firm pressure were entirely responsible for stopping lactation in this patient—time and infection may well have played a part—it is suggested that this is a logical approach in this type of injury. The result would be similar to firm bandaging applied to the normal lactating breast which is a known effective measure in the suppression of lactation.

This type of procedure could reasonably be carried out soon after injury in any similar case. The use of adhesive sponge considerably aided the application of firm pressure and it could be peeled off with only moderate discomfort when the breast was restrapped as it became smaller.

It is of interest that on analysis of the breast secretion 7 days before drainage ceased the report was: 'Only a trace of lactose. This indicates that it is a true milk, but one which is rapidly reverting to colostrum.'

Acknowledgement.—I am indebted to Dr. J. S. Dossett for his advice and encouragement in the treatment of this patient.

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RUPTURED ANGIOMATOUS SPLEEN PRESENTING AS A SEVERE COAGULATION DEFECT

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SUMMARY

A case is described in which spontaneous rupture of an angiomatous spleen presented with an acute disorder of blood coagulation. Splenectomy was performed after successful correction of the coagulation defect by the administration of blood and blood-products. The presence of amyloidosis associated with myeloma may have increased the liability of the spleen to rupture. Indentation of the right lobe of the liver by the lower ribs produced a misleading appearance of the hepatic scintiscan.

THE association of a haemorrhagic diathesis with a large haemangioma was first described by Kasabach and Merritt in 1940. A number of cases have since been recorded and reviewed and the coagulation disorder has been shown to be a defibrination syndrome, sometimes associated with increased fibrinolysis (Thompson and Umlauf, 1964; Thatcher, Clatanoff, and Stiehm, 1968). The majority of these reports, however, were of infants or children with a long-standing history of bruising or a bleeding tendency where elective investigation of the coagulation process was possible and no great urgency was necessary in the correction of the coagulation defect. The present report describes the treatment of an adult presenting with an acute coagulation disorder associated with rupture of an angiomatous spleen.

CASE REPORT

The patient was an active 60-year-old married woman who had no significant medical or drug history. Twelve hours before her admission to hospital she had noticed bruising of both ankles. There had been no trauma. The bruising had spread up the legs and had also developed on the upper arms and shoulders. Some 4 hours after the bruising had first been observed the patient was aware of nausea and increasingly severe right-sided upper abdominal pain. There was no other significant history.

The patient was admitted in a state of hypovolaemic shock with a systolic blood-pressure of 65 mm. Hg. There was tenderness in the right hypochondrium, with no guarding. The bowel-sounds were normal and there were no intra-abdominal bruits. Plain radiographs of the abdomen were unrewarding and blood examination revealed a normal red-cell morphology, the presence of platelets, and normal total and differential white-cell counts. Coagulation studies (*Table I*) revealed a severe consumptive coagulopathy with no evidence of excessive

Table I.—THE BLOOD-COAGULATION STUDIES

TEST	BEFORE TREATMENT	BEFORE OPERATION	4 WEEKS AFTER OPERATION
Whole-blood clotting time (min.)			
Glass	11	6	6
Silicone	24	14	10
Clot lysis	Marked	Moderate	—
Clot retraction	Good	Good	—
Partial thromboplastin time (sec.)			
Normal	32·5	32·5	36·5
Patient	196·0	32·5	33·25
Normal : patient	80·0	31·5	35·25
Prothrombin consumption index	30 sec. 60 sec.	30 sec. 60 sec.	30 sec. 60 sec.
Plasma	18 30	11 12	7 10
Serum	20 25	68 74	46 44
	=90 per cent	=16 per cent	=16 per cent
Euglobulin lysis time (min.)	>30	>30	>30
Fibrinogen titre			
Control	1/64	1/64	1/128
Patient	1/16	1/64	1/64
Platelet count	50,000	190,000	295,000
Prothrombin ratio	1·2	1·5	1·0

fibrinolysis. Because of the gravity of the patient's condition transfusion was initiated before these results were available, with initial clinical improvement, but there was increasing distension in the abdomen and it was thought that there was continued intra-abdominal bleeding. A total of 1 litre of fresh frozen plasma, 3 litres of fresh blood, and 4 g. of fibrinogen was given over a period of 9 hours, after which the coagulation state had returned to normal and it was possible to proceed to laparotomy, through a right paramedian incision. Three litres of blood and clot were removed from the peritoneal cavity and the source of blood-loss was found to be a tear on the phrenic surface of the spleen which was enlarged and of a dark-purple colour. The liver was moderately enlarged and smooth. Splenectomy was therefore carried out through a left subcostal incision. The patient made an uncomplicated recovery from the operation.

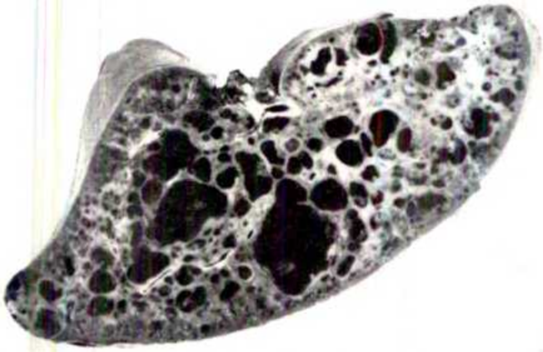

FIG. 1.—Cut surface of the spleen showing the numerous blood-filled spaces.

Pathological examination of the spleen showed that it was of the usual shape, moderately enlarged (385 g.), and contained a poorly defined haemorrhagic area in the region of a capsular laceration. The cut surface (*Fig.* 1) contained abundant blood-filled spaces, some of which measured between 1·0 and 1·5 cm. in diameter. Microscopic examination showed both cavernous and capillary types of vessel. The usual division into red and white pulp was lost and no Malpighian corpuscles were observed. Congo-red and thioflavine-T stains for amyloid showed subintimal deposits within the large vessels and a complete infiltration of the capillary walls. The vessels were devoid of thrombus; sections stained by the acid picro-Mallory and Martius yellow–soluble blue techniques (Lendrum, Fraser, Slidders, and Henderson, 1962) showed remarkably little fibrin.

Plasma electrophoresis showed an abnormal band in the fast γ-globulin region, and the bone-marrow contained an increased number of plasma-cells and some abnormal forms. There was no Bence-Jones protein in the urine, but a radiograph of the bony skeleton revealed collapse of the twelfth thoracic vertebral body and loss of the trabecular pattern in the first lumbar vertebra. These features suggest that the amyloidosis was associated with myeloma.

Postoperatively a disturbing feature was the progressive enlargement of the liver, which 3 weeks after the operation was firm, smooth, and clearly palpable 6 cm. below the right costal margin. The hepatomegaly was confirmed by a technetium-colloid scintiscan which suggested reduced uptake in the lateral aspect of the right lobe of the liver (*Fig.* 2). Abdominal aortic angiography showed no evidence of a vascular abnormality within the liver. In view of the finding of a rapidly enlarging liver and the possibility of a lesion in the right lobe further exploration was indicated.

At laparotomy there was now gross enlargement of both lobes of the liver and biopsies were taken. The lateral surface of the liver was clearly indented by the lower ribs and costal cartilages and it was deduced that this anatomical abnormality accounted for the apparent absence of uptake of isotope in this region of the liver. Histological examination of the liver biopsies showed extensive amyloid deposits forming a thick hyaline layer in the subendothelial spaces adjacent to the sinusoidal lumen.

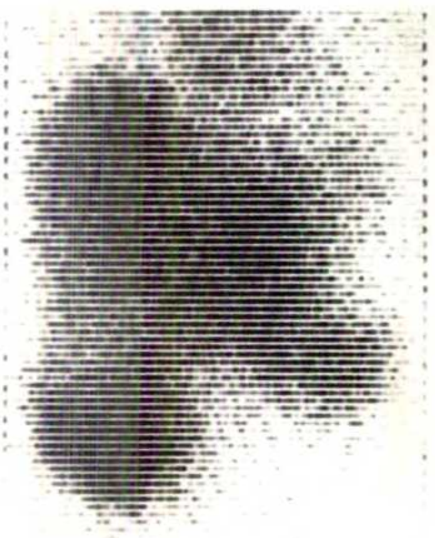

FIG. 2.—Technetium-colloid scintiscan showing reduced uptake in the lateral aspect of the right lobe of the liver.

DISCUSSION

There are several interesting and rather unusual features in this case. Although rupture is a recognized complication of splenic angiomatosis, the number of recorded cases is small (Husni, 1961). The usual clinical presentation is as an acute abdominal emergency and there appears to be no previous report of an associated abnormality of blood coagulation. Haemorrhagic shock, myeloma, and amyloidosis have all been associated with the defibrination syndrome (Hardaway, Brewster, and Elovitz, 1966; Rosner and Ritz, 1966), but in the patient described here spontaneous bruising undoubtedly preceded the development of haemorrhagic shock by several hours, and the return to a normal coagulation state after initial treatment and splenectomy suggests that the myeloma and amyloid were not primarily responsible. The patient is thus believed to have exhibited an acute form of the coagulation disturbance described with large haemangiomata.

It is generally agreed that complete surgical excision of an angioma is the most successful means of correcting the associated coagulation abnormalities. However, the successful initial correction of the coagulation disorder in this case by the administration of blood-products alone is in contrast to previous reports of defibrination associated with angiomata where it is suggested that anticoagulation with heparin (Hillman and Phillips, 1967) or phenindione

(Blix and Jacobsen, 1963) is required. Even so, complete correction has not always been achieved. Hillman and Phillips (1967) suggest that some danger may be associated with the use of blood-products alone since an induced imbalance of coagulation and lysis may result in rapid clotting within the angioma and infarction of the organ, but in spite of the considerable transfusion no infarction or clot formation was found in the spleen of our patient. Thus there is no evidence that the administration of blood products alone was potentially hazardous in this case.

The association of amyloidosis with myeloma is well known (Cohen, 1967) and this aspect of the case requires no further comment. However, it is possible that the deposition of amyloid in the spleen of this patient may have increased its susceptibility to trauma and it is notoriously difficult to exclude minimal trauma in cases of 'spontaneous' rupture of the spleen. The case also provides a convincing illustration of the rapidity with which hepatic enlargement due to amyloid deposition may occur, and in this context it is of interest that splenectomy appears to facilitate the experimental production of amyloidosis in animals (Calkins, Cohen, and Larsen, 1960). The unusual and rather misleading appearance of the scintiscan from the large liver of this patient emphasizes the need to take anatomical variations into account in the interpretation of such investigations.

Acknowledgements.—We are grateful to Mr. T. J. McNair and Professor R. H. Girdwood for permission to report this case.

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VISCERAL NEUROFIBROMATOSIS

AN UNUSUAL CAUSE OF OBSTRUCTIVE JAUNDICE

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SUMMARY

A case of visceral neurofibromatosis presenting as obstructive jaundice is described. Laparotomy revealed an ampullary tumour which was presumed to be malignant. A palliative cholecystojejunostomy was performed but death occurred 10 days postoperatively as a result of obstructive jaundice. At necropsy the ampullary tumour was found to be a benign neurofibroma.

THE association of visceral lesions with von Recklinghausen's neurofibromatosis is an uncommon but nevertheless a well-recognized entity. Perhaps many more cases remain unidentified because the visceral lesions do not produce clinical symptoms. The more commonly described presenting clinical features are chronic anaemia (Burton and Fitzgerald, 1970), gastro-intestinal bleeding, atypical dyspepsia and abdominal pain, a palpable mass, or bowel obstruction which may be due to intussusception, intraluminal encroachment, external compression, annular stenosis, or even volvulus (Logan, 1964; Lukash and Johnson, 1969; von Vroonhaven, 1970). One case of perforation due to an intestinal neurofibroma has been described (Warshauer and Nelson, 1953). Recently we have seen visceral neurofibromatosis which manifested itself as obstructive jaundice. This appears to be the first recorded case of such a combination.

CASE REPORT

The patient was a 61-year-old female who had attended hospital on a number of occasions. Her first admission in 1949 was for hysterectomy because of menorrhagia. She was admitted in 1950 for amputation of the right little finger following traumatic rupture of the flexor and extensor tendons.

In 1959 she was investigated as an in-patient for her complaint of multiple small skin nodules over the chest and arms and vague ill health accompanied by a productive cough. Her skin showed raindrop freckling with numerous soft subcutaneous nodules, several of which were pedunculated. Radiology showed a sliding hiatus hernia and unresolved pneumonia which responded to treatment. A diagnosis of cutaneous neurofibromatosis was made. There was no family history of von Recklinghausen's disease.

Her next admission in 1963 was for drainage of an appendix abscess, when she was advised that further surgery would be necessary. She failed to report back until 1965 when elective appendicectomy was carried out. On both occasions she had postoperative basal pneumonic consolidation.

In 1970 the patient presented with jaundice, epigastric pain, anorexia, and recurring bouts of diarrhoea of several weeks' duration. She had lost 19 kg. in weight over a period of 5 months. On examination she was deeply jaundiced and the liver was enlarged to three fingers below the right costal margin. There was a firm painless epigastric mass. Von Recklinghausen skin lesions were noted together with scratch marks over the abdomen and both arms. Liver-function tests indicated obstructive jaundice. Occult blood was found in the stools and there was an *Escherichia coli* urinary infection. The peripheral blood picture revealed a very marked neutrophil polymorph leucocytosis (24,000–30,000 per c.mm.) but no anaemia. Barium studies were unhelpful. A provisional diagnosis of carcinoma of the head of the pancreas was made and laparotomy was carried out.

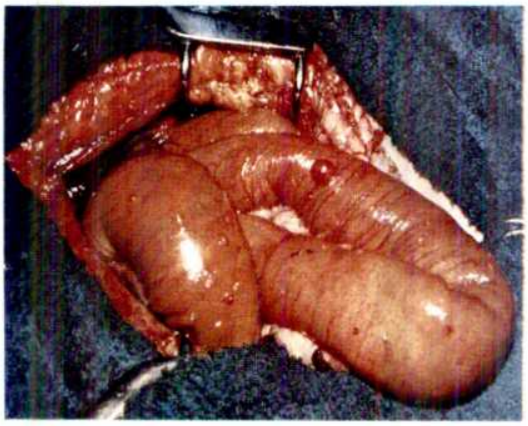

FIG. 1.—Jejunal neurofibromatosis at operation.

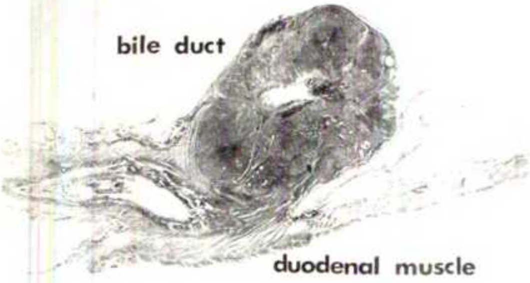

FIG. 3.—Low-power view of neurofibroma of ampulla of Vater. H. and E. (× 3.)

OPERATION.—The abdomen was opened through a right paramedian incision. An enlarged green liver with a greatly dilated common bile-duct and a distended gall-bladder were found. Approximately twelve discrete nodules were present along the proximal small bowel (*Fig.* 1) and a large irregular-shaped mass obstructed the duodenal ampullary region. The lymph-nodes alongside the duct and in the porta hepatis were enlarged.

It was considered that there had been malignant change in a neurofibromatous lesion; palliative cholecystojejunostomy was performed, a lesion in the small bowel was biopsied, and the abdomen was closed without drainage.

The patient's postoperative course was poor and apart from slight improvement in the degree of jaundice she gradually deteriorated, despite supportive therapy, and died 10 days later.

BIOPSY OF BOWEL TUMOUR.—The specimen submitted for histology was a discrete, smooth nodule, 10 mm. in diameter. The cut surface was pale yellow with a slightly whorled appearance.

Microscopy showed a simple neurofibroma which was not encapsulated and was incompletely surrounded by smooth muscle.

NECROPSY REPORT.—Externally there was deep jaundice, diffuse freckling of the skin, and numerous small polypoid subcutaneous nodules on the trunk, thighs, and arms.

The relevant findings were confined to the abdominal cavity. There was a generalized peritonitis with a bile-stained exudate in the peritoneal cavity. Along the duodenum and antimesenteric border of the upper small bowel there were approximately twelve small discrete tumours, the largest being 15 mm. in diameter. Most of them formed polypoid protrusions on the serosal surface. Proceeding distally along the bowel the lesions appeared with decreasing frequency and there was none in the distal small or entire large bowel. A 25-mm. diameter submucosal nodular tumour protruded into the duodenum around the ampullary opening, extending through the duodenal muscle to form a similar-sized nodular mass on the adventitial surface with the distal common bile-duct lying to the left lateral side. The bile-duct was dilated and contained submucous gas bubbles. The lymph-nodes in this area were enlarged. The gall-bladder was thick-walled, congested, and friable. The cholejejunostomy anastomosis appeared intact but was separated easily during handling. The liver (2460 g.) was enlarged, deeply bile-stained, soft, and crepitant. Both the spleen and the pancreas were soft and focally cystic. The kidneys were deeply bile-stained.

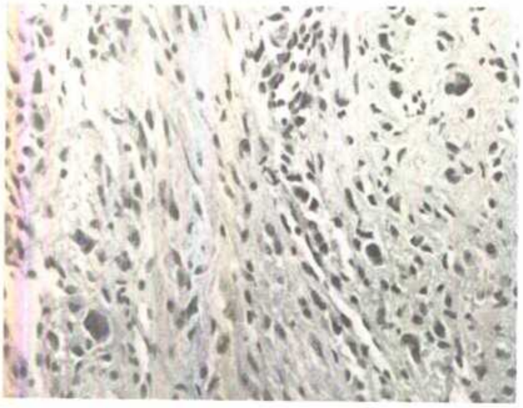

FIG. 2.—High-power view of area of neurofibroma showing several pleomorphic nuclei. H. and E. (× 134.)

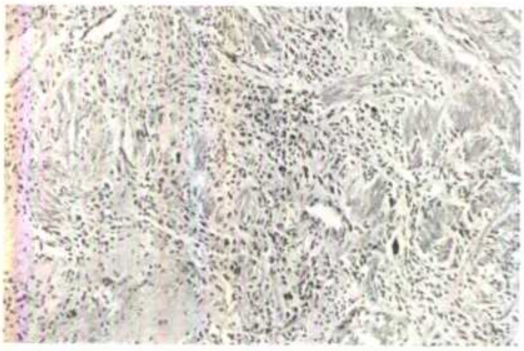

FIG. 4.—Low-power view showing neurofibromatous tissue intermingled with ampullary smooth muscle. H. and E. (× 92.)

There were no tumours in other organs.

HISTOLOGY.—The ampullary tumour, a neurofibroma, was partially encapsulated with several markedly sclerosed lobules. Small groups of ganglion cells were included in the submucosal tumour margin. Some areas showed a prominent vascular pattern with thrombus in many of the vascular channels. The tumour was very oedematous and contained a mild chronic inflammatory infiltrate. The cellular pattern was variable with some areas of attempted cellular regimentation and others where nuclear atypism was marked (*Fig.* 2). No mitotic figures were found.

The course of the bile-duct through the ampullary tumour was traced by means of serial sections. It was found in the centre of the submucosal portion of the tumour (*Fig.* 3). The mucosal lining was completely autolysed; some mucus glands and a chronic inflammatory infiltrate were present in the submucosa, and immediately subjacent to this the tumour intermingled with the ampullary muscle (*Fig.* 4). In the underlying duodenal muscle coat microscopic neurofibromatous nodules were studded at intervals along the myenteric plexus, and in sections showing the main tumour in this layer, direct continuity could be demonstrated between large abnormal nerves, the neurofibromatous nodules arising in the myenteric plexus, and the main ampullary tumour. Using Glees and Marsland's method, small numbers of nerve-fibres were demonstrated running through the tumour.

The oesophagus contained a microscopic neurofibroma at its lower end. Histology of one of the ileal nodules showed a poorly circumscribed neurofibroma which contained several small groups of ganglion cells. Random blocks of stomach and large bowel showed no neural abnormality.

Microscopically the kidney showed proximal tubular necrosis.

A section from a skin nodule showed a discrete but unencapsulated tumour with plexiform neuromatous and neurofibromatous components; pilar smooth muscle and sweat glands were included in the tumour. Microscopic neurofibromatous nodules and large abnormal nerves were present in the surrounding dermis.

DISCUSSION

The incidence of malignant degeneration in visceral neurofibromatosis is difficult to assess but it has been reported to be as high as 15 per cent (Levy and Khatib, 1960). At laparotomy in the present case the ampullary tumour was thought to have undergone malignant change because of its relatively large size and its irregular, craggy shape. Histologically the tumour was not discrete but merged and became closely intermingled with normal structure of this area, this being characteristic of von Recklinghausen's disease (Willis, 1967).

The number of simple duodenal neurogenic tumours which have been recorded as giving rise to clinical symptoms is very small. Three were submucosal polypoid ganglioneuromas (Dahl, Waugh, and Dahlin, 1957; Gemer and Feuchtwanger, 1966; Goldman, 1968), one of which had associated cutaneous neurofibromatosis; all were situated several centimetres proximal to the ampulla of Vater. Two cases of duodenal neurofibroma have been described: one presented as a gastro-intestinal haemorrhage (Curran and Forsythe, 1961) the second, as in the present case, had cutaneous neurofibromatosis and preoperatively was diagnosed on the basis of clinical and radiological findings as carcinoma of the head of the pancreas (von Vroonhaven, 1970). It differed from the present case in that the clinical presentation was of a high bowel obstruction, and at operation the lesion was situated about 3 cm. distal to the ampulla of Vater.

Only 1 case of obstructive jaundice due to a benign neurogenic tumour has previously been described (Oden, 1955). This was a neurolemmoma arising in the extraduodenal portion of the common bile-duct; there were no features of generalized neurofibromatosis. Non-epithelial tumours of the duodenal ampulla are rare (Nitshe and Suckie, 1947; Edmondson, 1967), and in particular no previous ampullary neurofibroma has been described.

The distribution of the visceral lesions in this patient was also unusual. The terminal ileum followed by the stomach are commonly cited as being most frequently involved (Logan, 1964; Mazare, Champetier, Micoud, and Verdier, 1968). Recorded lesions in the oesophagus are very rare; Russell and Rubinstein (1970) mention 1 case. Visceral ganglioneuromatosis is an uncommon association of von Recklinghausen's neurofibromatosis.

Acknowledgement.—We are grateful to Mr. A. Litton, F.R.C.S., for permission to publish clinical details.

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REVIEWS AND NOTICES OF BOOKS

Management of Constipation. Edited by SIR FRANCIS AVERY JONES, C.B.E., M.D., F.R.C.P., and EDMUND W. GODDING, F.P.S. 8⅞ × 6 in. Pp. 197 + xi. 1972. Oxford: Blackwell Scientific Publications. £2.

THIS excellent paperback is the first serious attempt at a comprehensive treatment of constipation since Sir Arthur Hurst's monograph of over fifty years ago. Constipation appears both as a primary disorder (simple constipation) and as a symptom secondary to a large number of medical and surgical conditions. This presents obvious difficulties in producing a coherent account of its many manifestations. That this has been achieved is due to the physiological approach which has been maintained throughout this book—an approach which must make a special appeal to surgeons.

The book proceeds logically from a description of normal colon physiology (A. N. Connell) to therapeutic agents (E. W. Godding), diagnosis (J. M. Hinton), and constipation management in adults (F. Avery Jones), in paediatrics (T. E. Oppé), in geriatrics (A. N. Exton-Smith), and in obstetrics (D. E. Burgess).

Much important new knowledge of colon physiology and the pharmacology of drugs has been gained during recent years and this has had a marked influence on the character of this book. However, it is clear that there is still a long way to go before a completely scientific basis of bowel movement can be laid down. The alimentary canal has to function, not only as a digestive, absorptive, and excretory organ, but also as a modulator and regulator of the diverse exogenous and endogenous stimuli, and of the many insults, to which it is constantly subjected. The mechanisms involved are, of necessity, highly flexible and complex and are seen as part of the homeostatic requirements of the body as a whole. It is not surprising that motility studies, which now employ a wide range of techniques, have only partly succeeded in evaluating the components of intestinal neuromuscular activity.

In the chapter on therapeutic agents an analytical method based on physiological principles and known pharmacology has produced order out of chaos. In the case of laxatives the indictment of a number of laxatives, some old, some new, is forthright and fairly stated. As would be expected, Senokot is revealed as the most physiologically acceptable of the chemical laxatives.

The section on per rectum evacuants is timely and the condemnation of soap enemata will be strongly supported by proctologists; their total prohibition would seem overdue.

This book is the most authoritative statement on the subject of constipation which has yet appeared in English or in any other language, and with its publication the dea of constipation as no more than a minor ailment should disappear. There are few who will not find something of value in it, including medical, nursing, and pharmaceutical practitioners. It has a special place in postgraduate teaching.

Conférences de Séméiologie Chirurgicale. Vol. 5. By JEAN MOUÏEL, Paris, and CLAUDE REGENSBERG, Paris. 10¼ × 8 in. Pp. 225. Illustrated. 1971. Paris: Baillière et Fils. No price given.

THIS synopsis is meant to serve as a guide while preparing for examinations in surgery as part of the French medical curriculum. It is a kind of programmed instruction, bringing together step by step the information required. The layout is most professional and the text very expert, admitting an impressive amount of factual knowledge within a comparatively limited space. Twelve volumes have been planned, the present one being the fifth to appear. It deals with gynaecology and the mammary gland, the emphasis being on the pathology and the signs and symptoms. The illustrations are limited in number and are rather mediocre. The student wishing to acquire insight and wanting to sharpen his wits will find this book of little use, but he who has to 'cram' will find that it has a great deal to offer. The language is so concise that a limited knowledge of French is sufficient.

Handbook of Orthoptic Principles. Second edition. By G. T. WILLOUGHBY CASHELL, M.B., B.S. (Lond.), F.R.C.S. (Edin.), F.R.C.S. (Eng.), Reading, and ISOBEL M. DURRAN, D.B.O.T., Oxford. 8½ × 5½ in. Pp. 136 + x. Illustrated. 1971. Edinburgh: Churchill Livingstone. £1·50.

THE second edition of this useful paper-back has been very carefully revised, and it will retain its place as a most useful handbook for all those who have to undertake the treatment of the various forms of squint. There can be no doubt that this small book fulfils its purpose admirably. The illustrations are well chosen and are of a high order. The index is new and complete.

Pädiatrischer EKG-Atlas. Second edition. By J. STOERMER, Göttingen, and W. HECK, Bremen. 11½ × 8¼ in. Pp. 316 + xi, with 256 illustrations. 1971. Stuttgart: Georg Thieme Verlag. DM.130.

THIS second edition of an atlas relating to the paediatric electrocardiogram has been totally revised. The authors have illustrated all standard congenital abnormalities and acquired diseases of the cardiovascular system in relation to the electrocardiogram, and there are numerous case histories to illustrate the electrocardiographic findings.

The book is beautifully illustrated by serial electrocardiograms and is well printed. There is a very extensive bibliography and the quality of the illustrations is excellent throughout.

This volume should be of considerable interest to cardiologists and cardiac surgeons involved in paediatric cardiac surgery, but the text could be enhanced by the comments of a paediatric cardiac surgeon and by the addition of radiological illustrations.

A Text-book of X-ray Diagnosis. Fourth edition. Vol. 6. Edited by S. COCKRANE SHANKS, C.B.E., M.D., F.R.C.P., F.F.R., Consulting Radiologist, University College Hospital, London, and PETER KERLEY, C.V.O., C.B.E., M.D., F.R.C.P., F.F.R., D.M.R.E., Consulting Radiologist, Westminster Hospital and National Heart Hospital, London. 9⅜ × 7⅛ in. Pp. 859 + xvi, with 904 illustrations. 1971. London: H. K. Lewis. £11.

THE new Volume 6 of this great work is devoted to bones and joints, and consists of 11 parts.

Part 1 is concerned with the normal bones and joints, including the spinal column. The radiographs are of a high quality.

Part 2 deals with the important problem of the general pathology of bone. The photomicrographs illustrating the various pathological conditions of bone could not be bettered.

In Part 3 the congenital deformities of bones and joints come under review, while in Part 4 the traumatic conditions of these structures are considered.

Part 5 deals with the inflammatory conditions of bones and joints and the illustrations in this section are excellent.

Part 6 is devoted to the important condition of osteochondritis, while Part 7 deals with static and paralytic lesions of bones and joints.

Part 8 is concerned with tumours and cysts and is well set out and illustrated.

In Part 9 the constitutional diseases of bones and joints come under review.

Part 10 is concerned with the soft tissues and includes calcification and ossification of the soft tissues.

Part 11 is devoted to the localization of foreign bodies.

This comprehensive work by the cream of British radiologists is a great credit to British medicine. When it is considered that the first edition appeared just before the Second World War and was reprinted five times the usefulness of this work is evident.

As a reference volume this book could not be bettered.

Actions of Alcohol. Vols. 1 and 2. By HENRICH WALLGREN, Helsinski, and HERBERT BARRY, III, Pittsburgh. 9 × 7 in. Pp. 870 + xxvi, with 18 illustrations. 1970. Amsterdam: Elsevier Publishing Company. $55.50.

THIS two-volume work is a comprehensive review of the experimental work on the effects of alcohol on the living organism, based on an integration of knowledge in the fields of biochemistry, physiology, and psychology.

Volume 1 details the biochemical, physiological, and psychological effects of alcohol (ethyl alcohol), while volume 2 is devoted to the chronic and clinical aspects.

Volume 1 deals with a wide variety of subjects, including alcoholic beverages, lethal blood levels, temperature regulation, and the metabolism of ethanol. At the end of each chapter there is a summary and a very full list of references.

Volume 2 is concerned with the detectability of alcohol, physical dependence, joint action of drugs and alcohol, characteristics of alcoholics, and the chronic effects and clinical aspects of alcohol.

This work is a compilation of international research and it will appeal to scientists in all branches of alcohol research. As a reference work it could not be bettered.

An Atlas of the Anatomy of the Ear. By BRANISLAV VIDIĆ, S.D., St. Louis, and RONAN O'RAHILLY, M.D., Wayne State. 9½ × 6½ in. Pp. 110, with 50 illustrations and 50 additional colour slides. 1971. London: W. B. Saunders Co. Ltd. £10·20.

THERE can be little doubt that the anatomy of the middle and internal ear is difficult to visualize for the average student and practitioner. Now that operations are frequently performed on the middle ear, it is important that the anatomy of this part of the human body should be understood. This atlas with its 50 colour slides (2 × 2 in.) and a small viewing box contributes enormously to the easy understanding of the middle and inner ear.

A black-and-white drawing with levels on the various structures is supplementary to each colour slide. This enables the viewer to see the relationship of the various anatomical structures.

The book contains an author index as well as a subject index. There is also a glossary of eponymous terms.

This is a useful atlas for students and also for all those who are contemplating becoming aural surgeons.

Critical Surgical Illness. Edited by JAMES D. HARDY, M.D., F.A.C.S., Mississippi. 10 × 7 in. Pp. 679 + xv, with 206 illustrations. 1971. London: W. B. Saunders Co. Ltd. £11·90.

THIS is a book for surgeons, for the various contributors, all experts in their own surgical field, discuss in detail the treatment of certain conditions and especially the post-operative treatment.

The 30 comprehensive chapters range over a large number of surgical conditions, from post-traumatic pulmonary insufficiency to haematologic crises in surgery. At the end of each chapter there is a useful list of references so that the reader may increase his knowledge of the particular subject under discussion. The illustrations throughout the book are good and do enhance the written word.

Quite a feature of this book is the inclusion of a brief biographical sketch of the author of each separate chapter.

This book should be in the library of every surgeon both at home and abroad, for it contains a wealth of sound practical surgery as practised in the United States of America.

Clinical Heart Disease. By SAMUEL ORAM, M.D. (Lond.), F.R.C.P. (Lond.), Senior Physician and Director of the Cardiac Department, King's College Hospital, London. 9½ × 7 in. Pp. 920 + vii. Illustrated. 1971. London: William Heinemann Medical Books Ltd. £12.

THIS book is a 'classic' and is by far the best that has so far been published on the important subject of clinical heart disease. The author has a long clinical experience of all varieties of heart disease. His book gives in one volume a comprehensive account of modern cardiology, including applied embryology, anatomy, and physiology. The emphasis is on clinical cardiography and it is stimulating to read the indications for surgical treatment in certain cardiac conditions.

The illustrations throughout this book are excellent: the line drawings are clear and concise, the radiographs have been well chosen, the electrocardiograms are definite, and the clinical pictures are telling.

At the end of each chapter the main points have been summarized under the heading Salient Features, and readers, especially students, will find these most useful. Another feature of this book is the advice on selected reading from books, monographs, and papers.

A very comprehensive and useful appendix on cardiorespiratory data is given at the end of the volume. These important facts and figures are difficult to remember as they are so numerous. The various pressures, oxygen saturation, oxygen capacity, cardiac output, and circulation times are but a few of the items recorded in these data.

An excellent production and a great credit to British medicine.

Vascular Disorders of the Intestine. Edited by SCOTT J. BOLEY, M.D., New York. 10 × 7 in. Pp. 657 + xviii. Illustrated. 1971. London: The Butterworth Group. £13·75.

MUCH progress has been made in the past 20 years regarding the causation and results of vascular disorders of the intestine. In this book, with its many contributors from all over America, the accumulated clinical evidence regarding all aspects of mesenteric vascular disease is considered.

This large volume is divided into six sections.

Section 1 deals with the anatomy, physiology, and pathology of the mesenteric circulation. The histopathology of intestinal ischaemia is discussed at length and the electron microscope has helped in this investigation.

Section 2 is devoted to the radiological aspects of mesenteric vascular disease. The value of magnification arteriography in intestinal vascular disease is stressed and is beautifully illustrated.

In Section 3 the experimental aspects of the mesenteric circulation come under critical review, and the effects of mesenteric ischaemia are carefully considered, including acute superior mesenteric vascular insufficiency.

Section 4 deals with the diagnosis and treatment of alterations of the mesenteric circulation, including the rate of flow.

Section 5 is devoted to vascular disorders of the small bowel, including the coeliac axis syndromes, while Section 6 is given over to a consideration of vascular disorders of the colon.

This volume is full of new and important information regarding the splanchnic circulation. Physiologists, pathologists, radiologists, and clinicians will find this book a mine of information.

Color Atlas of Cancer Cytology. By Masayoshi Takahashi, M.D., Tokyo. 11¾ × 8¼ in. Pp. 354 + v. Illustrated. 1971. Stuttgart: Georg Thieme Verlag. DM.178.

This large atlas contains some 652 beautifully coloured pictures of sections of cancer cells from various organs of the body. The volume is divided into two parts dealing with general cancer cytology in one section and practical cytology as it is applied to various organs and tissues in the other. The electron microscope plays an important part today in establishing the diagnosis of malignant disease when only a small clump of cells are available in a specimen. The author discusses the general outline of cancer cytology and the criteria of malignancy. The description of cell typing of malignant cells is excellent and the instructions for the preparation of smears and fixation are very clear.

In the central nervous system aspiration cytology directly from a tumour or cyst is advocated. Imprint smears can be made from the fresh-cut surface of an excised tissue specimen and may be valuable.

This is the most comprehensive atlas of cancer cytology that has so far been published and it should prove a most valuable reference volume.

At the end of the book there is an extensive list of references, but one is surprised to find no mention of J. Bamforth's book on cytological diagnosis which was published in 1966.

Clinical Otology. An International Symposium. Edited by Michael M. Paparella, M.D., Albert Hohmann, M.D., and John S. Huff, M.D., Minneapolis. 9¾ × 6½ in. Pp. 249 + xiv. Illustrated. 1971. London: Henry Kimpton. £13·25.

This volume represents the published proceedings of the first International Symposium of Clinical Otology sponsored by the Department of Otolaryngology, University of Minnesota School of Medicine, held in June, 1970.

The book is divided into five parts. Part 1 deals with audiology and diagnostic considerations. The techniques of stapedectomy are well described and illustrated, and the complications of this operation are discussed at some length.

Part 2 is devoted to the subject of congenital deafness. There is an excellent chapter on prostheses for microtia and other deformities of the ear. In Part 3 reconstructive surgery is considered at some length, including transplants in otology.

Part 4 deals with vestibular deafness in all its aspects.

Part 5 is devoted to sensorineural hearing loss, including noise-induced deafness, and the management of sudden deafness.

Although the great majority of contributors come from many centres in America there are chapters by Italian otologists and others from Denmark.

This is a book which every medical library should have on its shelves for reference purposes.

Concepts of Disease. Edited by Joel G. Brunson, M.D., Mississippi, and Edward A. Gall, M.D., Cincinnati. 10 × 7 in. Pp. 1134 + xiii. Illustrated. 1971. London: Collier-Macmillan. £11·95.

This large work, in which the 38 contributors have covered the whole field of general pathology, is an authoritative volume.

Professor Brunson contributes an excellent chapter on the cell and its ecology and in the considerable list of references at the end one is somewhat surprised to find the name of Roy Cameron omitted. Cameron's enormous volume on *The Cell* is surely the most important work on that subject that has so far been published.

The chapter on cytopathology by William Christopherson makes stimulating reading. Other interesting chapters are devoted to the effects of ionizing radiation, nutritional factors in disease, thrombosis, embolism, infarction, immunity, neoplasms revisited, and diseases peculiar to pregnancy and the neonatal period.

As one would expect in a work such as this, photomicrographs predominate and the electron micrographs are excellent. At the end of each chapter there is a complete list of references, mostly American.

This is a standard textbook of human pathology and it is an excellent reference volume. It should prove of real value to medical students and all clinicians.

Aspirin, Platelets and Stroke. Background for a Clinical Trial. Compiled and edited by Williams S. Fields, M.D., Houston, and William K. Hass, M.D., New York. Pp. 163 + xii. 1971. Missouri: Warren H. Green. $10.50.

This is an interesting volume containing 12 chapters by 29 contributors, all of whom are interested in the treatment of the ischaemic stroke syndrome. Many investigators consider that the treatment of this syndrome should consist of the giving of aspirin, which has been shown *in vitro* to produce marked collagen-induced platelet aggregation and the subsequent platelet release reaction. Also, animal experiments have clearly demonstrated a reduction of intra-arterial clotting following the administration of aspirin in comparatively small doses. When there is a marked constriction of the extracranial carotid vessels as shown by angiography, then surgery is clearly indicated.

Care of the Surgical Cardiopulmonary Patient. Edited by William E. Neville, M.D., New Jersey. 9 × 6 in. Pp. 313 + ix. Illustrated. 1971. London: Lloyd-Luke (Medical Books) Ltd. £8·20.

The importance of this book today is self-evident, for the increasing number of operations on the heart and lungs demands an ever-ready vigilance. Also thoracic trauma is common in road accidents and from war wounds.

The ten contributors to this book have covered in a most comprehensive manner the modern methods of pre- and postoperative treatment of the cardiopulmonary patient. The problems of cardiopulmonary arrest, myocardial revascularization, thoracic trauma, and acute renal failure are all considered in detail. The action of and indications for adrenergic drugs are dealt with in a lucid and interesting way.

This book will appeal to all those who have to work in intensive care units as well as to house-surgeons and surgical registrars.

Spinal Dysraphism. Spina Bifida Occulta. By C. C. MICHAEL JAMES, Ph.D. (Edin.), F.R.C.S. (Edin.), Newcastle upon Tyne, and L. P. LASSMAN, M.B., B.S. (Lond.), F.R.C.S., Newcastle upon Tyne. 8½ × 5½ in. Pp. 144 + viii. Illustrated. 1972. London: The Butterworth Group. £4·40.

THIS is a useful monograph on a subject that is not well known amongst the general practitioners of today. So often children with this defect are allowed to develop severe disabilities without the apparent possibility of treatment of the primary condition.

The authors of this book have wisely refrained from publishing their clinical records until they had collected 100 cases and had fully investigated these cases before and after operation.

The book is divided into two parts. Part 1 is devoted to clinical considerations, including the embryology and pathology of the condition. The principles of surgery are discussed fully and the postoperative care and complications are described in some detail.

Part 2 consists of an analysis of 100 cases and the results after laminectomy during the period 1957 to 1965.

This book is written in a clear, lucid style and is illustrated with good clinical pictures, radiographs, and excellent photographs of operative techniques.

This book will be in demand by paediatric physicians and surgeons, as well as orthopaedic surgeons and neurosurgeons.

Basic Skills for Surgical Housemen. By KENNETH C. CALMAN, Lecturer in Surgery, Western Infirmary, Glasgow. 7⅛ × 4⅘ in. Pp. 126 + vii. Illustrated. 1971. Edinburgh: Churchill Livingstone. £1.

THIS is a useful paper-back for the guidance of students, house-officers, and nurses. The techniques and procedures which are required by medical residents are described in some detail and are illustrated by clear line drawings. Procedures such as venepuncture, arterial blood sampling, urethral catheterization, the insertion of chest drains, the management of cardiac arrest, abdominal paracentesis, bronchoscopy, and tracheostomy are well described.

This pocket-book contains much useful information for the resident, student, and nurse, and its price is moderate.

Biological Tissue in Heart Valve Replacement. Edited by M. I. IONESCU, M.D., Consultant Thoracic Surgeon, General Infirmary; Leeds, D. N. ROSS, B.Sc., M.B., Ch.B., F.R.C.S., Consultant Surgeon, Guy's Hospital, London; and G. H. WOOLER, T.D., M.D., M.A., F.R.C.S., Honorary Thoracic Surgeon, General Infirmary, Leeds. 8½ × 5½ in. Pp. 925 + xxix. Illustrated. 1972. London: The Butterworth Group. £22.

THIS is an important book, for it marks the progress that has taken place during the past few years concerning heart-valve replacement. It is pleasing to note that this book is edited by three outstanding British thoracic surgeons. The numerous contributors to this volume come from Canada, France, Holland, Roumania, Switzerland, United States of America, and Great Britain. The majority are thoracic surgeons from various centres in England.

The enormous collection of material concerned with biological tissue in heart-valve replacement speaks for itself, and the various contributors have given their clinical experience with many types of valves. The various techniques used in heart-valve replacement are well described and illustrated. There can be no doubt that this book provides a critical account of our present knowledge of this type of surgery. The book is a great credit not only to the editors but also to the numerous contributors.

This is an ideal reference volume and should be found in every medical library.

The Complete Handbook for Medical Secretaries and Assistants. By ROBERT LEE DENNIS, M.D., San José, and JEAN MONTY DOYLE, R.R.L., San José. 11 × 8½ in. Pp. 559 + xiii. Illustrated. 1971. Edinburgh: Churchill Livingstone. £4·50.

THIS is a comprehensive volume giving essential information regarding medical terms and reports, and also the format of letters to doctors and the filing of medical notes, book-keeping, and insurance. There is also an up-to-date list of surgical instruments, dressings, drugs, and anaesthetics. There are sections on tumours and the electrocardiogram.

Any secretary knowing the contents of this large volume would be worth her weight in gold.

Ergebnisse der Bluttransfusionsforschung. Vol. 11. Edited by M. MATTHES, Freiburg i. B., N. KLEINE, Freiburg i. B., and L. P. HOLLANDER, Basel. 9½ × 6½ in. Pp. 466 + viii, with 117 illustrations. 1971. Basel: S. Karger. £12·65.

THIS massive volume reports the proceedings of the fourteenth meeting of the German Society for Blood Transfusion held in April, 1970. The papers presented cover a wide field with particular reference to immunology. Apart from 58 separate papers, the book contains a special lecture by Dr. R. Race on blood groups in human genetics, a long opening speech, and a panel discussion on exchange transfusion in adults. Unfortunately, the papers have been presented as they were read and have not been edited or shortened. None of the papers contains a summary and the majority are in German. The book is beautifully printed and well illustrated and is likely to be of interest to those who attended the meeting.

Geburtshilfliche Operationen. Eleventh edition. By HEINRICH MARTIUS and GEHARD MARTIUS, Berlin. 9 × 6 in. Pp. 189 + xvi, with 177 illustrations. 1971. Stuttgart: Georg Thieme Verlag. DM.24.

THIS is the eleventh edition of a classic textbook for students and practitioners about obstetric procedures. It was first published in 1933. The book is generously and well illustrated by half-tone diagrams, and various obstetric manœuvres are well described.

It is perhaps unfortunate that the book deals only with technical procedures and it leaves out entirely the problems of antenatal and postnatal care, and it does not discuss at all the management of the newborn baby. However, because of the clarity of the diagrams it must be a success with medical students.

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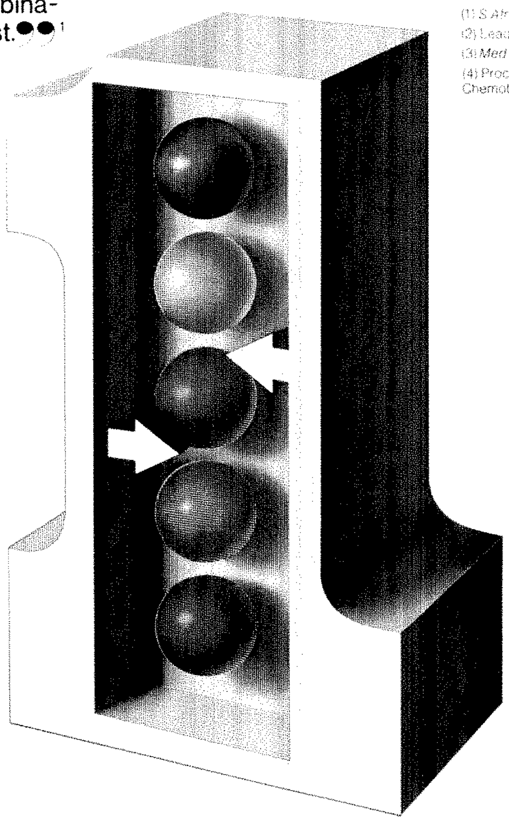
(1) *S Afr med J*, (1970) **44**, Supplement (August) 12

(2) Leading Article, *Brit med J*, (1969) **1**, 525

(3) *Med J Austr* (1971) **1**, 526

(4) Proceedings of the V International Congress of Chemotherapy, (1967), **1**, 1, (A1 - 5a/3) 293



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The purpose of this book is to offer a concise aid to the study of clinical surgery rather than such comprehensive cover of the subject as is already available in the many standard texts. To this end every effort has been made at impartiality and clarity, with deliberate restriction of the subject matter to common clinical fields. Consideration of the surgical specialities of orthopaedics, urology, cardio-thoracic surgery and otorhinolaryngology has been limited to certain aspects of general concern.

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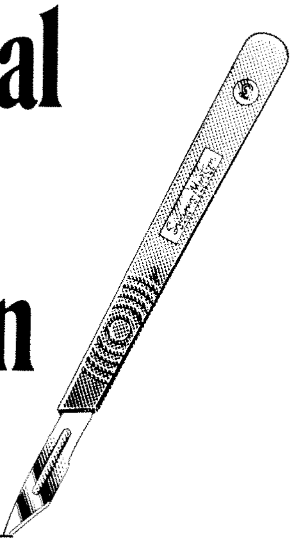

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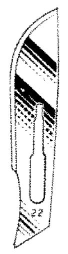

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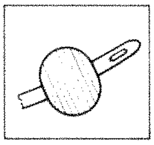

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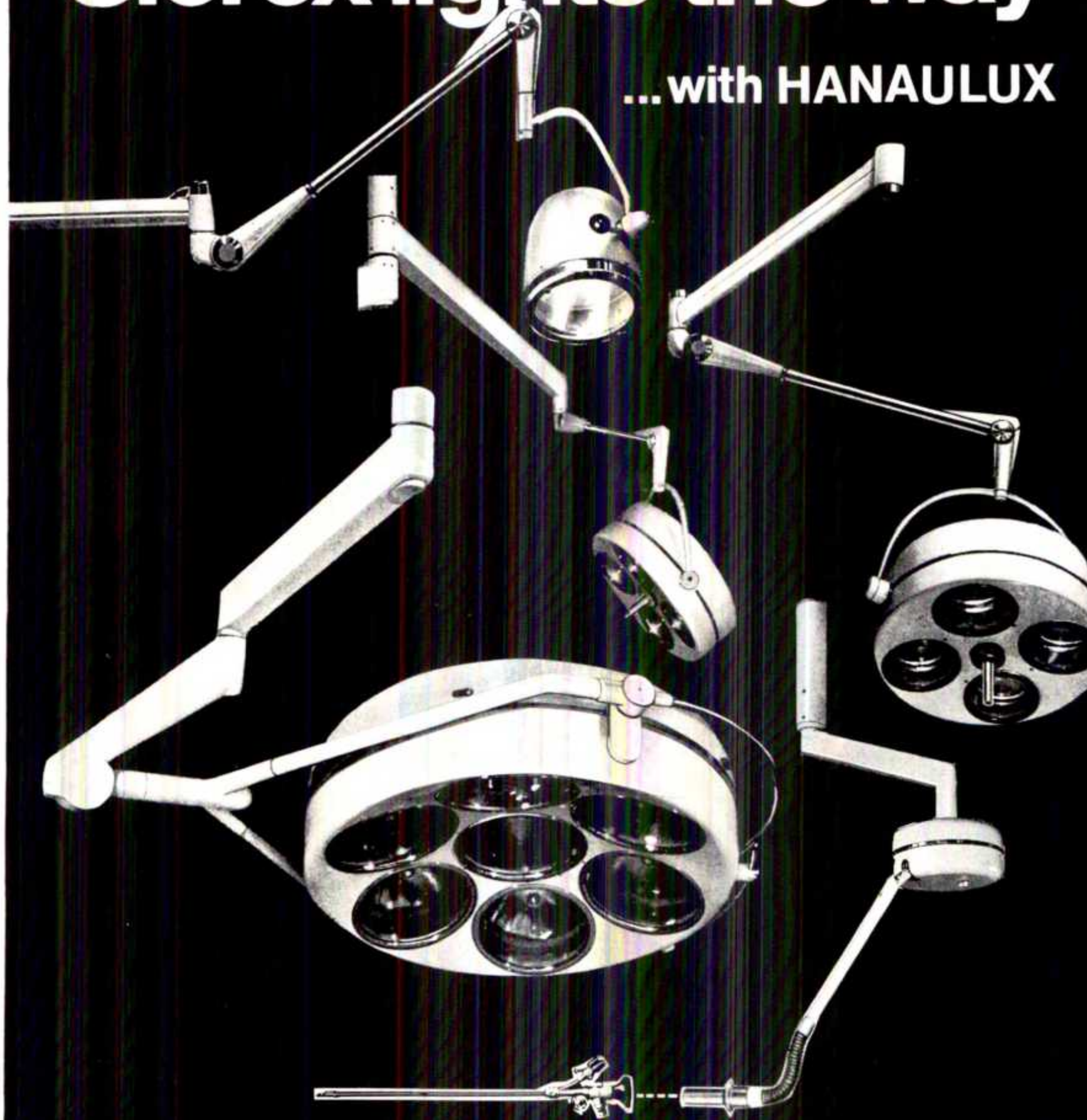

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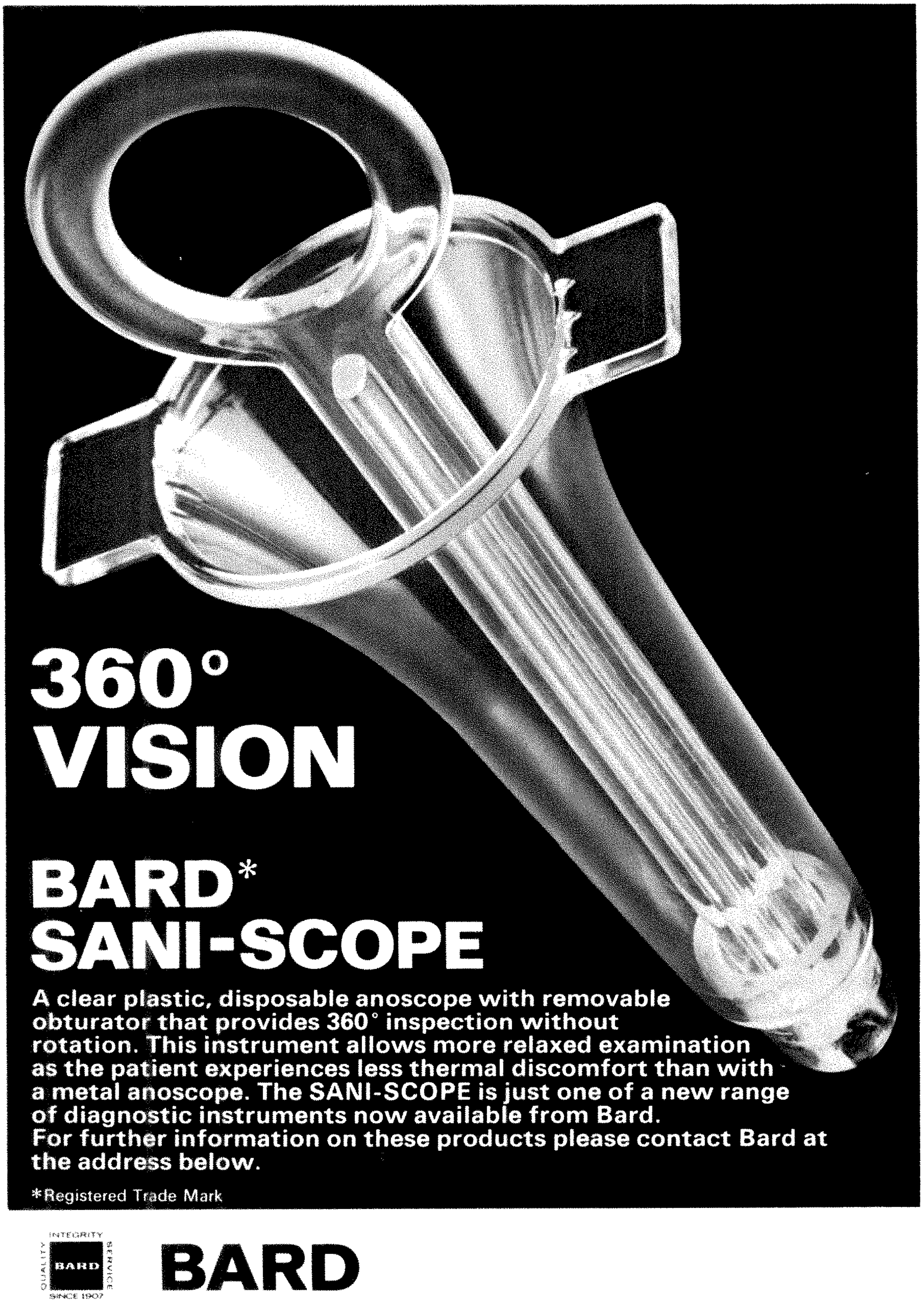

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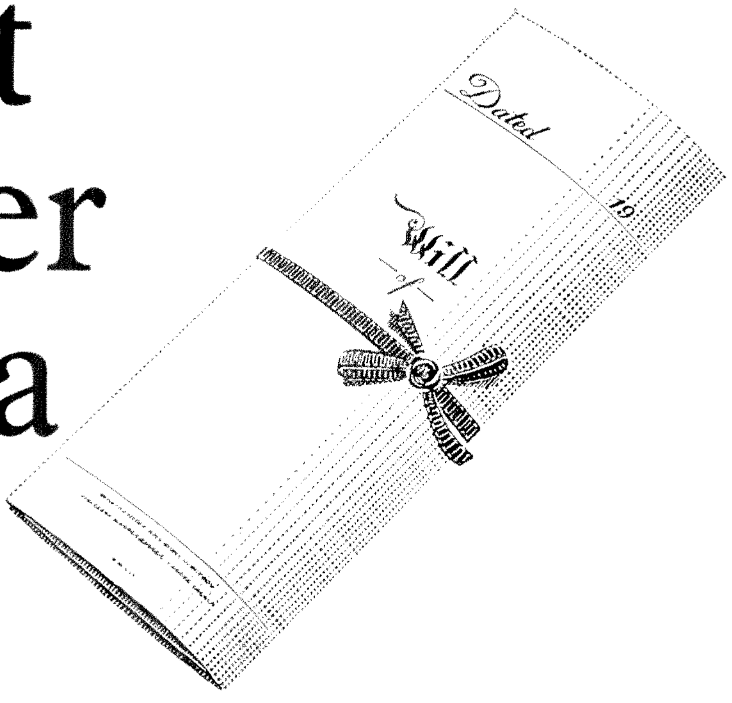

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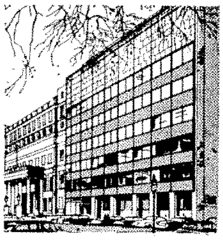

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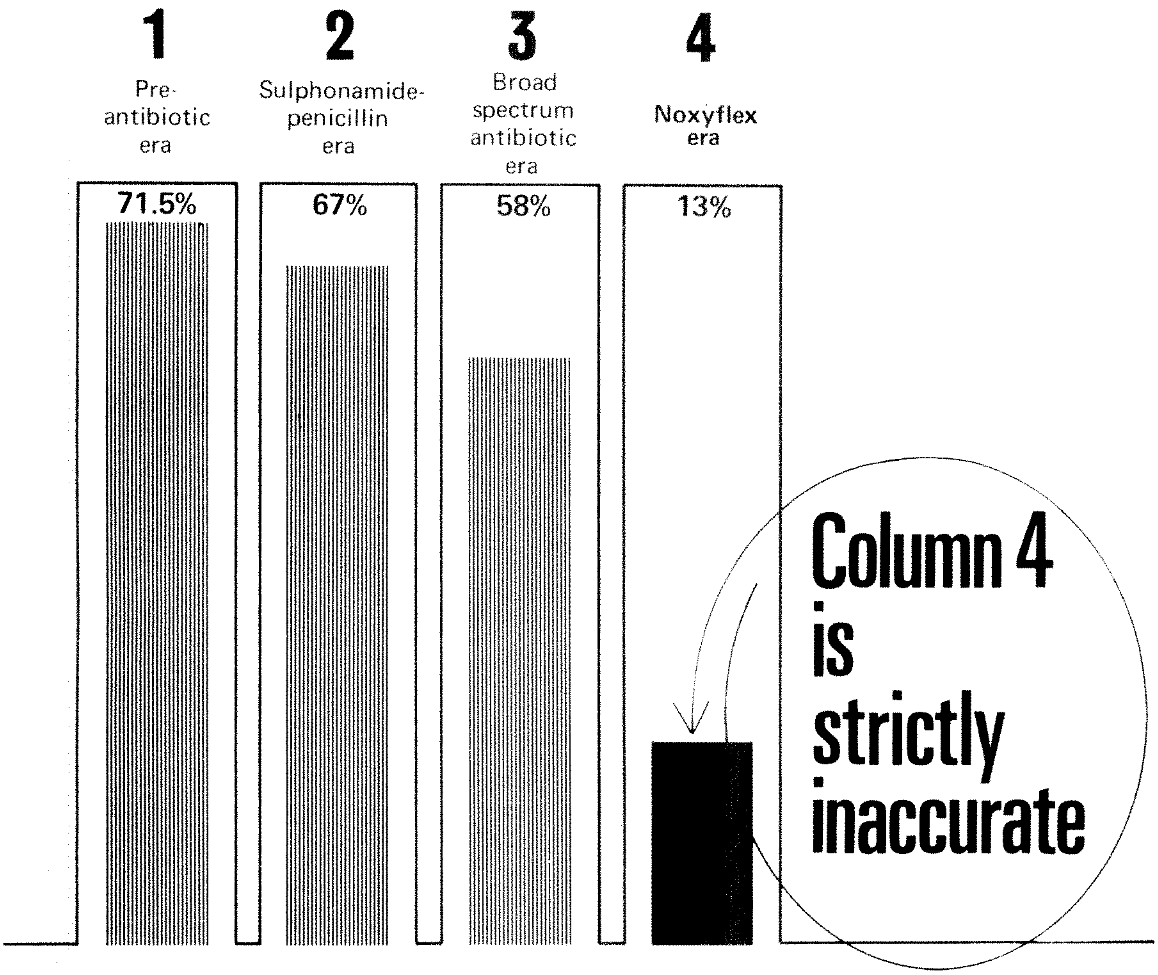

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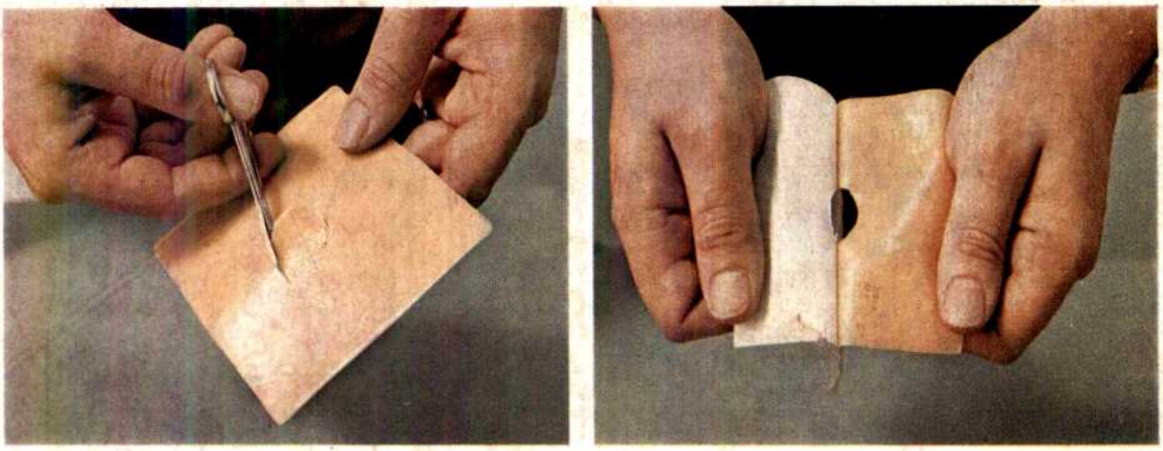

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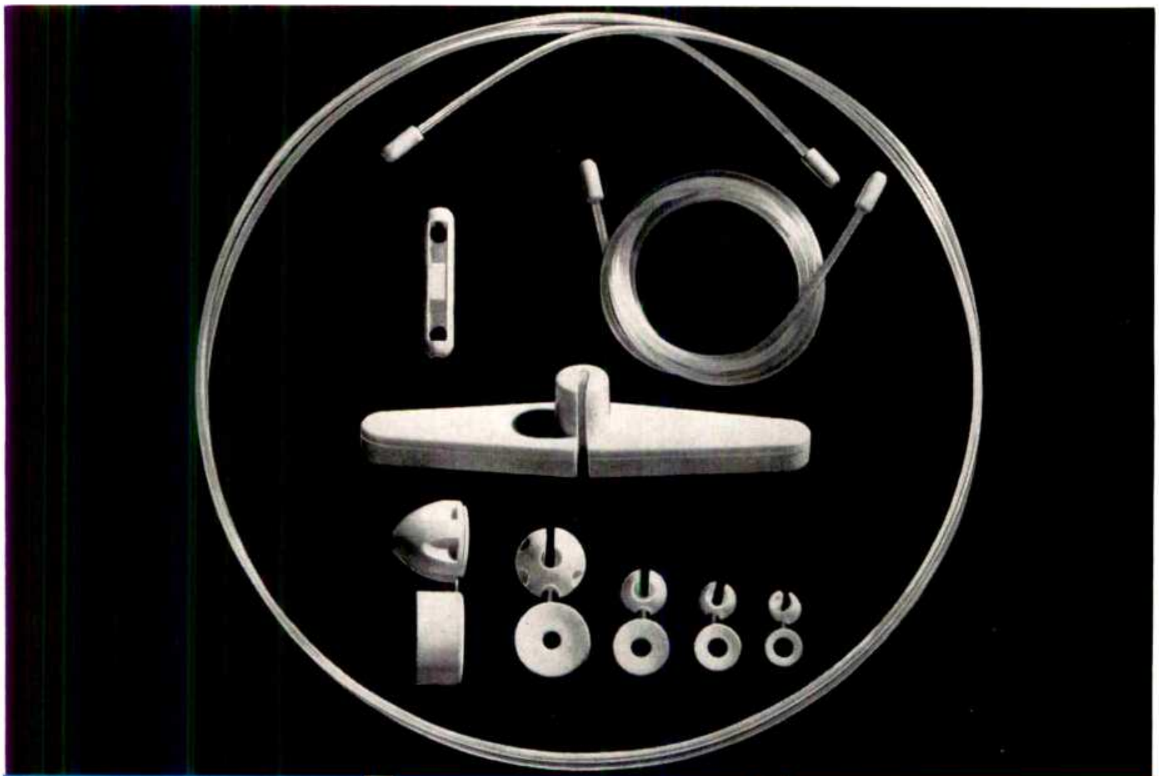

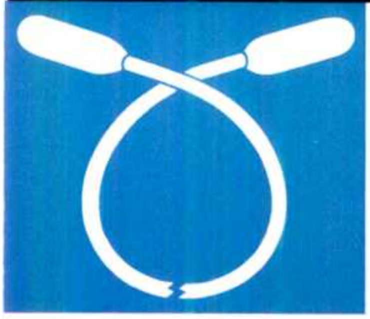

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CONTENTS

PAGE

ORIGINAL PAPERS

MALIGNANT TUMOURS OF THE BILE-DUCTS *Kenneth W. Warren, John C. Mountain, and William Lloyd-Jones* 501
THE DELAYED HYPERSENSITIVITY RESPONSE IN PRIMARY BREAST CARCINOMA AS AN INDEX OF HOST RESISTANCE *Roger J. Mitchell* 505
SURGICAL OBJECTIVES IN UNRESECTED CANCER OF THE HEAD OF THE PANCREAS *R. G. Elmslie and A. H. Slavotinek* 508
ABDOMINAL AORTIC ANEURYSM AND HORSE-SHOE KIDNEY *John E. Frawley, G. H. Dickson, C. W. Jamieson, and H. H. G. Eastcott* 513
THE DIAGNOSIS OF PARATHYROID OVERACTIVITY IN A POPULATION OF RENAL STONE FORMERS *Roy Scott, Frances Dryburgh, Robert Wilson, Ian T. Boyle, and David Pollock* 517
THE EFFECT OF THE FIBRINOLYTIC INHIBITOR EPSILON-AMINOCAPROIC ACID ON THE INCIDENCE OF DEEP-VEIN THROMBOSIS AFTER PROSTATECTOMY - - *I. C. Gordon-Smith, J. A. Hickman, and S. H. El Masri* 522
REPAIR OF THE LARYNGOPHARYNX AND CERVICAL OESOPHAGUS AFTER IRRADIATION - - *H. J. Shaw* 524
THE ROLE OF RADIOTHERAPY IN THE MANAGEMENT OF MALIGNANT THYMOMA *C. R. H. Penn and H. F. Hope-Stone* 533
BRACHIAL PLEXUS LESIONS ASSOCIATED WITH TRAUMATIC ASPHYXIA - - *Peter Leech and Hugh Cuthbert* 539
A COMPARISON OF PORTAL AND SYSTEMIC VENOUS DRAINAGE IN PORCINE RENAL ALLOGRAFTS *G. Mazzoni, C. Di Martino, A. Demofonti, A. Valli, S. Pellegrini, B. Gentili, and M. Melis* 541
THE SINGLE THYROID NODULE *A. Psarras, S. N. Papadopoulos, D. Livadas, A. D. Pharmakiotis, and D. A. Koutras* 545
THE RELATIONSHIP BETWEEN BLOOD-FLOW AND FAILURE OF FEMOROPOPLITEAL RECONSTRUCTIVE ARTERIAL SURGERY - - - - - - - - - *H. J. Terry, J. S. Allan, and G. W. Taylor* 549
THE EFFECTS OF POSTURE, EXERCISE, AND BANDAGE PRESSURE ON THE CLEARANCE OF ^{24}Na FROM THE SUBCUTANEOUS TISSUES OF THE FOOT - - - - - - - - - - - *A. D. B. Chant* 552
PERSISTENT AND RECURRENT HYPERPARATHYROIDISM - - - - *Orlo Clark and Selwyn Taylor* 555
THE EFFECT OF REMNANT SIZE ON THE OUTCOME OF SUBTOTAL THYROIDECTOMY FOR THYROTOXICOSIS *A. J. Hedley, W. Michie, T. Duncan, G. Hems, and J. Crooks* 559
THE EFFECT OF EXPERIMENTAL BILE-DUCT OBSTRUCTION ON CRITICAL BIOSYNTHETIC FUNCTIONS OF THE LIVER *Emanoel Lee, B. D. Ross, and J. R. Haines* 564
PERIPHERAL TUBERCULOUS LYMPHADENITIS IN THE ELDERLY - - - - - - *A. L. G. Peel* 568

SHORT NOTES OF RARE OR OBSCURE CASES

TUMORAL CALCINOSIS - - - - - - - - - - - - *Derek Berg* 570
RUPTURED MYCOTIC ANEURYSM OF THE SPLEEN - - - *Heather M. Dukes and John M. Mynors* 572
A CASE OF GALL-STONE ILEUS IN THE ABSENCE OF A BILIARY-ENTERIC FISTULA - - - *J. H. Newman* 573
HAEMOPERITONEUM COMPLICATING SECONDARY CARCINOMA IN THE LIVER *Ali Ahmed and C. Metcalfe-Gibson* 576
LUMBOSACRAL AGENESIS IN A 60-YEAR-OLD MAN - - - - - - - *W. J. Nicol* 577
LEIOMYOMA OF THE APPENDIX - - - - - - - - - *T. H. Cullen and H. J. Voss* 579

REVIEWS AND NOTICES OF BOOKS

Orthopaedics for the Undergraduate. Fractures—*W. A. Crabbe.* Tracheostomy and Artificial Ventilation—ed. *Stanley A. Feldman and Brian W. Cramley.* Ano-rectal Malformations in Children—*F. Douglas Stephens and E. Durham Smith.* Patients, Hospitals and Operational Research—*G. M. Luck, J. Luckman, B. W. Smith, and J. Stringer.* Progress in Pediatric Surgery, Vol. 3—ed. *P. P. Rickham, W. Ch. Hecker, and J. Prévot.* Facial Prostheses—*Alan Clive Roberts.* Handbuch der Medizinischen Radiologie; Encyclopedia of Medical Radiology, Part 3: Spezielle Strahlentherapie Maligner Tumoren—ed. *A. Zuppinger.* Congenital Deformities of the Testis and Epididymis—*C. Gordon Scorer and Graham H. Farrington:* Schweitzer. A Biography—*George Marshall and David Poling.* Physiology of the Eye—*Hugh Davson.* Shands' Handbook of Orthopaedic Surgery—ed. *R. Beverly Rancy and H. Robert Brashear.* The Lacrimal System—ed. *Everett R. Veirs.* Current Concepts of the Histology of Oral Mucosa—ed. *C. A. Squier and Julia Meyer.* Notes on Dental Materials—*E. C. Combe.* Fundamental Skills in Surgery—*Thomas F. Nealon.* Die Fettembolie—*Dr. Gyorgy Szabo.* Ileostomy Care—*Marshall Sparberg.* Surgery and the Allergic Patient—ed. *Claude A. Frazier.* 581

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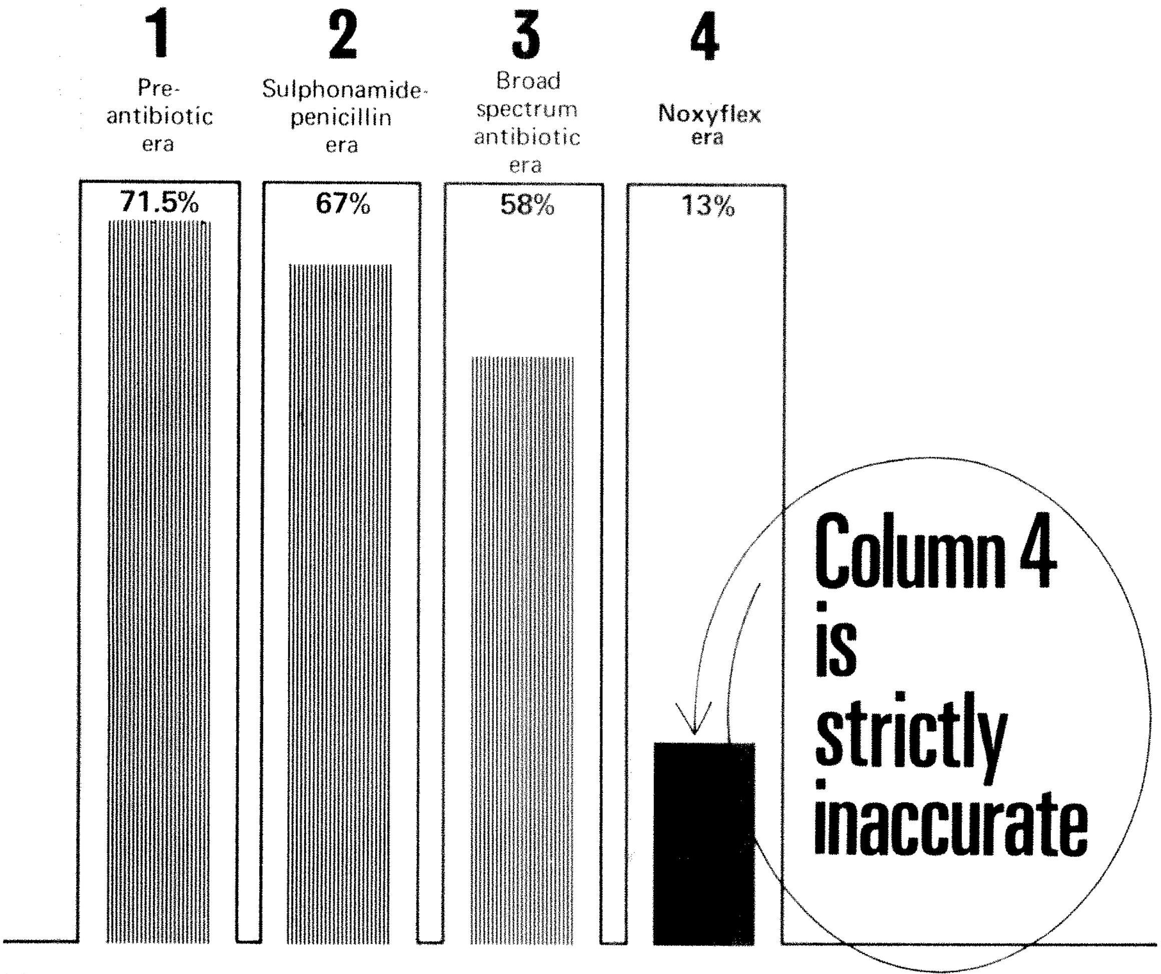

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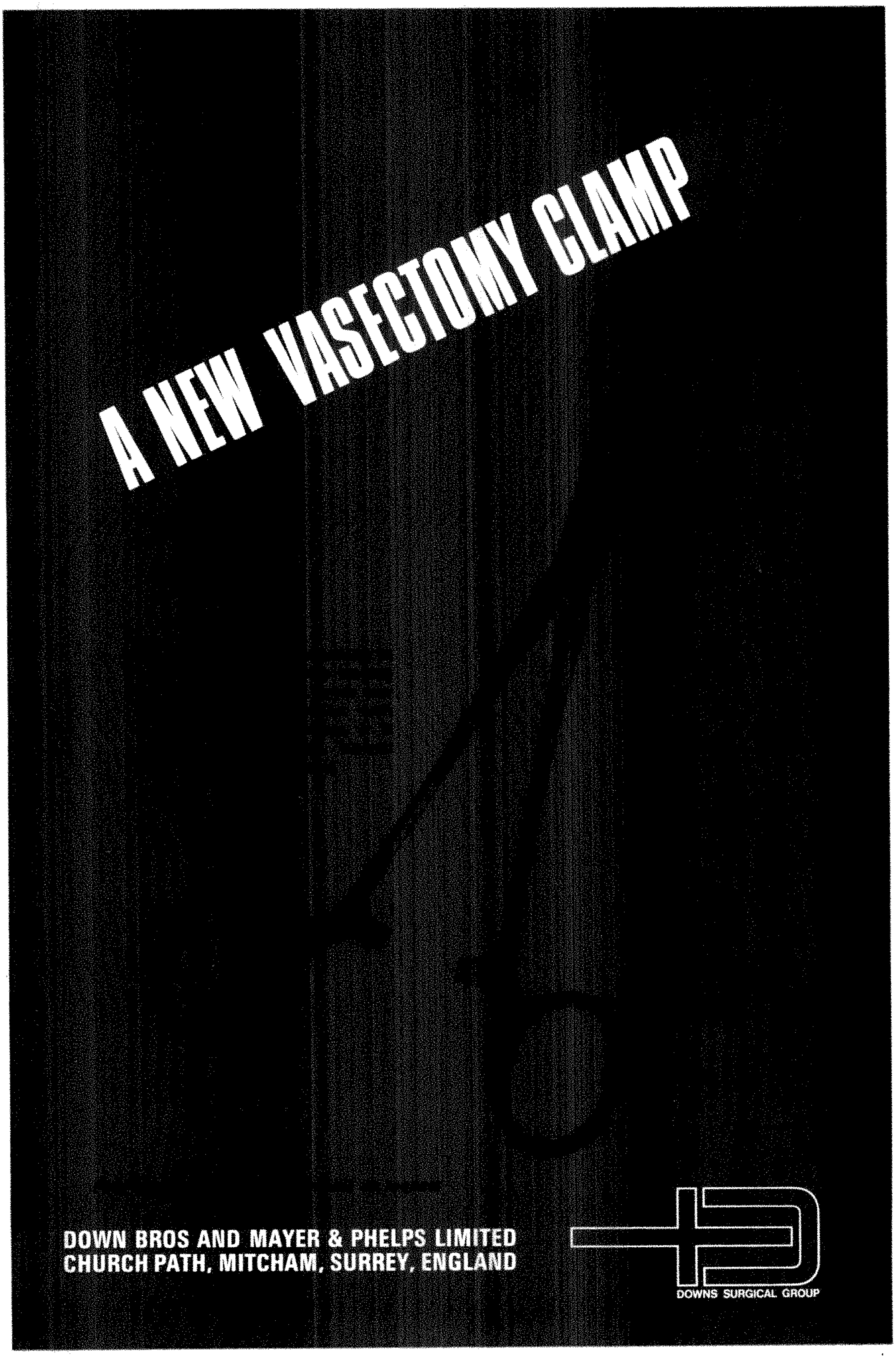

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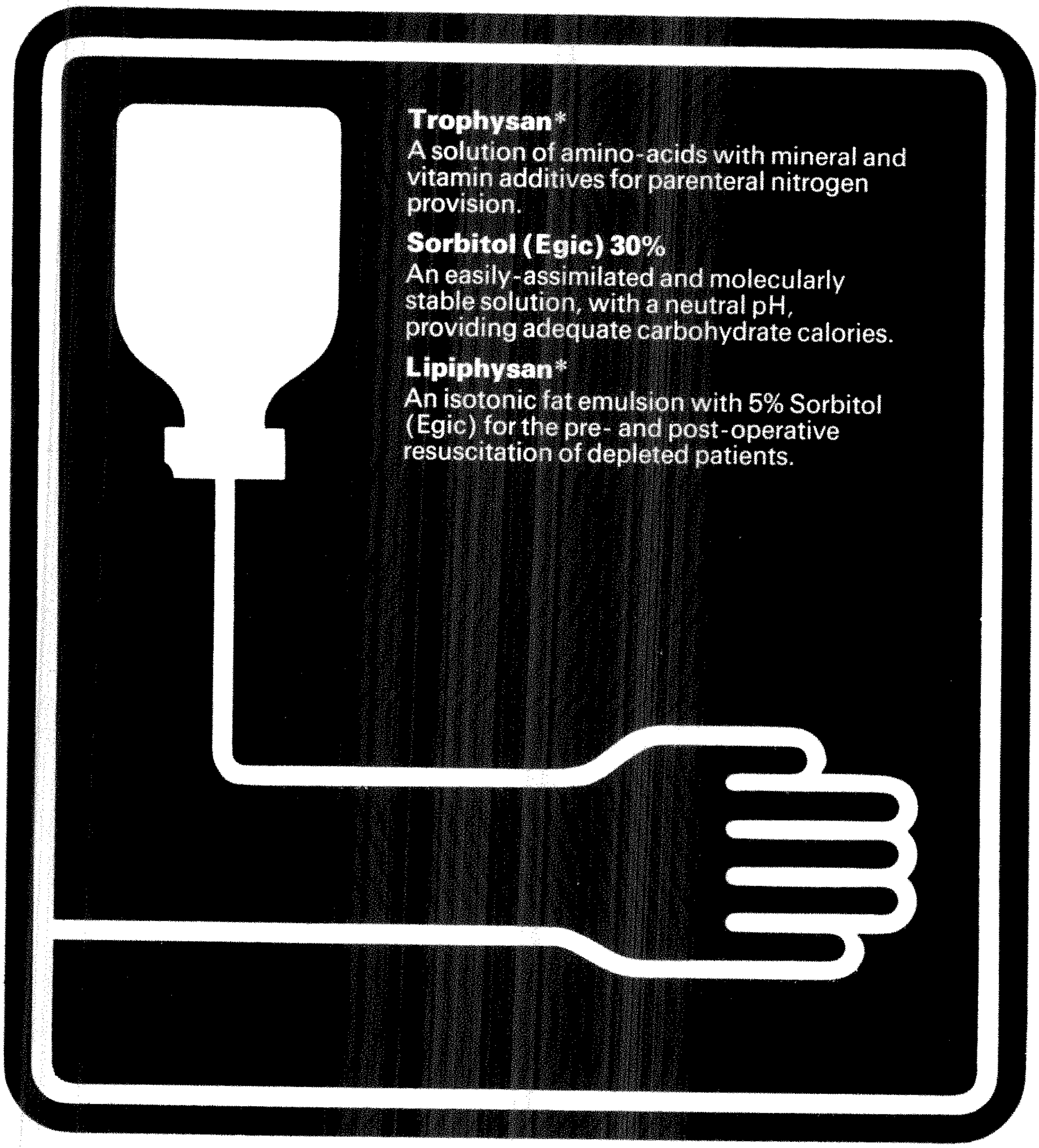

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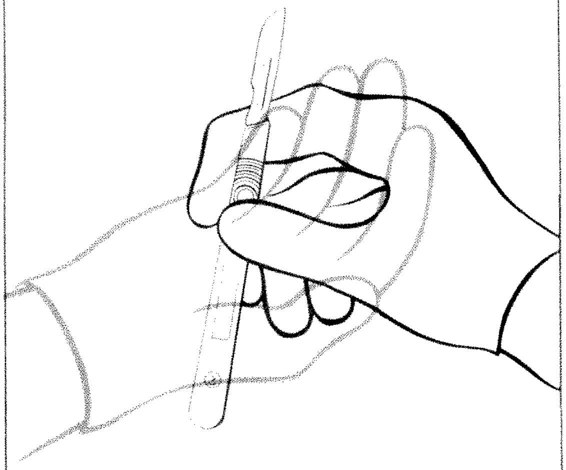

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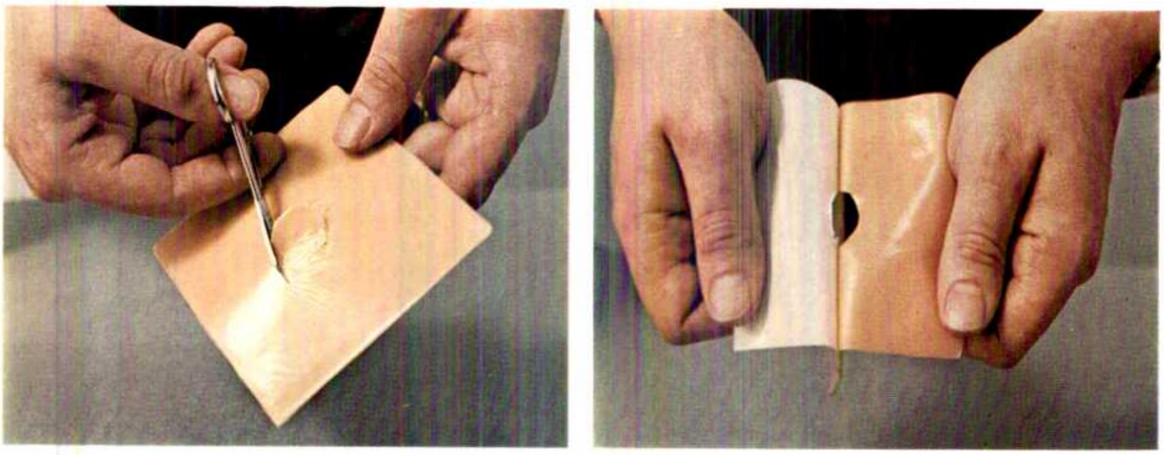

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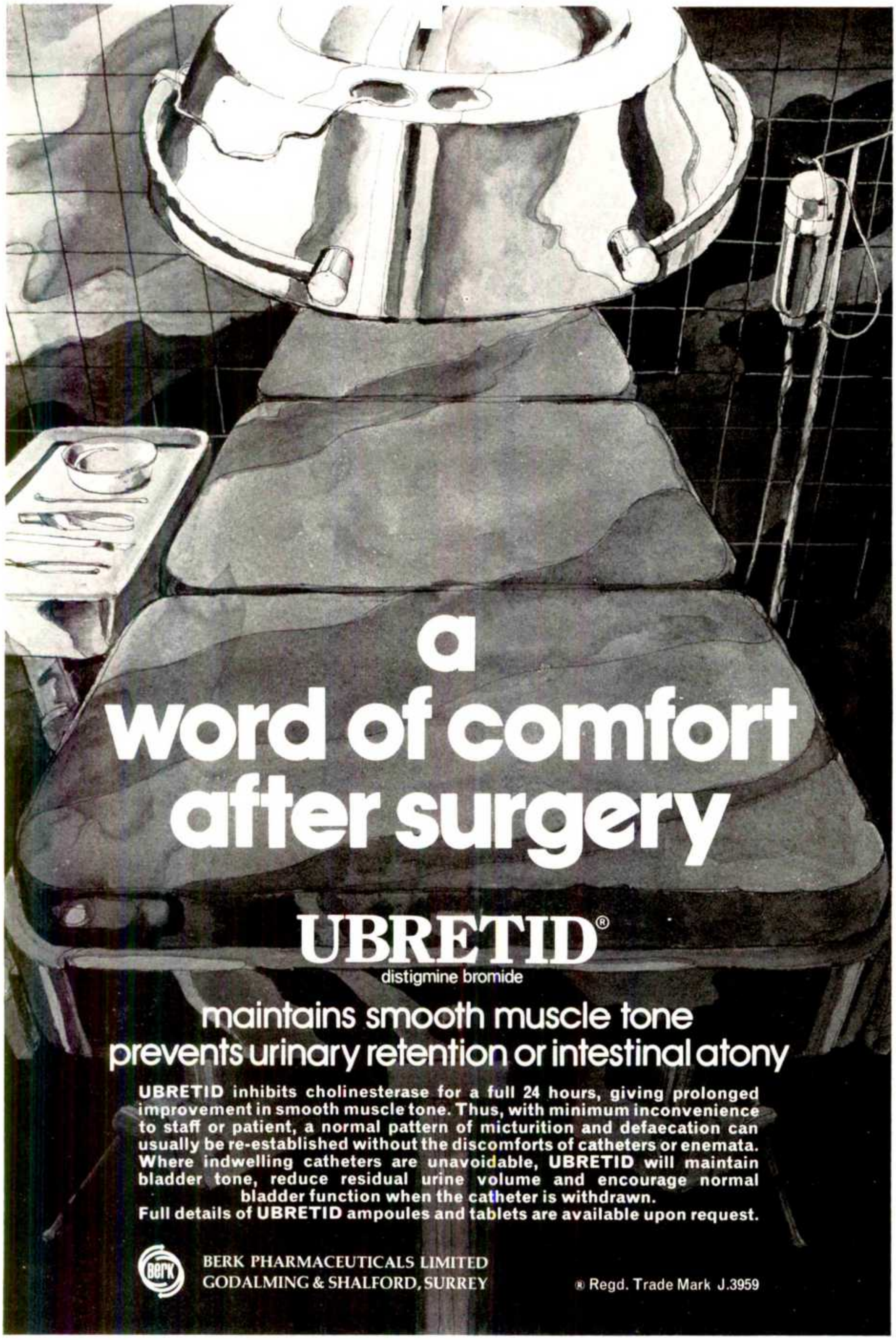

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ORIGINAL PAPERS

MALIGNANT TUMOURS OF THE BILE-DUCTS

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SUMMARY

The 77 cases of malignant neoplasm of the extrahepatic bile-ducts treated at the Lahey Clinic between 1965 and 1969 are reviewed. Exploratory laparotomy was performed in 68 cases, although in 9 cases operation was not indicated because of the patients' poor condition. Of the 68 surgical patients, 24 (35 per cent) had a radical procedure, of which 17 survived for more than 1 year and 5 are still alive more than 3 years later, 3 having no evidence of recurrent disease. Forty-one patients had palliative treatment usually with some form of decompression procedure of the obstructed common bile-duct, and in 15 patients this was combined with hepatic artery infusion chemotherapy. Of these patients, 16 survived for more than 1 year, including 9 from the group treated by hepatic artery infusion chemotherapy. Only 1 patient is still alive after more than 3 years.

Of all the patients, 44 per cent survived for more than 1 year, 23 per cent for more than 2 years, and 8 per cent for more than 3 years. The mean survival time was 13 months. These results compare favourably with those of the previous survey from the Lahey Clinic, and it is concluded that the improvement is the result of the increase in the radical resection rate from 18 to 31 per cent and in the institution of hepatic artery infusion chemotherapy in palliative cases.

MALIGNANT tumours of the bile-ducts have been associated with a very poor prognosis despite the fact that the majority of these tumours tend to be slow growing without widespread metastases. This is mainly because of the difficulty of early diagnosis and the proximity of these tumours to vital structures. Braasch, Warren, and Kune (1967) reviewed the total experience of the Lahey Clinic in treating neoplasms of the bile-ducts from 1920 to 1965 and reported 173 cases. Only 25 patients (14 per cent) were known to have survived 1 year or more and only 7 for more than 3 years.

During the past 5 years an attempt has been made whenever possible to be more radical in the surgical management of this condition as suggested by Quattlebaum and Quattlebaum (1965). Hepatic artery infusion chemotherapy was first performed for non-resectable lesions in 1965. We have therefore reviewed the records of patients treated from 1965 to 1969 to determine whether this more radical surgical approach together with infusion chemotherapy for the non-resectable lesions has resulted in a better prognosis.

RESULTS

Between 1965 and 1969 77 patients (44 men and 33 women) with primary malignant neoplasms of the bile-ducts were treated at the Lahey Clinic Foundation. The youngest patient was 31 years, the oldest 79 years, and the average age was 57 years. The peak incidence was in the sixth decade (*Fig.* 1).

The site of origin of the neoplasms is shown in *Fig.* 2. The commonest site was found to be the common hepatic duct (28 cases), followed by the retroduodenal portion of the bile-duct (18 cases) and the supraduodenal portion of the common bile-duct (11 cases). In 7 patients the neoplasm arose from the left hepatic duct, but in no patient did a neoplasm arise in the right hepatic or cystic duct. In 13 patients it was impossible to determine the site of origin of the neoplasm because the entire extrahepatic ductal system was involved.

Of the 77 patients, 69 were found to have adenocarcinoma, of which 49 were well-differentiated infiltrating lesions, 18 were anaplastic infiltrating tumours, and 2 were papillary tumours. One patient had a leiomyosarcoma. Insufficient material was obtained in 5 patients to classify the tumour. In 2 other patients, although obvious widespread malignant disease was present at laparotomy, biopsy revealed negative findings.

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Definite metastases were present in 35 of the 77 patients (45 per cent). The periductal lymph-nodes were involved in 25 patients and the coeliac lymph-nodes in 12. Direct extension into the liver occurred in 18 patients, of whom both lobes were involved in 13, the left lobe in 3, and the right lobe in 2. The peritoneum was obviously involved in 7 patients, and 1 patient also had osseous metastases.

The commonest presenting symptom was jaundice, occurring in 71 patients (92 per cent). Loss of weight and anorexia were also common. Upper abdominal pain was present in 23 patients (30 per cent) and chills and fever occurred in 22 patients (29 per cent). Jaundice was present on examination at the Lahey Clinic in 61 patients (79 per cent). The discrepancy between the presence of jaundice on examination at the Lahey Clinic and a history of recent jaundice is due to the fact that 60 of the 77 patients had had previous exploratory surgery elsewhere, and 21 (27 per cent) had a biliary drainage tube in situ or a biliary fistula on arrival. Except for hepatomegaly, which was present in 42 patients (55 per cent), other signs were usually absent. A palpable gall-bladder was present in only 3 patients (4 per cent), an enlarged spleen occurred in 2 patients (2 per cent), and a palpable abdominal mass and ascites were present in 1 patient each.

The liver-function tests showed evidence of bile-duct obstruction in almost all the cases. The serum bilirubin was raised above 1·5 mg. per 100 ml. in 55 out of 70 patients (79 per cent), with a maximum level of 47 mg. per 100 ml. in 1 patient. The serum alkaline phosphatase was raised above 4 Bodansky units in 67 out of 69 patients (97 per cent), and the level was more than 20 Bodansky units in 32 patients (46 per cent). The serum glutamic oxaloacetic transaminase was raised above 50 U. in 21 out of 37 patients (57 per cent). In only 6 patients, however, was it raised above 100 Somoygi units, and the highest recorded value was 177 Somoygi units. A low serum-protein level less than 5·6 g. per 100 ml. was found in only 4 patients, although the serum albumin was less than 3·5 g. per 100 ml. in 26 patients. The serum prothrombin level was less than 65 per cent in 20 patients.

Straight roentgenograms of the abdomen were not helpful in making the diagnosis of extrahepatic biliary tract neoplasia. It was performed in 36 patients and was reported as being normal in 29. Only 4 patients were shown to have hepatomegaly, and another 2 who had had previous biliary-tract surgery had air in the biliary tree. Intravenous cholangiography was also unhelpful. Of the 13 patients on whom it was performed, only 2 showed a dilated common bile-duct, 3 patients had a normal-calibre duct delineated, while the remainder showed no opacification. T-tube cholangiography on patients who had been operated on elsewhere was performed in 15 cases; in 13 of these a dilated bile-duct was demonstrated, the exact site of the obstruction being obvious in 10. In 2 patients the procedure was unsuccessful. In 32 patients an upper gastro-intestinal series was performed; 20 were reported as being normal, while the remaining 12 (38 per cent) showed extrinsic pressure deformity of the stomach or duodenum. Hepatic scintiscanning was performed in 8 cases, 7 of which were reported as being abnormal, showing cirrhosis in 2 and hepatic metastases in 5. These preoperative diagnoses were found to be correct in 6 of the 7 patients. Coeliac angiography was performed in 9 patients. It was unsuccessful in 1, normal in 3, and showed hepatic metastases in 5. Percutaneous cholangiography was performed in only 2 patients. It was unsuccessful in 1 and successful in the other. Operative cholangiography was usually performed using a No. 18 Foley catheter with the balloon inflated. It was performed in 15 patients and was successful in delineating the site of the stricture in 13 of them.

Table I.—TREATMENT AND SURVIVAL OF 77 PATIENTS WITH A MALIGNANT TUMOUR OF THE BILE-DUCT

PROCEDURE	TOTAL NO. OF CASES	SURVIVAL				
		0–4 wk.	5–26 wk.	27–52 wk.	1–3 yr.	3+ yr.
Pancreatoduodenectomy	15	1	1	4	7	2*
Hepatic artery infusion chemotherapy with or without tube	15	2	1	3	8	1
Hepatico-enterostomy by-pass with or without tube	11	4	1	3	3	—
Tube with or without biopsy	10	—	3	3	4	—
Resection with end-to-end anastomosis or hepatico-enterostomy	7	—	—	1	3	3†
External drainage	5	4	1	—	—	—
Biopsy alone	3	2	—	—	1	—
Pancreatic hepatectomy	2	—	—	—	2	—
No surgery	9	5	2	2	—	—
Total	77	18	9	16	28	6

* One patient has not had a recurrence.

† Two patients have not had a recurrence.

Summary of survival:—
12 months or more, 34 patients (44 per cent).
24 months or more, 18 patients (23 per cent).
36 months or more, 6 patients (8 per cent).
No recurrence, 3 patients.

Of the 77 patients, 60 had had an exploratory operation for obstructive jaundice before their referral to the Lahey Clinic for further assessment and treatment (*Table I*). Resection of the tumour was accomplished in 24 patients, the majority of which were tumours of the distal duct treated by pancreatoduodenectomy (15 patients). It was possible, however, to perform a resection and hepatico-enterostomy or end-to-end anastomosis in 7 patients and a left hemi-hepatectomy and hepatico-enterostomy in 2 others for neoplasms of the proximal duct.

A palliative procedure was performed in 41 patients. This entailed dilating the neoplastic stricture and inserting a rubber stent, either a T-tube or a Y-tube depending on the position of the stricture, in 10 patients, creating a by-pass biliary intestinal anastomosis proximal to the tumour with or without the insertion of a rubber stent in 11 patients, and using hepatic artery infusion chemotherapy associated with the insertion of a stent in 15 patients. Only external drainage of the proximal obstructed duct was possible in 5 severely ill patients, and in 3 patients only biopsy of the neoplasm was possible. On 9 occasions no surgery was attempted as the patient was too ill on admission to the hospital.

Of the 68 patients who underwent surgery, 10 (15 per cent) died in the postoperative period. The principal causes of death were hepatic coma in 3 patients; biliary peritonitis, 2; pneumonia, 2; endotoxic shock, 1; pancreatitis, 1; and secondary haemorrhage, 1.

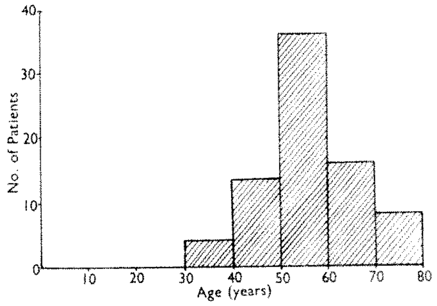


FIG. 1.—Age and sex incidence of 77 patients with malignant tumours of the bile-ducts (1965–9).

Non-fatal morbidity occurred in 16 patients (24 per cent). Several of these patients had more than one complication. Complications included wound infection in 6 patients; pneumonitis and atelectasis, 6; biliary fistula, 3; wound dehiscence, 2; subphrenic abscess, 2; intraperitoneal abscess, 2; pancreatic fistula, 1; and duodenal fistula, 1.

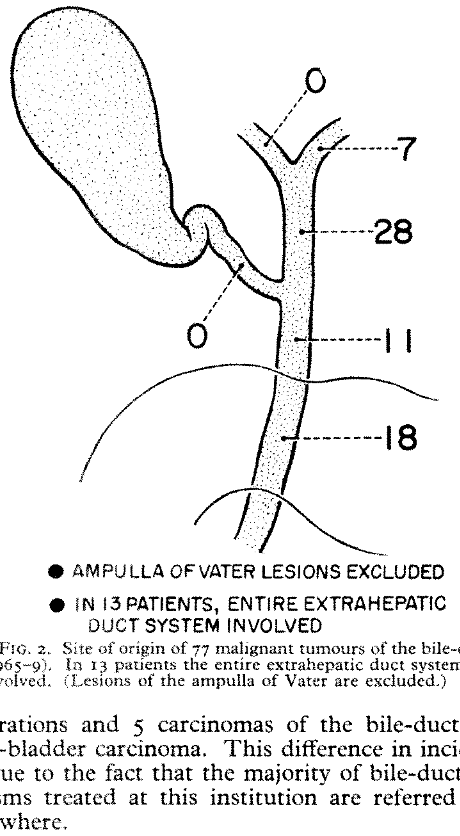
Of the 77 patients, 34 (44 per cent) survived for more than 1 year and 18 (23 per cent) survived for more than 2 years. Six patients (8 per cent) are known to be alive after more than 3 years, but only 3 are apparently still free of a recurrence of the disease. Of these 6 long-term survivors, 5 had a resection procedure while 1 was treated by hepatic artery infusion chemotherapy. The average survival period for all the patients was 13 months.

DISCUSSION

Malignant neoplasms of the bile-ducts are rare tumours. According to Courvoisier (1890) the first case was described in 1508. Renshaw (1922), however, considered the first recorded case to be that reported by Fardel in 1840, and that the first hepatic duct carcinoma was described by Schneppel in 1878.

Several large series of cases have been reported in recent years by Kuwayti, Baggenstoss, Stauffer, and Priestley (1957), Sako, Seitzinger, and Garside (1957), Lippman, McDonald, and Longmire (1959), Thorbjarnarson (1959), Strohl, Reed, Diffenbaugh, and Angerson (1963), and Braasch and others (1967). According to Sako and others (1957), 564 cases of primary carcinoma of the extrahepatic bile-ducts with microscopic proof of diagnosis had been recorded up to June, 1954.

The exact incidence of this condition is difficult to determine. The reported autopsy incidence ranges between 0·01 and 0·85 per cent (Mohardt, 1939; Kirshbaum and Kozoll, 1941; Sako and others, 1957). Neibling, Dockerty, and Waugh (1949) found 1 carcinoma of the bile-ducts in every 210 biliary-tract operations, while Thorbjarnarson (1959) found approximately 3 carcinomas of the gall-bladder to every 1 bile-duct carcinoma. Between 1965 and 1969, 1766 biliary-tract operations were performed at the Lahey Clinic, and 16 carcinomas of the gall-bladder were seen, giving an incidence of 1 carcinoma of the bile-duct for every 23 biliary-tract operations and 5 carcinomas of the bile-duct to 1 gall-bladder carcinoma. This difference in incidence is due to the fact that the majority of bile-duct neoplasms treated at this institution are referred from elsewhere.


0
7
28
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11
18
● AMPULLA OF VATER LESIONS EXCLUDED
● IN 13 PATIENTS, ENTIRE EXTRAHEPATIC DUCT SYSTEM INVOLVED

FIG. 2. Site of origin of 77 malignant tumours of the bile-ducts (1965–9). In 13 patients the entire extrahepatic duct system was involved. (Lesions of the ampulla of Vater are excluded.)

The slightly higher incidence in the male sex which has previously been reported (Sako and others, 1957; Braasch and others, 1967) is again seen in this series. The present series also confirms that the majority of cases occur in the 50–70 age-group (*Fig.* 1). The average age of 57 years is similar to that of the previous series reported from the Lahey Clinic. The youngest reported case was a 23-year-old woman (Neibling and others, 1949), and the oldest was 93 years of age (Thorbjarnarson, 1959).

The majority of malignant neoplasms of the bile-ducts can be classified into well-differentiated, papillary, and anaplastic adenocarcinomas. In our series all the tumours, except for one, on which positive histology was obtained were adenocarcinomas. The exception was a leiomyosarcoma. This incidence is similar to that reported in a previous series. Cases of leiomyosarcoma were also reported by Thorbjarnarson (1959) and Braasch and others (1967). Other rare neoplasms that have been reported include adenoacanthoma (Braasch and others, 1967), squamous-cell carcinoma (Braasch and others, 1967), and rhabdomyosarcoma (Horn, Yakovac, Kaye, and Koop, 1955; Farinacci, Fairchild, Sulak, and Gilpatrick, 1956).

The macroscopic pathological appearance of carcinoma of the bile-ducts has been classified into medullary, infiltrating, and papillary types (Lippman and others, 1959), but it is difficult to classify any case into one type as areas of each type of tumour may be seen. The infiltrating type is usually slow growing and may incite a surrounding fibroblastic reaction that will make it particularly difficult to differentiate from a benign stricture. According to Altemeier, Gall, Zinninger, and Hoxworth (1957) and Thorbjarnarson (1958), this type of tumour is more common than was once thought, and differentiation from sclerosing cholangitis may be almost impossible.

In the present series the commonest site for the origin of bile-duct tumours was the common hepatic duct (*Fig.* 2), but previous series have recorded the distal common bile-duct as being the commonest site (Sako and others, 1957; Braasch and others, 1967). In all the reported series, however, it has been impossible to determine the exact site of origin of the neoplasm in 10-20 per cent of the cases, and it is often difficult to be sure whether the tumour has originated from the duodenum or the gall-bladder and not the bile-ducts. These factors probably account for the variability of site incidence in different series. In this present study, however, it is interesting that there were 7 cases in which the neoplasm arose from the left hepatic duct while none originated in the right hepatic duct. No tumour was considered to have arisen from the cystic duct.

The incidence of metastases in the present series of 45 per cent of the cases is similar to that found by previous workers (Renshaw, 1922; Thorbjarnarson, 1959), although an incidence of over 70 per cent has been recorded (Neibling and others, 1949; Kuwayti and others, 1957). We also confirmed that in nearly all the cases the spread was localized to the vicinity of the bile-duct, with involvement of the liver, peritoneum, and local lymph-nodes, and that widespread metastases occur extremely late in this disease. The patient with osseous metastases was only diagnosed as having a primary bile-duct carcinoma at autopsy.

The clinical features on initial examination were very similar in incidence to those recorded in the previous series from the Lahey Clinic (Braasch and others, 1967). Although obstructive jaundice was present in nearly all our patients, there were rarely any features that would lead to the correct diagnosis being made before operation. In carcinomas of the distal bile-duct an enlarged gall-bladder may be palpated, but this also occurs with carcinoma of the head of the pancreas. Kuwayti and others (1957) found a palpable gall-bladder in 32 per cent of their cases, but it occurred in only 4 per cent in the present series. This discrepancy is due in part to the fact that 60 of our patients had been referred from elsewhere having already had exploratory surgery.

Radiology is rarely useful in making a correct preoperative diagnosis, although an upper gastrointestinal series may show distortion of the stomach or duodenum. It may, however, be of considerable help to the surgeon in determining the correct procedure applicable in a particular patient. Preoperative hepatic scintiscanning and coeliac angiography have been performed with increasing frequency at the Lahey Clinic over the years of this study. Although it is impossible to differentiate metastatic lesions in the liver from metastases from another primary neoplasm or from a hepatoma, the extent of the spread of the tumour can be assessed preoperatively by this investigation. Whether or not the hepatic pathology is the result of a bile-duct neoplasm can only be determined by laparotomy.

If a previous exploration has been performed operative cholangiography or T-tube cholangiography is an essential and accurate procedure in determining the site and extent of the neoplastic stricture. This information may also be obtained preoperatively, and a differential diagnosis from other causes of obstructive jaundice may be obtained by percutaneous transhepatic cholangiography. This procedure has rarely been performed at the Lahey Clinic for neoplastic obstruction of the bile-duct because in these cases usually no doubt exists that the patients have 'surgical jaundice' requiring an operation; the procedure is not without risk, and as a result of the procedure the proximal dilated duct is partially decompressed and may make delineation of the duct at operation more difficult. Percutaneous cholangiography, however, may prove more effective with increasing experience.

Even at operation it may be difficult to confirm the diagnosis, especially in the infiltrating type of lesion that is liable to be confused with sclerosing choledochitis (Altemeier and others, 1957) or with a benign biliary-duct stricture if previous biliary or gastric surgery has been performed. The diagnosis can only be excluded after multiple biopsies of the bile-duct have been reported to be negative.

The types of operative procedures that are available for the treatment of bile-duct neoplasms were summarized in the previous report from the Lahey Clinic (Braasch and others, 1967). The type of operation performed depends on the site of the neoplasm and the extent of the spread of the disease. The procedures can also be classified into radical, when an attempt is made to excise the neoplasm completely, and palliative, when the obstructive jaundice is relieved by insertion of a rubber stent through the neoplastic stricture or by performing a by-pass biliary-intestinal anastomosis. Until recently the majority of the radical procedures performed were for neoplasms of the distal duct, when a pancreatoduodenectomy is often possible, but radical resection for hepatic duct and supraduodenal bile-duct tumours was rarely attempted. In the series of Braasch and others (1967) 32 of 173 patients had a radical resection, of which 27 were pancreatoduodenectomies, while in the current series it was possible in 24 of 77 patients with only 15 pancreatoduodenectomies. The number of resections of the proximal ducts has therefore increased.

Since 1965 hepatic artery infusion chemotherapy has been used with increasing frequency for non-resectable malignant lesions of the bile-ducts at the Lahey Clinic after its introduction by Watkins and Sullivan (1964) for primary and secondary hepatic carcinoma. In the series reported by Braasch and others (1967) only 2 patients had received a course of hepatic artery infusion chemotherapy and no conclusions could therefore be made regarding its use. Fifteen patients have now received this treatment and it is therefore possible to assess its effect on the prognosis.

The prognosis after operation for carcinoma of the bile-ducts has been very poor in all the reported series. Braasch and others (1967) found that only about 14 per cent of patients survived for 1 year or more and 4 per cent for more than 3 years. All but 1 patient had had a distal common-duct tumour treated by pancreatoduodenectomy. One of the longest survivors after operation was reported by Altemeier and others (1957). Their patient lived for 5½ years and required seven operations. One of the patients reported in the previous series from the Lahey Clinic (Braasch and others, 1967), who was alive 3 years after undergoing a pancreatoduodenectomy for a distal duct carcinoma, eventually survived 7 years. He required two further surgical procedures for obstructive jaundice secondary to recurrent disease during this time. The poor prognosis of bile-duct tumours was also shown by Neibling and others (1949), who reported a mean survival period of only 3 or 4 months.

The present series reports considerable improvement in the immediate prognosis compared with the previous report from the Lahey Clinic; 44 per cent of the patients in the present series were alive at 1 year compared with 14 per cent in the previous series, while 8 per cent were alive at 3 years compared with 4 per cent. The average survival period of 13 months in the present series also compares favourably with that reported by Neibling and others (1949). This improvement in the immediate prognosis appears to be associated with the increased performance of radical operation especially for the proximally situated tumours: radical operations were performed in 18 per cent of the cases in the series of Braasch and others (1967) while they were carried out in 31 per cent of the cases in the present report. It therefore confirms the suggestion made by Quattlebaum and Quattlebaum (1965) that an attempt at more radical operation would improve the prognosis of this condition. Hepatic artery infusion chemotherapy has also resulted in an improvement in the prognosis of those patients receiving palliative treatment. Of the 15 patients who were thus treated, 9 were still alive after 1 year and 1 patient is still alive more than 3 years later.

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THE DELAYED HYPERSENSITIVITY RESPONSE IN PRIMARY BREAST CARCINOMA AS AN INDEX OF HOST RESISTANCE

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SUMMARY

An attempt has been made to correlate the Varidase test with possible immunological phenomena as assessed histologically. It would appear statistically that the test is more likely to be negative in the presence of poor differentiation, suggesting that there may be some form of immunological suppression in these cases. In the majority of these poorly differentiated cases there was an absence of lymphocytic involvement of the tumour. However, no obvious connexion between Varidase and lymphocytic infiltration of the tumour or sinus histiocytosis has been found.

The Varidase test cannot therefore be assumed to be a reliable guide of the accepted histological criteria of host-defence reactions. Any information as to why this test should be so consistently depressed in the presence of malignant disease has not been forthcoming. This work is a preliminary report and is an attempt to assess the total immune competence of a group of adult patients in the presence of mammary carcinoma. It is freely acknowledged that further work into the long-term survival of these patients is necessary before further conclusions can be drawn.

IT is recognized that the delayed hypersensitivity response may be reduced in malignant disease.

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Hughes and Mackay (1965) showed depression of the response to tuberculin in patients with carcinoma, and this depression became more marked as the disease progressed. Roberts and Williams (1968), using streptokinase, reported that the delayed hypersensitivity response was increasingly suppressed as the malignancy disseminated. Stjernswärd and Clifford (1970) also showed that the delayed hypersensitivity response to dinitrochlorobenzene (DNCB) is depressed in large Burkitt lymphoma tumours. In respect of humoral immunity Lytton, Hughes, and Fulthorpe (1964) showed that the circulating antibody response to tetanus toxoid was reduced in patients with malignant disease compared with patients equally debilitated but not suffering from malignancy.

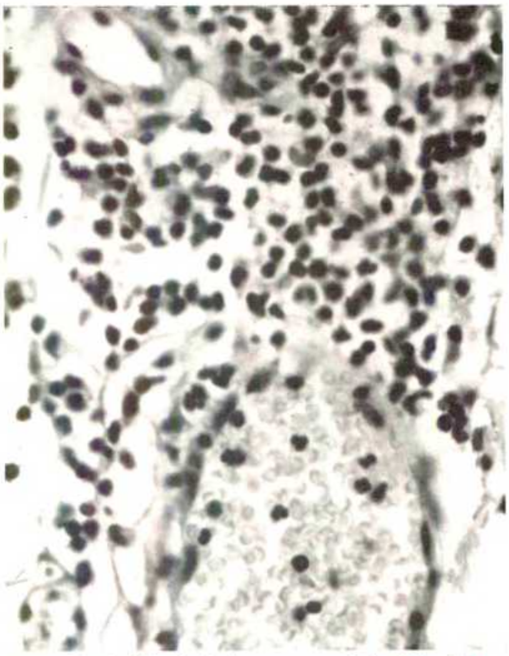

FIG. 1.—Typical histological appearance of the delayed hypersensitivity response.

The present study was undertaken to assess the cellular immune competence of a group of patients with primary carcinoma of the breast compared with a similar group of patients without known malignant disease. In addition, an attempt has been made to correlate these findings with appearances of suggested immunological significance in the primary tumour and regional nodes.

MATERIALS AND METHODS

A group of 45 women seen at the United Bristol Hospitals with primary breast carcinoma was studied. Patients with known secondary deposits from mammary carcinoma were not included in the present work.

The group was tested intradermally with streptokinase-streptodornase solution (Varidase, Lederle) following the work of Roberts and Williams (1968). Assuming that the adult population has at some time developed an immunity to the streptococcus, streptococcal antigen should when injected intradermally produce an immune reaction at the cellular level. Suppression of this response in the presence of malignancy becomes more marked as the disease progresses and is more evident in the group studied than in a group of controls without known malignancy. The two groups had a similar incidence of streptococcal infections in their past histories. The carcinoma group included 2 patients who had had rheumatic fever compared with the controls who included 1 case of rheumatic fever. There were no cases of acute nephritis in either group. The Varidase test was performed in order to provide an index of possible host resistance.

Nature of the Varidase Test.—The Varidase test was assumed by Roberts and Williams (1968) to indicate a delayed hypersensitivity response. This is confirmed by histological study of a reaction at 48 hours in a sample removed from the author's arm. There is perivascular cuffing with lymphocytes and invasion by round cells and macrophages. This histological appearance is characteristic of a delayed hypersensitivity response (Turk, 1967) (*Fig.* 1).

Technique.—Normal saline, 0·1 ml., containing 5 U. of Varidase was injected intradermally into the forearm. The reaction was read at 48 hours and compared with a normal saline control in the opposite arm. A response greater than 25 mm. with erythema and swelling was regarded as positive. Any transient erythema which was fading at 24 hours was regarded as negative, as were reactions of less significance.

Assessment.—Four variables were assessed in each patient:—

1. Delayed hypersensitivity (Varidase test).
2. Lymphocytic invasion of the tumour.
3. Sinus histiocytosis.
4. Grade of malignancy of the tumour.

1. *Varidase Test.*—This was recorded as either positive (+) or negative (−).

2. *Lymphocytic Invasion of the Tumour.*—This was graded as follows:—

An occasional lymphocyte	0
Scattered foci of lymphocytes, or a thin scattering	1
Numerous foci or germinal centres	2

3. *Sinus Histiocytosis* was graded as follows:—

No sinusoids	0
Sinusoids less than 5 cells thick	1
Sinusoids more than 5 cells thick	2
As above but with mixed cellularity	3

4. *Histological Grade of Tumour*:—

Well differentiated	1
Intermediate	2
Poorly differentiated	3

This assessment was based on the work of Patey and Scarff (1928). They graded tumours by consideration of tubule formation, hyperchromatism, and nuclear pleomorphism. The difficulties of grading tumours on morphological grounds have for the present purposes been accepted.

The histology of the tumour and the lymph-nodes was assessed on this basis by the author and compared with an independent histopathological opinion.

RESULTS

1. Varidase Test.—The results of the Varidase test are shown in *Table I*. The higher incidence of

Varidase negative in the carcinoma group is statistically significant ($\chi^2 = 4{\cdot}921$, $P < 0{\cdot}05$). Roberts and Williams (1968) showed that up to 70 per cent of patients with widespread disease were Varidase negative.

2. Varidase Test and Scarff Grading.—The results of the Varidase test compared with the Scarff grades (Patey and Scarff, 1928) are shown in *Table II*. These results suggest that the Varidase test is more likely to be suppressed in the presence of poor differentiation. This is statistically significant ($\chi^2 = 4{\cdot}213$, $P < 0{\cdot}05$).

Table I.—RESULTS OF THE VARIDASE TEST

VARIDASE	CARCINOMA OF THE BREAST	CONTROLS
V+	24	35
V−	21	10

Table II.—RESULTS OF THE VARIDASE TEST COMPARED WITH SCARFF GRADES*

VARIDASE	SCARFF GRADE		
	1	2	3
V+	1	11	12
V−	2	2	17

* Patey and Scarff (1928).

Table III.—RESULTS OF VARIDASE TEST COMPARED WITH SINUS HISTIOCYTOSIS

VARIDASE	SINUS HISTIOCYTOSIS			
	0	1	2	3
V+	2	9	6	7
V−	6	3	5	7

3. Varidase and Sinus Histiocytosis.—Sinus histiocytosis was present in very comparable degrees in all stages, irrespective of the Varidase test (*Table III*). From this study there is no evidence that the Varidase test has any correlation with sinus histiocytosis and this is confirmed statistically ($\chi^2 = 1{\cdot}906$).

4. Varidase and Lymphocytic Involvement of Tumour.—There is no apparent connexion between the Varidase test and the degree of lymphocytic involvement of the tumour (*Table IV*). This is confirmed statistically ($\chi^2 = 0{\cdot}122$).

5. Lymphocytic Involvement of the Tumour and Scarff Grading.—Comparing the Scarff grade with lymphocytic involvement of the tumour (*Table V*), poorly differentiated tumours were more likely to show no lymphocytic involvement. Comparing groups 1 and 2 with group 0 this is statistically significant ($\chi^2 = 4{\cdot}245$, $P < 0{\cdot}05$).

DISCUSSION

Host resistance to malignant disease has been under consideration since the early papers of Bashford, Murray, and Cramer (1908) and Lambert and Haines (1911), but it was not until recent years that the implications of reactive lymph-nodes or round-cell infiltration within and around the tumour came to be appreciated. Foote and Stewart (1946) first suggested that the lymphocytic invasion of a primary tumour might represent an immunological defence mechanism, and some series have shown this to be indicative of a favourable prognosis (Moore and Foote, 1949; Richardson, 1956). Black, Opler, and Speer (1955) noted that those patients with marked lymphocytic infiltration of the tumour had an observed survival of at least twice that expected from his series.

Table IV.—RESULTS OF VARIDASE TEST COMPARED WITH LYMPHOCYTIC INVOLVEMENT OF TUMOUR

VARIDASE	LYMPHOCYTIC INVOLVEMENT OF TUMOUR		
	0	1	2
V+	8	14	2
V−	9	6	6

Table V.—LYMPHOCYTIC INVOLVEMENT OF THE TUMOUR COMPARED WITH SCARFF GRADES

SCARFF GRADE	LYMPHOCYTIC INVOLVEMENT OF TUMOUR		
	0	1	2
2	3	11	2
3	13	8	6

Geschickter (1945) first drew attention to the so-called 'medullary breast cancer with lymphoid infiltration' as a new clinical entity. This type of breast carcinoma is known to be associated with a good prognosis (Bloom, Richardson, and Field, 1970). According to Richardson's (1956) histological criteria there were no cases in this series which fell into the medullary group. In the series of Bloom and others (1970) there was an incidence of 7 per cent.

The majority of reports concerning sinus histiocytosis regard it as a favourable prognostic sign (Black, Kerpe, and Speer, 1953; Black, Opler, and Speer, 1954, 1956). Berg (1956) doubted whether sinus histiocytosis was an index of host resistance, regarding it as a normal structural feature of lymph-nodes. This was disputed by Black and Speer (1958), who regard sinus histiocytosis as an uncommon finding in lymph-nodes removed from non-cancerous patients. Sinus histiocytosis is a reactive change in the tissue of a host and if it is associated with an improved survival rate it may rightly be termed an expression of host resistance. This view was endorsed and developed by Hamlin (1968) in her extensive survey of possible host resistance based on histological criteria. She found a distinct correlation between marked sinus histiocytosis and good survival. Black (1970) again emphasizes the improved survival in a more recent report.

The degree of malignancy of the primary tumour has long been assumed to affect long-term survival. Following the work of Broders (1920), Patey and Scarff (1928) graded breast carcinomas into groups depending on their histological appearance. A high grade of malignancy is not, however, incompatible with long survival, and these subdivisions only serve further to demonstrate the unpredictability of forecasting long-term survival.

Acknowledgements.—I wish to thank the surgeons of the United Bristol Hospitals for access to their patients, and to Mr. A. J. Webb for his advice and encouragement. My thanks are also due to Dr. A. C. Hunt, lately Consultant Pathologist to the United Bristol Hospitals, for his help in the interpretation of the histology and to Miss E. H. L. Duncan of the University of Bristol Statistical Department for her advice.

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SURGICAL OBJECTIVES IN UNRESECTED CANCER OF THE HEAD OF THE PANCREAS*

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SUMMARY

Twenty-seven patients with obstructive jaundice due to unresected cancer of the pancreas have been reviewed. The surgical objectives in treating this sort of patient were taken as the need to make a positive diagnosis and to palliate until death. There was failure to establish the diagnosis of cancer at operation (17 patients), failure to attain permanent biliary decompression (1 patient), failure to anticipate duodenal obstruction (3 patients), and failure to relieve pancreatic pain (8 patients). As a result of this review we have evolved a set of guide-lines which should be considered when treating patients with irresectable cancer of the pancreas.

SINCE Robson and Cammidge's (1907) dismal survey, in which only 2 of 66 patients with irresectable cancer of the pancreas survived cholecysto-enterostomy, there has been a gradually growing enthusiasm for palliation of irresectable cancer of the head of the pancreas. Indeed today the treatment of these patients is, or should be, an exercise in short-term palliation.

The objectives of surgical treatment in jaundiced patients presumed to have irresectable cancer of the pancreas are to make a firm diagnosis and to relieve distressing symptoms. Although most of these patients have only a short time to live, the scope of the operation should be extended to prevent anticipated symptoms which might otherwise necessitate a second operation. We have reviewed a series of such patients in order to find the reasons for failure to achieve these objectives. As a result we now feel that the traditional quick laparotomy and gall-bladder decompression can be justified only in the critically ill terminal patient.

THE PRESENT SERIES

This review concerns 27 patients with obstructive jaundice thought to be due to cancer of the head of the pancreas who were operated on between 1964 and 1970 by one of us. All but 1 patient had a biliary decompression procedure. Eleven patients were lost to follow-up. One patient died shortly after operation; the other patients survived to be discharged from hospital. The review took into account the following features: histological diagnosis, adequacy of biliary decompression, duodenal decompression, and relief of pancreatic pain.

DIAGNOSIS

The diagnosis of cancer of the pancreas was made histologically in 19 patients, either from operation biopsy specimens (6 patients) or at post-mortem examination (9 patients) or both (4 patients). The remaining 8 patients were considered to have cancer of the pancreas primarily because a dilated, blue, thin-walled common bile-duct was found at operation. Operative biopsies were taken from any obvious secondary deposit in the abdomen, from the paraduodenal peritoneum if it appeared abnormal, or from the coeliac and common-duct nodes; on one occasion a pancreatic biopsy was considered justified.

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* Part of this paper was read at the Forty-fourth General Scientific Meeting of the Royal Australasian College of Surgeons held in Sydney in May, 1971.

Case 1.—A. S., a 63-year-old landowner, had a laparotomy and cholecystojejunostomy in June, 1967, elsewhere for presumed cancer of the head of the pancreas, and was told the likely course of events. A year later he was well, although extremely concerned about his future and about the timing of personal decisions concerning his estate. At a re-exploration in May, 1968, the pancreas was hard throughout. Biopsies of the peritoneum and lymph-nodes were negative for cancer but a transduodenal biopsy of the pancreas showed adenocarcinoma.

The unconfirmed operative diagnosis of cancer of the head of the pancreas was challenged in another 2 patients who developed pancreatitis 3 and 11 months after their initial operation. The provisional diagnosis was later proved: in the first patient by biopsy at a subsequent operation; in the second at a post-mortem examination.

Case 2.—E. G., a 78-year-old female, presented with jaundice in April, 1969. At laparotomy the pancreas was hard throughout and enlarged. The common duct was 4 cm. in diameter, thin-walled, and blue. Although biopsies of the paraduodenal peritoneum and the coeliac lymph-nodes did not contain malignant tissue, we still thought that the patient had cancer of the pancreas. In January, 1970, she developed severe upper abdominal pain with the serum amylase raised to 667 Somogyi units. In view of her good general health and a weight-gain of 6 kg. since operation the original diagnosis was questioned. However, when she finally died in December, 1970, a well-differentiated adenocarcinoma of the pancreas was found.

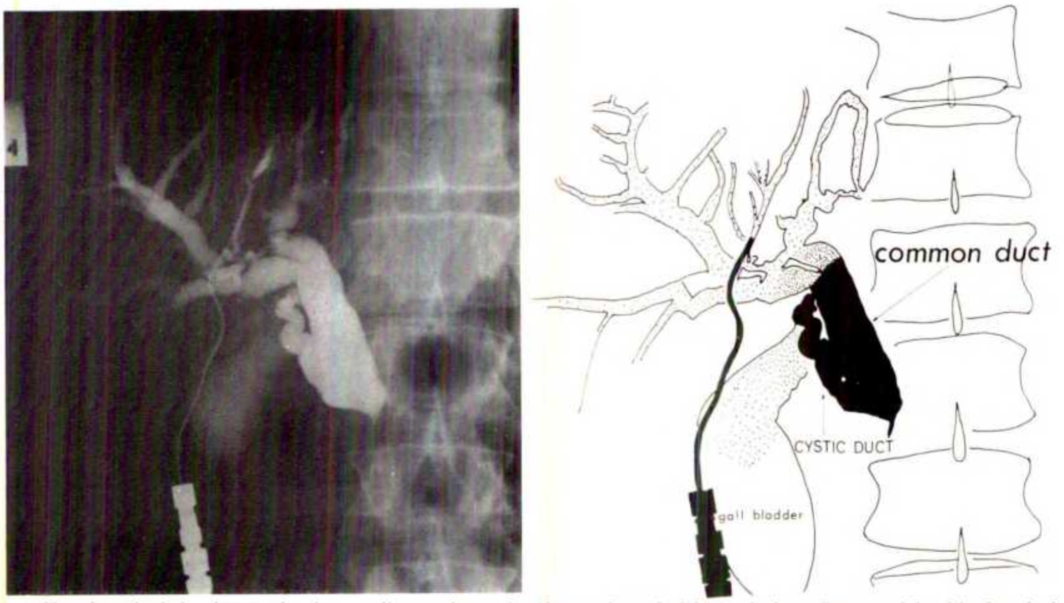

FIG. 1.—Transhepatic cholangiogram showing a malignant obstruction close to the end of the cystic duct. Because of the risk of cystic duct occlusion the gall-bladder was removed and the common duct used for decompression.

BILIARY DECOMPRESSION

One patient in the series had a massive tumour in the porta hepatis and did not undergo biliary decompression. Eighteen patients underwent biliary decompression via the gall-bladder. Nine patients had decompression of the hepatic duct because of either a previous cholecystectomy or a diseased gall-bladder, or a low cystic duct termination (*Fig.* 1). Despite precautions aimed at preventing the return of obstructive jaundice during the postoperative period, 1 of the patients who was followed up (*Case* 3) became jaundiced owing to extension of the growth to the cystic duct.

Case 3.—W. W., a 68-year-old male, developed obstructive jaundice. At laparotomy in January, 1969, a cholangiogram taken through the gall-bladder (*Fig.* 2) showed obstruction of the common bile-duct well below the presumed site of entry of the cystic duct; a cholecystenterostomy was performed. Six months later jaundice reappeared. At reoperation the gall-bladder was collapsed and the cancer (outlined by transhepatic cholangiography) now occluded the entry of the cystic duct (*Fig.* 2). A high decompression of the common hepatic duct produced permanent relief of jaundice until the death of the patient 5 months later.

DUODENAL DECOMPRESSION

Four patients in this series had a gastro-enterostomy at the time of their biliary decompression. One patient had frank duodenal obstruction, and the other 3 had distortion of the duodenum in the barium meal. Another 3 patients, each with a normal barium meal at the initial operation, developed duodenal obstruction with vomiting owing to extension of the tumour after the initial operation, and each subsequently underwent gastro-enterostomy. Two of these patients had a positive biopsy of the paraduodenal peritoneum at their first operation, and in the other

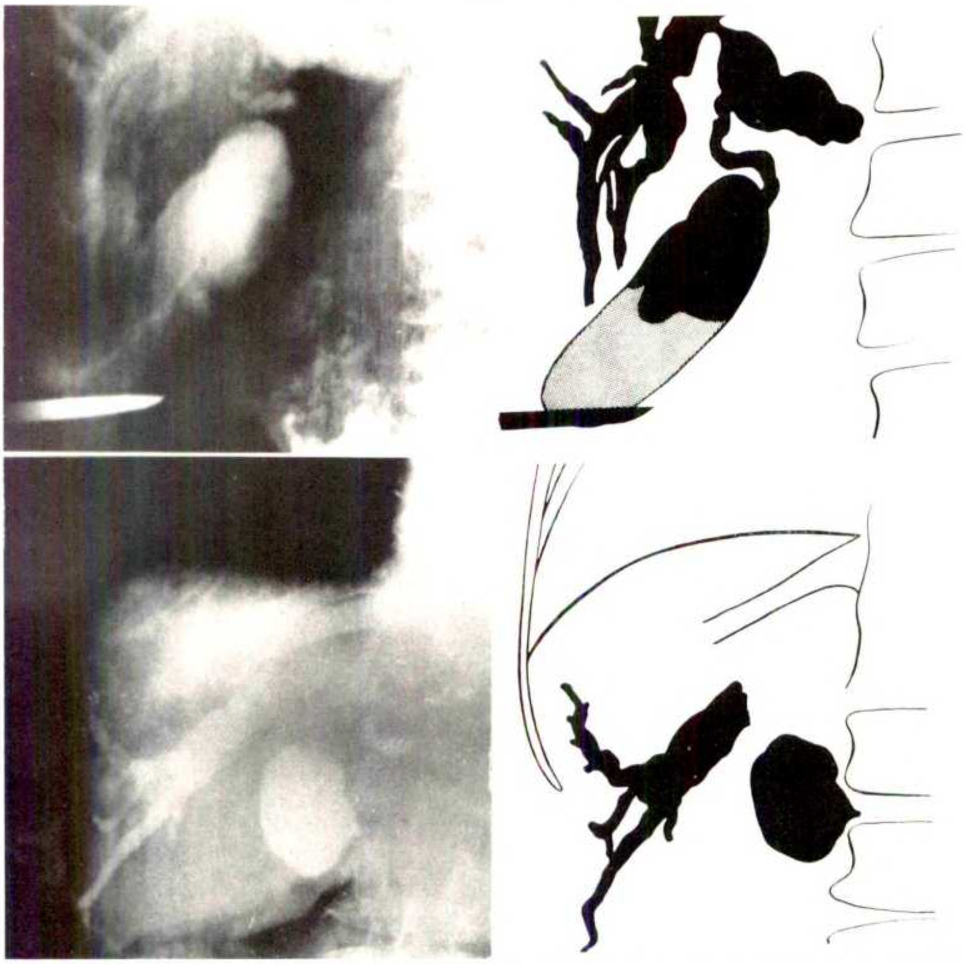

FIG. 2.—Cholangiograms of *Case* 3. The upper cholangiogram, taken at operation, appears to show a high cystic-duct termination well away from the obstruction. The lower cholangiogram taken just before the second operation fails to outline the gall-bladder or cystic duct which had become obstructed by upward extension of the growth.

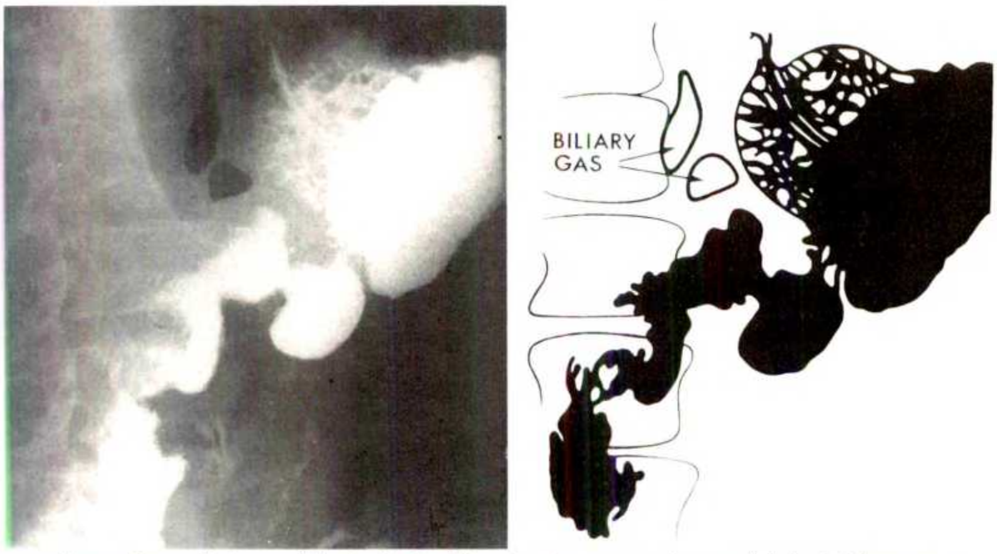

FIG. 3.—*Case* 5. Barium meal showing duodenal distortion due to presumed cancer of the head of the pancreas.

patient it was noted that the plane between the pancreas and the inferior vena cava was obliterated. Duodenal obstruction subsequent to the biliary decompression operation can be rapid and debilitating, and negate the palliative advantage of the relieving of jaundice, as the following case records show.

Case 4.—P. F., a 46-year-old male, had a cholecystoenterostomy and entero-anastomosis in June, 1967, for cancer of the head of the pancreas proved by paraduodenal biopsy. The preoperative barium meal was normal. Five weeks later the patient developed vomiting, and a barium meal showed a dilated stomach and a deformed second part of the duodenum. Gastro-enterostomy restored gastro-intestinal patency for the 4 remaining months of life.

Case 5.—D. Mc., a 69-year-old male, had a choledochoduodenostomy for presumed cancer of the pancreas in April, 1969. Attempted mobilization of the pancreas failed owing to obliteration of the plane between it and the inferior vena cava. The barium meal prior to operation was normal. Four months later the patient developed vomiting and the barium meal showed deformity of the antrum, pylorus, and duodenum (*Fig.* 3). In August, 1969, a gastro-enterostomy was performed. The patient was reasonably well until December, 1969, when he was lost to follow-up.

RELIEF FOR PANCREATIC PAIN

Nine patients had pancreatic pain preoperatively and were submitted to alcohol injection of the coeliac ganglia region during their biliary decompression operation. There was a fall in blood-pressure in all 6 patients in whom the pressure was closely monitored. One patient was relieved of pain until his death 3 months later. Six patients were unrelieved. Two patients obtained temporary relief.

Case 6.—R. O. H., a 43-year-old male with severe, persistent, deep epigastric pain, presented with jaundice which was initially diagnosed as being caused by chronic pancreatitis. A barium meal showed distortion of the duodenum. Because of increasing jaundice a transhepatic cholangiogram was performed and showed complete obstruction of the common bile-duct. At laparotomy in November, 1967, the paraduodenal peritoneum was biopsied and indicated the presence of cancer. In view of the cholangiogram findings of low cystic-duct entry, and duodenal involvement, as well as the severe pain experienced by the patient, a high hepaticojejunostomy, gastro-enterostomy, and injection of the coeliac ganglia region with 2 ml. of absolute alcohol were undertaken. Although there was an immediate fall in blood-pressure after the injection of alcohol, the pain was relieved for only 4 weeks. The patient died 5 months after the operation, unjaundiced and without vomiting, but with constant severe debilitating pain requiring morphine. At post-mortem examination the primary tumour occupied the whole pancreas; there were many lymph-node and hepatic metastases.

DISCUSSION

This survey is incomplete in two respects: the diagnosis of cancer was not always proved and the follow-up is incomplete. Despite this defect it does serve to emphasize the high number of surgical failures: failure to diagnose correctly, failure to relieve jaundice permanently, failure to anticipate duodenal obstruction accurately, and failure to combat pain.

Misgivings over the surgical treatment of irresectable cancer of the pancreas have been expressed by many authors. Cattell and Warren (1953), concerned about this aspect, listed four palliative procedures including ligation of part of the arterial supply of the pancreas. Since then the failure of gall-bladder decompression alone to palliate successfully has been considered by various authors (Warren, 1950; Glassman and Johnston, 1955; Elmslie, 1968; Gallitano, Fransen, and Martin, 1968; White, Murat, and Morgan, 1968).

The diagnosis of cancer of the pancreas is frequently elusive. Glenn and Thorbjarnarson (1964), using operation and autopsy data, reported metastases (including lung and skeletal metastases) in less than 143 patients in a series of 236 patients with cancer of the pancreas. When biopsies are not positive we have found the guide-line of Smith and Sherlock (1964) to be of great value. They stated: 'If there is jaundice and an irregular enlargement of the head of the pancreas which might be neoplastic, the surgeon should look at the common bile duct for the answer. The grossly dilated thin-walled, translucent, duct typical of obstruction by a tumour is very different from the white, opaque, thick-walled, adherent, duct typical of chronic pancreatico-biliary infection.' The transhepatic cholangiogram is also of value in making this distinction (Glenn and Thorbjarnarson, 1964; Elmslie and Newstead, 1969). In exceptional circumstances, as in the present *Case* 1, if doubt still exists transduodenal needle biopsy can be employed on the understanding that if chronic pancreatitis alone is found in the specimen the primary disease could still be cancer of the pancreas (Schultz and Sanders, 1963).

Although jaundice does sometimes appear as a terminal event owing either to hepatic metastasis or to extreme cholangitis, the failure of jaundice to remit or the reappearance of jaundice after operation is usually evidence of failure of the operative procedure to achieve biliary decompression. In one series (Gallitano and others, 1968) biliary drainage failed to relieve jaundice in 25 per cent of the patients; presumably the cystic duct was blocked in some of these patients. At operation it cannot be assumed that the distended gall-bladder is necessarily patent to the common duct. The advantage of cholangiography, either before or at operation, is twofold. Not only does it locate the upper limit of the block relative to the cystic duct but also it demonstrates whether or not the cystic duct is patent (Elmslie and Newstead, 1969). Reobstruction in 1 of our patients (*Case* 3) may have been due to misinterpretation of the original cholangiogram. We do not claim to have produced evidence in favour of routine common-duct decompression. However, it seems reasonable to advocate cholecystectomy and common-duct decompression if the patient is in relatively good health and if doubt exists about the termination of the cystic duct.

Occasional non-mechanical vomiting as an accompaniment of nausea is not uncommon in patients with cancer of the head of the pancreas. The progression of the disease towards duodenal obstruction is generally regarded as a signal for gastro-enterostomy at the time of biliary decompression. Our experience suggests that it should also be performed if at operation there is suspected spread to the paraduodenal peritoneum and if the plane between the pancreas and the inferior vena cava is difficult to display. In Glassman and Johnston's (1955) series of 20 patients 3 required gastro-enterostomy soon after biliary decompression; consequently they suggested gastro-enterostomy as a routine procedure. With this approach the patient at risk is the one with pancreatitis misidentified as cancer. One patient presumed now to have pancreatitis but initially thought to have cancer has developed ulceration at the gastrojejunal stoma (Proudman, 1971).

In the past abdominal surgeons operating on cancer have been particularly concerned with survival periods. Now that the technical advances in this sort of surgery have reached their limit, more emphasis is being placed on the quality of the survival period and nowhere is this better exemplified than in irresectable cancer of the head of the pancreas causing pain. In the present series alcohol was injected into the coeliac ganglia region if the pain was 'pancreatic' (boring, epigastric, or lumbar pain, occasionally paroxysmal, sometimes nocturnal, and frequently relieved by lumbar flexion). Pain due to biliary or hepatic distension (dull, mild, and in the right upper quadrant) was relieved by biliary decompression alone. The almost uniform failure of alcohol injection in our series should not be taken to represent a failure of the principle. Rather it could well be a measure of the technique used. Two possible reasons for failure were the volume of alcohol used and the preliminary dissection of the area before the injection was undertaken. The volume of absolute alcohol was 2 ml. in the earlier injections (1966–8) and 5 ml. in the later ones—volumes which are considerably less than those used by White and others (1968) (10 ml. of absolute alcohol) and by Bridenbaugh, Moore, and Campbell (1964) (50 ml. of 50 per cent alcohol). Furthermore, in our hands some dissection usually preceded the injection; sometimes in mobilizing the pancreas from the right and at other times by dividing the posterior parietal peritoneum above the pancreas thus opening the retroperitoneal space which contains the ganglia and their connexions. Presumably two reasons for the excellent results obtained by dorsal injection (Bridenbaugh and others, 1964) are the large volume and the integrity of the restraining peritoneum in front of the injection. None of the patients in our series was submitted to coeliac block by the dorsal route.

CONCLUSIONS

In the light of this review certain guide-lines can be given for the treatment of obstructive cancer of the head of the pancreas which is considered, for one reason or another, to be irresectable. First, a quick gall-bladder decompression is not a satisfactory palliative procedure unless the patient is near death. Secondly, a determined effort should be made to arrive at the correct diagnosis—by radiological display of the block, by looking at the common duct, by mobilization of the head of the pancreas, by biopsy of the surrounding peritoneum and lymph-nodes, and occasionally by transduodenal biopsy of the swelling. Thirdly, the relationship of the entry of the cystic duct into the common duct and the upper level of the growth should be considered. When they are adjacent, the common duct (rather than the gall-bladder) should be used for decompression. Fourthly, if at operation there is evidence of spread towards the duodenum a gastro-enterostomy should be undertaken. Finally, a small volume of absolute alcohol injected into the coeliac ganglia region at the conclusion of this sort of operation is unlikely to be of benefit, particularly if the posterior peritoneum has been divided. As a result of this review we will undertake alcohol injection via the dorsal route postoperatively (Bridenbaugh and others, 1964) in those patients who have pain whether or not they have had an attempted block at operation. These measures may not prolong the patient's life but they should make it more tolerable.

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ABDOMINAL AORTIC ANEURYSM AND HORSE-SHOE KIDNEY

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SUMMARY

Successful abdominal aortic replacement for aneurysm in 3 patients with horse-shoe kidney is reported. The anatomy of the horse-shoe kidney, particularly in relation to its blood-supply, is described. Because of the lack of correlation between the radiological and operative findings it is suggested that the final decision for replacement of the aorta must be taken at operation. Techniques for grafting which obviate the need to divide the isthmus of the horse-shoe kidney and decrease the operating time are described.

THE horse-shoe kidney is prone to acquired disease in 80–90 per cent of cases and with advancing years the likelihood of this increases. Atherosclerotic aneurysm of the abdominal aorta is seen in the elderly, frequently as one manifestation of generalized atheroma, and such patients must be considered as liable to some diminution of renal reserve owing to renal artery atherosclerosis or hypertensive arteriosclerosis (Szilagyi, Smith, and Whitcomb, 1959). Since the blood-supply to a horse-shoe kidney is frequently anomalous and may arise from multiple sites on the abdominal aorta or iliac arteries the combination of horse-shoe kidney with abdominal aortic aneurysm poses a difficult problem in the preservation of renal function with operative treatment of the aneurysm. We report here our experience of 3 patients with this rare combination, which has previously been reported in only 18 cases (Julian, 1956; Phelan, Bernatz, and De Weerd, 1957; Szilagyi and others, 1959; Wilder, Kock, and Stein, 1963; Mannick, Brooks, Bosher, and Hume, 1964; Lynn and Bruce, 1965; Minken and Rob, 1967; Cox and Machado, 1968; Killen, Scott, and Rhamy, 1968; Cohn, Stoney, and Wylie, 1969; Scott, De Bakey, and Mani, 1969). In 16 of these replacement of the aneurysm was undertaken successfully.

The kidney develops from the urogenital ridge. Development is progressive in a caudal direction with the formation of primitive pronephros, followed by the temporarily functioning mesonephros, and finally the metanephros which forms the definitive kidney and derives its drainage system from a lateral bud from the mesonephric duct. With differential growth the kidney ascends to its definitive position. It is postulated (Arey, 1965) that convergent growth of the lateral buds of the mesonephric duct which are to form the drainage systems of the definitive kidneys may result in fusion of the metanephric masses across the midline, so that the definitive kidney is the horse-shoe type. Ascent of this fused kidney is impeded and it tends to be sited lower than normal with the isthmus usually at the level of the fourth or fifth lumbar vertebrae, that is, at or near the level of the abdominal aortic bifurcation.

The developing kidney derives a segmental blood-supply from the aorta. With progressive development the more cephalad vessels disappear along with the mesonephros and maximal development occurs caudally in the region where the definitive kidney will develop. In this region the arteries form a network, the rete arteriosum urogenitale, which supplies in varying degrees the developing suprarenal and urogenital organs. Eventually some roots from the aorta degenerate and the area which they have supplied is taken over by a neighbouring root. Finally, the kidney comes to be supplied by one artery from the aorta, which divides in the hilum to supply the five definitive segments of the kidney. Graves (1971) has suggested that the persistence of some of these segmental roots from the aorta accounts for the variation of origin of the segmental renal arteries which may be manifest by a number of separate vessels from the aorta supplying particular segments of the kidney. These anomalous vessels are not 'accessory' or 'extra' arteries but normal segmental arteries supplying a particular segment of the kidney. Such arteries are true end arteries, there being no communications between them from segment to segment within the kidney.

Graves (1971), in a precise study of the renal blood-supply by arteriography and injection of coloured resins, has shown that the supply of the horse-shoe kidney is similarly segmental in nature. His studies indicate that the isthmus of the horse-shoe kidney represents the posterior segment of the lower pole and that vessels running to the isthmus from the iliac arteries or aorta below the isthmus represent the posterior branches of the lower segment artery which have taken origin from the nearest point on the aortic axis to the fused developing metanephros.

Venous drainage of the horse-shoe kidney may also be anomalous and the common variations are the isthmus vein running across the front of the aorta to the inferior vena cava and the left renal vein coursing behind the aorta to the inferior vena cava, an anomaly which occurs in about 2 per cent of patients (Culp and Bernatz, 1961).

POSSIBILITY OF AORTIC REPLACEMENT

Papin (1914) recorded 139 horse-shoe kidneys in 126 of which the arterial supply was accurately documented (*Table I*). He divided the arterial supply of the horse-shoe kidneys into three major groups:—

Group 1: Normal renal arteries (20 per cent of cases).

Group 2: Three to five renal arteries (66 per cent of cases).

Group 3: More than five renal arteries (14 per cent of cases).

In group 1 replacement of the abdominal aorta below the level of the renal arteries should not pose a problem in the preservation of the renal blood-supply.

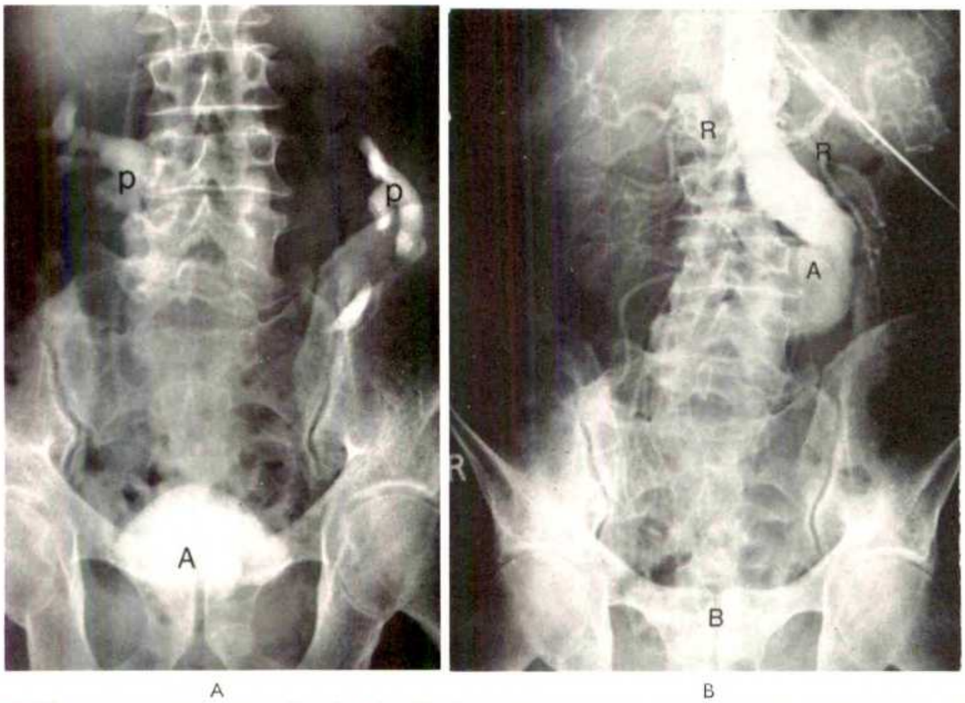


FIG. 1.—A, The intravenous pyelogram outlines the pelves (P) of the horse-shoe kidney and the low position of the kidney is well demonstrated. On the left the kidney is rotated with the calices medial and the pelvis lateral, while the right half of the horse-shoe is not rotated. The ureters are not seen. B, The aortogram shows two renal arteries (R) arising from the aorta above the aneurysm (A).

Table I.—ARTERIAL SUPPLY OF 126 HORSE-SHOE KIDNEYS (PAPIN, 1914)

No. of Arteries	*No. of Cases*	
1	1	Group 1 (20 per cent)
2	26	
3	40	Group 2 (66 per cent)
4	23	
5	20	
6	9	Group 3 (14 per cent)
7	3	
8	2	
9	0	
10	2	

In group 2 the horse-shoe kidney was supplied by three to five renal arteries and in all of these there were two arteries at the normal site and additional vessels from varying sites distal to these. The aorta was the commonest site of origin of additional arteries (73 per cent), the remainder arising from the common iliac arteries except in 2 cases (internal iliac and middle sacral). The additional vessels were distributed equally between the main renal substance and the isthmus. In this group replacement of the aorta below the level of the vessels at the normal site is theoretically possible, but additional vessels from the aorta may have to be sacrificed and one or more segments of the kidney will be rendered ischaemic. Additional vessels from the iliac arteries may well be preserved if the iliac vessels are not to be replaced with the aorta, but division of such vessels may be necessary for mobilization of the horse-shoe kidney in gaining access to the aorta. Again, a segment of the kidney will be rendered ischaemic. From Graves's (1971) studies it would seem that in this group the supply to the apical, upper, middle, and posterior segments of both kidneys would be preserved in most cases, and that ischaemia would be confined to the lower segments which include the isthmus.

In group 3 the renal vessels were small and multiple, and from the description would almost certainly render surgical replacement of the aorta with the preservation of renal function impossible.

It would seem, then, that aortic replacement in a patient with a horse-shoe kidney without producing renal ischaemia is possible only in the group with normal renal arteries, that is, in 20 per cent of cases of horse-shoe kidney. In the remaining 80 per cent of cases some degree of renal ischaemia is likely to result from aortic replacement, which seems possible in those with three to five arteries (60 per cent), and is probably impossible in those with more than five renal arteries (14 per cent).

CASE REPORTS

Case 1.—A 65-year-old man presented complaining of intermittent claudication in both legs at 200 m. and a thumping sensation in the lower abdomen. There were no other symptoms or any past history of cardiovascular disease. Examination revealed hypertension of the order of 230/135 without cardiomegaly. In the mid-abdomen there was a pulsatile mass 10 cm. in diameter and the peripheral pulses below the femoral were absent in both legs. Harsh bruits were audible over the abdominal aorta and over both common femoral arteries. The patient was admitted to hospital for assessment for aneurysm replacement.

An intravenous pyelogram (I.V.P.) revealed the presence of a horse-shoe kidney (*Fig.* 1 A). In view of this an aortogram was obtained which showed an aneurysm of the abdominal aorta below the level of two renal arteries (*Fig.* 1 B). The blood-urea was 40 mg. per 100 ml.

It was decided to delay aortic replacement until the hypertension had been controlled. However, in spite of vigorous treatment the hypertension did not improve and the aneurysm increased in size over the following 3 months. The patient was therefore readmitted for an aortic replacement graft on 8 Feb., 1971.

At operation (*Fig.* 2) the findings were not as expected from the radiological appearances. There was a left common iliac aneurysm and an aortic aneurysm. The kidney was supplied by two renal arteries as suggested on the aortogram. A large isthmic vein crossed the aneurysm to the junction of the left renal vein with the inferior vena cava. The kidney had three pelves. On the right side a single ureter descended in front of the isthmus to the bladder. The left half of the kidney had two pelves, one from the isthmic region and one from the lateral aspect of the kidney (the lateral position being due to rotation), the ureters joining below the kidney to descend to the bladder. The renal substance appeared normal and there were no palpable calculi.

The aortic aneurysm and left common iliac aneurysm were isolated by clamping the aorta below the level of the renal arteries, the right common iliac artery, and the left internal and external iliac arteries. The aortic aneurysm was opened and the lumbar arteries were controlled by oversewing from within. A bifurcation graft was sutured to the neck of the aneurysm from within, and after division of the right common iliac artery and left common iliac aneurysm the limbs of the graft were passed intraluminally from the aneurysm and brought out through

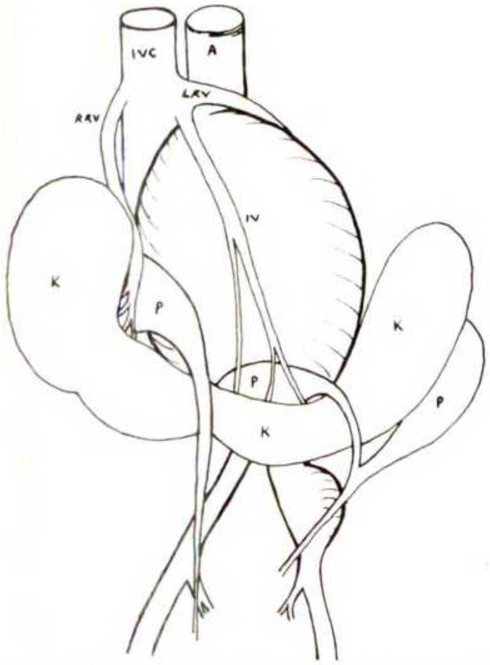
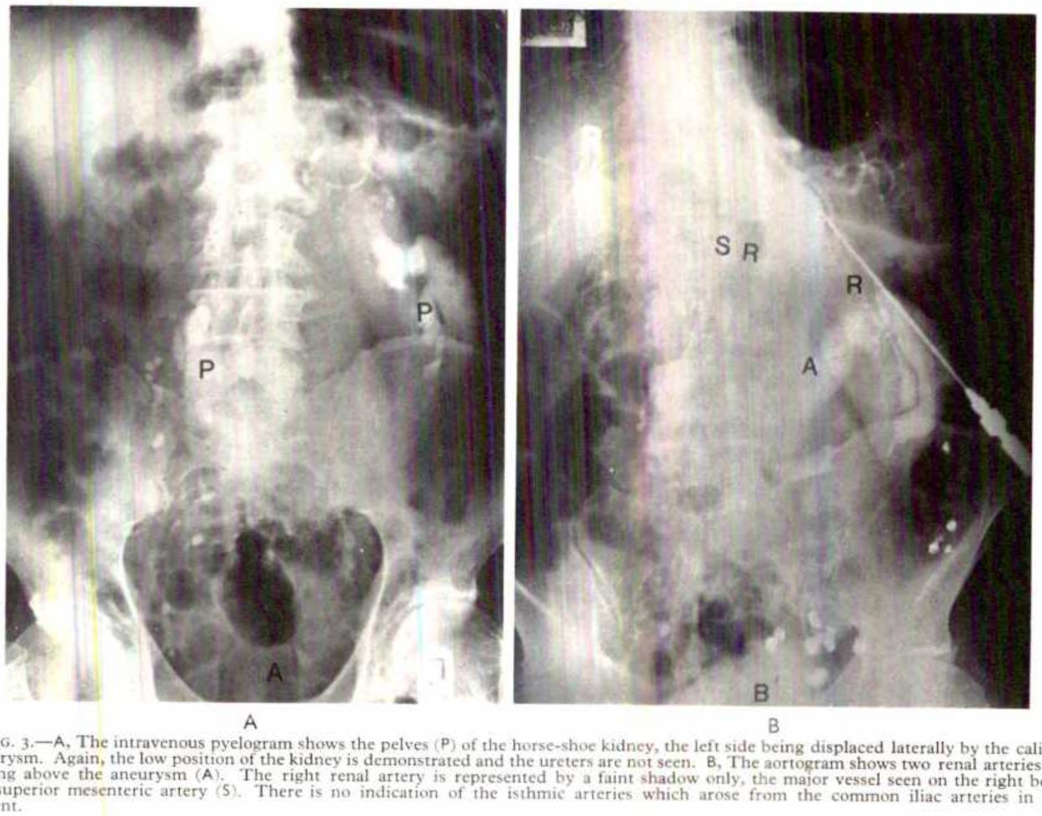


FIG. 2.—Diagrammatic representation of the operation findings in *Case* 1. The renal arteries were behind the aneurysm on the left side and behind the vena cava on the right side. IVC, Inferior vena cava. IV, Isthmic vein. A, Aorta. RRV, Right renal vein LRV, Left renal vein. K, Kidney. P, Pelvis.



A B

FIG. 3.—A, The intravenous pyelogram shows the pelves (P) of the horse-shoe kidney, the left side being displaced laterally by the caliceal aneurysm. Again, the low position of the kidney is demonstrated and the ureters are not seen. B, The aortogram shows two renal arteries (R) arising above the aneurysm (A). The right renal artery is represented by a faint shadow only, the major vessel seen on the right being the superior mesenteric artery (S). There is no indication of the isthmic arteries which arose from the common iliac arteries in this patient.

the divided ends. The right limb of the graft was sutured end to end to the common iliac artery, and the left limb end to side to the external iliac artery after ligation of the common iliac stump below the aneurysm. Occlusion time to the right leg was 35 minutes and to the left 50 minutes. The total operating time was 2 hours 10 minutes. Using this technique it was not necessary to mobilize the kidney from the aneurysm and the isthmus did not require division. The patient had an uneventful recovery and has remained well. His hypertension has settled to 160/100 without hypotensive therapy.

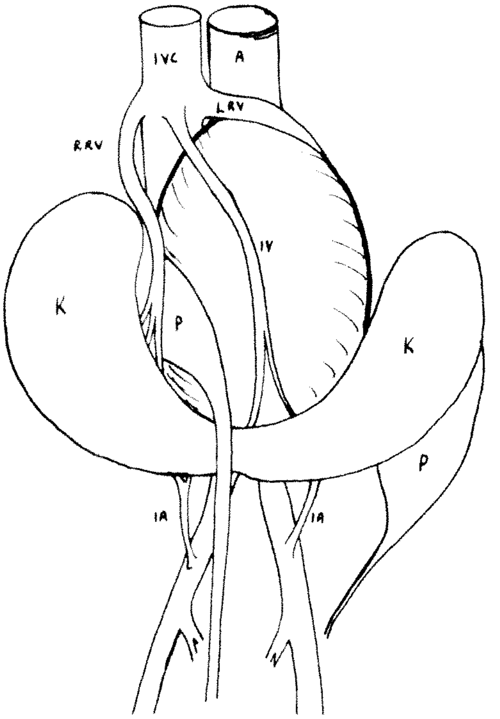


FIG. 4.—Diagrammatic representation of the operation findings in *Case* 2. The renal arteries were behind the aneurysm on the left side and behind the vena cava on the right side. IVC, Inferior vena cava. IV, Isthmic vein. A, Aorta. RRV, Right renal vein. LRV, Left renal vein. K, Kidney. P, Pelvis. IA, Isthmic artery.

Case 2.—A 75-year-old man presented with anorexia and weight-loss. There were no other symptoms or any past history of cardiovascular disease. On examination there was marked pallor, a large, pulsatile, mid-abdominal mass, 16 cm. in diameter, and normal peripheral pulses in both legs. There were no bruits. The patient was admitted to hospital for assessment for aneurysm replacement.

Investigation revealed a hypochromic, microcytic anaemia with a haemoglobin level of 50 per cent. Examination of the stool for occult blood proved positive and barium studies of both the upper and lower alimentary tract revealed diverticulosis coli. A horse-shoe kidney was seen on I.V.P. and a subsequent aortogram showed a large aneurysm of the abdominal aorta below the level of two renal arteries (*Fig.* 3 A, B). The blood-urea was 28 mg. per 100 ml.

The anaemia was considered to be due to poor diet combined with bleeding from diverticulosis coli and it responded well to iron therapy. Replacement of the abdominal aorta was undertaken on 21 June, 1971.

As in the first case the operation findings were not as expected from the radiological appearances (*Fig.* 4). The aneurysm was confined to the aorta. A large isthmic vein crossed the aneurysm to the inferior vena cava. In addition to two renal arteries at the normal site there were two isthmic arteries each arising from the corresponding common iliac artery and not suspected from the aortogram. A vein from the isthmus accompanied each of these vessels and drained into the common iliac vein. Two ureters descended to the bladder in front of the isthmus. The renal substance appeared normal and there were no palpable calculi.

The aortic aneurysm was isolated by clamping the aorta below the level of the renal arteries and each common iliac artery proximal to the origins of the isthmic arteries. The technique used was as in the first case except that it was possible to place a tube graft within the aneurysm, the lower end being sutured to the aortic bifurcation. The isthmic arteries were preserved. Occlusion time to both legs was 40 minutes and the total operating time was 3 hours. Again, it was not necessary to mobilize the kidney from the aneurysm and the isthmus did not require division. The patient had an uneventful recovery and has remained well.

Case 3.—A 68-year-old man had been noted to have a large abdominal aortic aneurysm when he had suffered a left hemiplegia 2½ years previously. The aneurysm had increased in size over the month before consideration for operation and had been accompanied by abdominal discomfort and tenderness of the sac. Rupture was considered to be imminent. On examination he was a frail man with a mild residual left hemiplegia. There was a large, pulsatile, central abdominal mass and all his peripheral pulses were present.

Investigation by high lumbar aortography and intravenous and retrograde pyelography confirmed that he had a large aortic aneurysm and revealed a horse-shoe kidney with some small radiolucent calculi in the left renal pelvis. The renal arteries seemed normal in their site of origin.

The findings were again not accurately predicted by investigation. Three isthmic veins and two small isthmic arteries were associated with the common iliac vessels. There was no isthmic vein draining proximally in this case and large renal vessels connected fairly normal renal hila to the aorta and inferior vena cava at the normal anatomical level and just proximal to the aneurysm.

It was necessary to divide the small isthmic vessels to obtain access to the distal extremity of the aneurysm. The kidney was then lifted up like an apron to expose the anterior surface of the aneurysm. The aorta and common iliac arteries were controlled, the aneurysm opened, and a Dacron tube graft was then sutured within the aortic lumen. The patient's postoperative course was stormy but he survived the procedure and his renal function remained good.

DISCUSSION

Because the horse-shoe kidney embraces the abdominal aorta and may present as an apparently pulsatile mid-abdominal mass, and because the presence of a horse-shoe kidney may not be suspected in a patient with an obvious aneurysm a clinical diagnosis of an aortic aneurysm and horse-shoe kidney is unlikely. Such a diagnosis can be made accurately only on radiology or at operation. Indeed, of the 18 cases reported in the literature, a clinical diagnosis was not made in any, a radiological diagnosis was made in 9 cases, and an operative diagnosis in 9 cases. In the 3 patients reported here a clinical diagnosis was not made. Routine I.V.P. established the presence of a horse-shoe kidney and subsequent aortograms confirmed renal arteries arising from the aorta above the aneurysm, indicating operability of the aneurysm with preservation of at least some renal blood-supply. However, owing to inadequate demonstration of distal additional arteries and anomalous venous drainage the technique for aortic replacement was of necessity decided at operation.

Our investigation of patients with aortic aneurysms normally includes intravenous pyelography but not lumbar aortography. An aortogram was, however, obtained in these patients because of the presence of a horse-shoe kidney. Nevertheless, preoperative assessment of the problems involved was difficult and inaccurate. Scott and others (1969) have stressed the importance of both intravenous pyelography and aortography in these patients. We agree with this, but add that the operative technique cannot always be planned accurately on the basis of these investigations and can be defined only after exposure at operation. Minken and Rob (1967) have pointed out that the renal blood-supply must be demonstrated at operation to ascertain the resectability of the aneurysm. They have also shown in their case the value of preoperative aortography in demonstrating renal arteries which could not be found by dissection.

Since the precise anatomy is unlikely to be established before operation, it is essential to spend time and care in defining the vascular supply of the kidney and especially the anatomy of the drainage system of the horse-shoe kidney. The danger of infection around the prosthetic graft in the event of a urine leak demands exposure of the drainage systems in the entire operative field to avoid inadvertent damage of a ureter or pelvis, and since the intrarenal caliceal pattern may also be distorted, division of the isthmus should be avoided if at all possible to obviate the danger of caliceal damage. Additional vessels of supply to the kidney should be preserved either by selective clamping (as in *Case* 2) or by reimplantation of large vessels from the aneurysm into the graft using the Carrell-patch technique. Smaller vessels from the aneurysm may be sacrificed provided, as in *Case* 3, that there is a major arterial supply arising above the aneurysm, but if the vessels sacrificed have not already been occluded by atheroma some degree of renal ischaemia is to be expected. We would recommend the technique of grafting described in *Cases* 1 and 2 whenever possible because it eliminates the need for division of the isthmus and greatly decreases the operating time, a factor which we believe is important in the postoperative recovery of the patient.

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THE DIAGNOSIS OF PARATHYROID OVERACTIVITY IN A POPULATION OF RENAL STONE FORMERS

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SUMMARY

In recent years most cases of primary hyperparathyroidism have been revealed as a result of 'metabolic screening' of patients with renal calculi. It is recognized that elevation of serum calcium is the single most important finding in such cases (Keating, 1961; McGeown, 1961; Boonstra and Jackson, 1962; Dent, 1962; Oakland, 1963). However, in primary hyperparathyroidism the serum calcium may be minimally elevated or may fall within the normal range (McGeown and Bull, 1957; Kyle, Schaaf, and Canary, 1958; Pyrah, Raper, and Smith, 1958; Nordin, 1962; Hodgkinson and Edwards, 1963; Parfitt, Higgins, Nassin, Collins, and Hilb, 1964), and because of this observation further evidence of parathyroid overactivity is necessary in assessing patients with renal calculous disease. Such evidence may be obtained by measurements of phosphate handling by the kidneys.

The present study was undertaken to define the practical value of correlating various parameters of calcium and phosphorus metabolism on a large outpatient population of renal stone formers.

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MATERIALS AND METHODS

The conditions of the biochemical screening are essentially those of Nordin and Smith (1965) except that the patient is fasted overnight. The patient is asked to report to the ward at 8.30 a.m. and a 4-hour collection of urine is undertaken. To promote a urine flow 100 ml. of water are given hourly, and at approximately the mid-point of the collection period a sample (25 ml.) of venous blood is withdrawn without occlusion. On completion of the test the patient is given a meal and can then return home or to the place of employment. Ward patients with marginal or frankly abnormal results have the biochemical screening repeated as indicated. The routine is similar to that for the group of out-patients and a few patients proceeded to more extensive tests, such as the phosphate deprivation test, ^{47}Ca uptake, the cortisone-suppression test, etc. Serum samples are analysed by standard laboratory techniques for calcium, inorganic phosphate, alkaline phosphatase, proteins, creatinine, urea, sodium, potassium, chloride, CO$_2$ content, uric acid, and magnesium. Urine was analysed for calcium, urea, phosphate, and creatinine.

Table I.—ANALYSES OF THE INITIAL METABOLIC SCREENING IN 205 CONSECUTIVE STONE FORMERS

RESULT OF SCREENING	MALE	FEMALE	TOTAL
Total No. screened	111	94	205
Hypercalcaemia	25	14	39
Parathyroid tumour	3	2	5
Exploration			
Parathyroid tumour	3	2	5
Parathyroid tumour positive	1	2	3
Parathyroid tumour negative	2	0	2
Not explored but with positive biochemistry	1	0	1

Table II.—RANGE OF SERUM CALCIUM AND URINE PHOSPHATE PARAMETERS IN THE GROUP CONSIDERED NOT TO HAVE PARATHYROID ADENOMAS (FIRST BIOCHEMICAL SCREENING)

PATIENTS	NO. OF PATIENTS	Ca	Cp	PERCENTAGE T.R.P.	P.E.I.	Mg. P. PER CENT
Male	18	10·4–13·4	8·9–70·5	70·7–97·0	−0·08–+0·17	1·5–3·6
Female	10	10·4–11·0	4·8–13·5	82·0–95·5	−0·07–+0·05	2·7–3·5

Key to abbreviations: Ca, serum calcium; Cp, phosphate clearance; T.R.P., tubular resorption of phosphate; P.E.I., phosphate-excretion index; Mg. P. per cent, mg. of phosphate reabsorbed per 100 ml. glomerular filtrate.

RESULTS

The findings in 205 consecutive out-patients investigated in the year 1968 are shown in *Table I*. Hypercalcaemia was found in 25 male and 14 female patients (range: male, 10·4–13·6 mg. per cent; female, 10·3–12·6 mg. per cent).

Correlating the radiological evidence of calculus formation with the biochemical parameters related to the calculated indices of phosphate excretion (viz.: the phosphate clearance, percentage tubular reabsorption of phosphate, the phosphate-excretion index, and the mg. of phosphate reabsorbed per 100 ml. of glomerular filtrate) it was obvious that 3 male and 2 female patients had unequivocal evidence of hyperparathyroidism. These were proved by the removal of a parathyroid adenoma at operation. The range of the various parameters under consideration in 28 patients with hypercalcaemia who were not explored is shown in *Table II*.

In each of these patients the screening was repeated on at least two occasions or repeated calculations of the serum calcium failed to show a sustained hypercalcaemia. Some patients, nevertheless, have had a recurrent stone problem and further metabolic studies including phosphate-deprivation tests and steroid-suppression tests were undertaken. However, no patient's clinical state by itself has been severe enough to warrant an exploration for possible parathyroid overactivity. Included in these studies are five phosphate-deprivation studies which have *not* provided conclusive evidence of parathyroid overactivity.

The results of the first screening in 6 patients are shown in *Table III*. When the test was repeated some patients showed a minimal hypercalcaemia and the phosphaturia persisted. Despite equivocal phosphate-deprivation tests in all 6 patients it was decided that exploration was justifiable.

As can be seen in *Table III*, on the initial biochemical screening all of these patients had calcium levels which fell within the equivalent ranges of a group of blood donors. Apart from normal or minimal hypercalcaemia, all of these patients had an elevation of the phosphate-excretion index and a reduction of the mg. of phosphate reabsorbed per 100 ml. of glomerular filtrate. Male patients 1 and 2 did not have a demonstrable cervical adenoma and following operation have not shown any further clinical or biochemical problems. Female patient 1 had hyperplasia of two parathyroid glands. Male patient 3 was not explored because he had a severe degree of aortic stenosis and was considered to be unfit for a general anaesthetic. Male patient 4 and female patient 2 each had a parathyroid adenoma removed from one cervical parathyroid gland.

Table III.—RESULTS OF FIRST BIOCHEMICAL SCREENING IN 6 PATIENTS WITH NORMAL OR MINIMAL HYPERCALCAEMIA AND PHOSPHATURIA

SEX AND PATIENT	SERUM		URINE			
	Ca	Phos	Cp	T.R.P.	P.E.I.	Mg. P. Per cent
Male 1	10·6	2·4	23·7	77·1	+0·17	1·9
Male 2	10·8	2·0	21·5	79·0	+0·17	1·6
Male 3	10·8	2·0	25·0	67·0	+0·29	1·34
Male 4	10·0	2·6	59·0	71·0	+0·13	1·8
Female 1	10·6	1·7	7·0	88·0	+0·10	1·50
Female 2	10·8	2·2	18·7	76·8	+0·18	1·70

See Table II for key to abbreviations; Phos, serum inorganic phosphate.

Control Subjects.—A group of 16 male and 7 female laboratory staff was submitted to the 'routine' metabolic screening. No person in this group gave any history which might suggest a renal calculus and all were found to have normal calcium and phosphorus parameters. *Table IV* shows the range of the various calcium and phosphorus parameters measured.

Table IV.—RANGE OF VALUES IN CONTROL SUBJECTS (LABORATORY STAFF)

PATIENT	NO. OF PATIENTS	Ca	Cp	PERCENTAGE T.R.P.	P.E.I.	Mg. P. PER CENT
Male	16	8·1–10·4	6·3–16·5	82·4–94·2	0·07–+0·08	2·3–3·8
Female	7	9·1– 9·4	7·0–13·0	84·9–93·3	0·06–+0·00	2·9–3·4

See Table II for key to abbreviations.

Table V.—RANGE OF VALUES FOUND IN PATIENTS WITH PROVED PARATHYROID LESIONS (FIRST BIOCHEMICAL SCREENING)

PATIENT	Ca	Cp	PERCENTAGE T.R.P.	P.E.I.	Mg. P. PER CENT
Male	10·0–13·6	16·2–59·0	66·8–81·0	+0·13–+0·25	1·3–1·8
Female	10·0–12·2	7 –19·3	72 –78	+0·10–+0·26	1·3–1·7

See Table II for key to abbreviations.

Table VI.—CALCIUM VALUES FOR A GROUP OF BLOOD DONORS

PATIENTS	NO. OF PATIENTS	SERUM CALCIUM LEVEL		95 PER CENT LIMITS		
		Mean	S.D.	Lower	Upper	Range
Total	243	9·53	0·43	8·7	10·4	8·5–10·8
Male	145	9·52	0·41	8·7	10·4	8·7–10·7
Female	68	9·45	0·38	8·7	10·2	8·5–10·8

The corresponding results for the group of patients who were found to have parathyroid lesions are shown in *Table V*.

Comparison of Serum Calcium Levels in Stone Formers and in Control Subjects.—In order to assess the significance of hypercalcaemia a comparison has been made between the non-hypercalcaemic group of stone formers and a group of non-stone formers matched for age and sex.

Table VI shows the results as obtained in a group of blood donors who did not give any history suggestive of renal calculous disease. *Table VII* shows the comparison between the group of stone formers who were non-hypercalcaemic and the blood donors when matched for age and sex.

DISCUSSION

In order to prevent recurrence of stone disease (Twinem, 1937; Williams, 1963; Sutherland, 1964) it has been emphasized that intensive study of the metabolism of the individual patient with a calculus is more likely to be of practical value than epidemiological surveys (Prien and Frondel, 1947). Harrison (1959) stated that insufficient metabolic screening was undertaken in stone formers and this has been emphasized as recently as 1968 (Leading Article, *British Medical Journal*). Perhaps the reason for this is the wide variety of metabolic factors which have to be considered (Rose, 1968). Many authors including Hellstrom (1953) have stressed the serious effects of delay in diagnosing parathyroid overactivity in stone formers. When the greatest effort is directed towards the uncovering of this latter condition the incidence of parathyroid overactivity has been found to range from 2 to 22 per cent in various series (Beard and Goodyear, 1950; Baker and Connelly, 1956; McGeown and Montgomery, 1956; Hodgkinson and Pyrah, 1958; Melick and Henneman, 1958; Harrison, 1959; Litin, Diessneig, and Keating, 1961).

Table VII.—COMPARISON OF SERUM CALCIUM LEVELS IN STONE FORMERS AND IN CONTROL SUBJECTS

PATIENTS	AGE-GROUP (years)	STONE FORMERS			NON-STONE FORMERS		
		No.	Mean	S.D.	No.	Mean	S.D.
Normocalcaemic male	18–20	2	9·8	0·28	33	9·69	0·40
	21–30	8	9·6	0·34	49	9·60	0·42
	31–40	23	9·6	0·38	16	9·40	0·34
	41–50	20	9·5	0·57	13	9·58	0·47
	51–60	25	9·6	0·44	11	9·32	0·38
	61+	16	9·4	0·77	2	9·25	—
Normocalcaemic female	18–20	2	9·7	0·42	20	9·51	0·43
	21–30	11	9·2	0·63	20	9·39	0·41
	31–40	14	9·3	0·61	7	9·44	—
	41–50	15	9·5	0·39	13	9·48	0·28
	51–60	18	9·6	0·51	6	9·47	—
	61+	10	9·1	0·86	—	—	—

If simple elevation of the serum calcium was all that was necessary to make the diagnosis of hyperparathyroidism then there would be no problem. Serum calcium can become elevated by conditions other than parathyroid overactivity, e.g., sarcoidosis, malignancy, thyrotoxicosis, multiple adenomatosis, and myeloma (Henneman, Demsey, Carrol, and Allbright, 1956; McGeown and Montgomery, 1956; Frei, Bentlel, Riesalbach, and Block, 1963; Goldsmith and Ingbar, 1966; Kerr and Smith, 1967; Anderson, Cooper, and Naylor, 1968; Dent and Watson, 1968; Buckle, Mason, and Middleton, 1969). In none of our patients with hypercalcaemia was there any evidence to suggest that any of the above causes was present. In addition to routine clinical screening, all the patients had a check of the erythrocyte sedimentation rate which was used as a non-specific method of revealing any gross pathology. Laboratory error, which is a possible cause of 'hypercalcaemia', must always be considered along with the clinical technique of withdrawing venous blood for biochemical estimations.

Estimation of urinary calcium values is not of value in making a definitive diagnosis because any of the above causes as well as idiopathic hypercalciuria can be associated with elevation of the urinary calcium output (Allbright, Henneman, Benedict, and Forbes, 1953; Henneman, Boweaccy, Forbes, and Dudley, 1958; Edwards and Hodgkinson, 1965; Chambers and Dormandy, 1967; Boyce, Garvey, and Goven, 1968; Bulusi, Hodgkinson, Peacock, and Nordin, 1970). It has become customary to relate serum calcium levels to certain measurements of phosphate excretion in the biochemical diagnosis of parathyroid tumour. It is necessary that such estimations be measured with the patient in hospital on a standard diet. Great difficulty arises in the interpretation of the different measurements of phosphate excretion in the urine (Yendt and Janorski, 1961; Wills, 1970).

That parathyroid hormone reduces the ability of the renal tubule to reabsorb phosphorus from the urine is undisputed, and because of this various authors have used the degree of phosphaturia as a measure of parathyroid overactivity. In 1953 Sirota showed the effect of removing a parathyroid adenoma on the tubular reabsorption of phosphate and in 1954 Schaaf and Kyle introduced the concept of measuring the percentage tubular reabsorption of phosphate as an indication of parathyroid overactivity. This parameter, however, varied according to the dietary phosphate and the degree of renal failure in addition to the effect of the parathyroid hormone. To overcome these difficulties Thomas, Connor, and Morgan (1958) introduced the clinical concept of measuring the actual mg. of phosphate reabsorbed per 100 ml. of glomerular filtrate. Kyle and others (1958) emphasized the value of measuring the total phosphate clearance as a measurement of phosphate excretion in making the diagnosis of parathyroid overactivity.

Another factor which causes problems in interpreting phosphaturia is that serum inorganic phosphate levels cause variations in the amount filtered across the glomeruli and the latter occurs in direct relationship to the former. To allow for this variable Nordin and Fraser (1956) introduced the mathematically derived phosphate-excretion index (P.E.I.), which allows a comparison of the relationship between serum inorganic phosphorus and tubular reabsorption of phosphate in the patient with the same relationship in a series of normal control subjects.

The reasons for such a multiplicity of estimations of phosphate excretion are that the degree of phosphaturia varies according to the phosphate intake, the vitamin-D intake, and renal function. To compensate for these factors and for the rate of glomerular filtration, or the effects of serum inorganic phosphate on the various indices, each of the authors cited devised a different index as a measurement of the parathyroid hormone control of tubule handling of phosphate. In addition there are more complicated tests based on either phosphate loading (Hyde, Jones, McSwiney, and Prutney, 1960; Anderson, 1964) or phosphate deprivation (Chambers, Gordan, Goldman, and Reifenstein, 1956).

These derived indices of phosphate excretion use essentially the same biochemical data, namely serum inorganic phosphorus and creatinine together with the coincident urine phosphate and creatinine excretion.

Considerable scepticism and doubt as to the value of these various phosphate indices exist (Hodgkinson and Pyrah, 1958; McGeown, 1961; Dent, 1962; Edwards and Hodgkinson, 1965), and these authors emphasize the value of an accurate estimation of serum calcium after meticulous withdrawal of a venous specimen.

In terms of economics and practical realities we feel that, while agreeing with the indubitable evidence of accurate and repeated estimations of serum calcium levels in making the diagnosis of hyperparathyroidism in a renal stone population, the index of suspicion can be greatly increased by the scheme outlined above. In addition, such screening can act as a means whereby only those requiring more detailed study are admitted to metabolic wards. This is important to the patient and to the use of beds in the hospital concerned.

Before submitting the patient to complicated procedures such as calcium-infusion tests (Kyle, Schaaf, and Erdman, 1954; Pronove and Bartter, 1961), steroid suppression of calcium (Dent, 1962), ^{45}Ca uptake studies (Cannigia, Genmari, and Cesari, 1965), and assay of parathyroid hormone (Buckle, 1969) some form of preliminary screening is essential if these complicated procedures are to yield the maximum information.

Examination of our figures shows that the suspicion of parathyroid overactivity in a renal stone former is greatly increased if the phosphate parameters are scrutinized, especially in those patients who are normocalcaemic or who have a mininally elevated serum calcium. We feel that repeated serum calcium estimations should inevitably reveal parathyroid overactivity but early diagnosis minimizes the urinary stone problem and also the systemic effects of parathyroid overactivity such as hypertension.

In addition, a considerable base-line knowledge of renal function is available for each individual patient and in the total management of a patient with a renal stone problem may serve as a guide in determining the surgical management of problems arising from the stone itself. It was not appreciated at the outset that the procedure could also be used to 'screen out' patients with hypercalcaemia who did not require exploration for possible parathyroid overactivity, although such patients obviously require careful supervision on a long-term basis. This group is still being carefully assessed at regular intervals.

A final difficulty in the interpretation of serum calcium levels in stone formers is that the mean value for calcium is often higher than in non-stone formers matched for age and sex (*Table VII*). This is invariably the case with males, with a progressive fall with age which is less obvious in the female population.

The clinical diagnosis of hyperparathyroidism, particularly when hypercalcaemia is minimal, causes considerable difficulties. Despite the galaxy of laboratory tests available, Strott (1968) suggested that the decision to submit a patient for operation for a possible parathyroid lesion should be dictated by the signs, symptoms, and prognosis rather than by the laboratory investigations. We disagree with this outlook. While the patient's clinical state is a very important guide to therapy, laboratory findings must not be ignored and early screening of patients with renal calculi for hyperparathyroidism should be as comprehensive as the scheme outlined here.

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THE EFFECT OF THE FIBRINOLYTIC INHIBITOR EPSILON-AMINOCAPROIC ACID ON THE INCIDENCE OF DEEP-VEIN THROMBOSIS AFTER PROSTATECTOMY

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SUMMARY

Sixty-two patients undergoing retropubic prostatectomy were examined for evidence of deep-vein thrombosis using the ^{125}I-fibrinogen technique. Patients were allocated randomly into two groups. The first group was given the fibrinolytic inhibitor epsilon-aminocaproic acid (EACA) during the perioperative period, while the second group of patients acted as a control. The administration of EACA did not increase the incidence of deep-vein thrombosis after prostatectomy. This finding is discussed together with the possible role of the fibrinolytic system in postoperative venous thrombo-embolic disease.

It has been demonstrated that the synthetic inhibitor of fibrinolytic activity epsilon-aminocaproic acid (EACA) reduces blood-loss following prostatectomy (McNicol, Fletcher, Alkjaersig, and Sherry, 1961a; Andersson, 1962; Sack, Spaet, Gentile, and Hudson, 1962; Vinnicombe and Shuttleworth, 1966a). This effect is considered to be a result of the inhibition of the urinary fibrinolytic enzyme urokinase which, after prostatectomy, digests clot forming in the prostatic bed, thus promoting haemorrhage. If given in larger doses EACA also inhibits systemic fibrinolysis and it has been claimed that this may reduce blood-loss further (Ladehof and Otte, 1963). In fact, many published studies employed EACA in larger doses. It has been suggested, however, that the administration of EACA carries the risk of inducing intravascular thrombosis. McNicol and Douglas (1964) have recommended that this drug should not be used as routine prophylactic treatment after prostatectomy, but should be reserved for patients in whom protracted haematuria is presenting a major problem.

Although a number of studies have failed to demonstrate an increased risk of deep-vein thrombosis in association with EACA, these were based on clinical evidence (Andersson, 1962; Vinnicombe and Shuttleworth, 1966b), which is now known to be inaccurate, or on isolated phlebography 2 weeks after operation (Becker, Borgstrom, and Saltzman, 1970). With the introduction of the ^{125}I-fibrinogen technique for the accurate detection of deep-vein thrombi it was decided to reinvestigate the risk of using EACA routinely at prostatectomy.

MATERIALS AND METHODS

Sixty-two patients, all aged over 50 years, undergoing retropubic prostatectomy with general anaesthesia were studied. Patients were allocated randomly to one of two groups. Thirty patients with even ages received EACA (treated group), while the remaining 32 acted as controls (control group). The age and weight distribution of the two groups was similar. The mean age of the treated group was 66·5 years (S.D. ± 6·7) and the mean weight was 72·7 kg. (S.D. ± 11·4). In the control group the mean age was 67·6 years (S.D. ± 7·7) and the mean weight was 70·9 kg. (S.D. ± 10·6).

EACA Régime.—Patients in the treated group were given 6 g. of EACA orally 5 hours before operation, followed by the intravenous infusion of 6 g. during operation, and a further 6 g. commencing 5 hours after the end of operation and continuing for 6 hours. Thus, a total of 18 g. was given over an 18-hour perioperative period.

Table I.—INCIDENCE OF THROMBO-EMBOLISM IN THE EACA-TREATED AND IN THE CONTROL GROUPS

GROUP	NO OF PATIENTS	DEEP-VEIN THROMBOSIS		PULMONARY EMBOLISM	
		No.	Per cent	No.	Per cent
Control	32	9	28	1	3
Treated	30	9	30	2	6

Detection of Deep-vein Thrombosis.—Patients were examined for evidence of deep-vein thrombosis using the ^{125}I-fibrinogen technique (Atkins and Hawkins, 1965). After operation each patient received intravenously 0·7 mg. fibrinogen containing approximately 100 µc. ^{125}I. This material was prepared by the Lister Institute from a pool of five donors who were accredited as free of the hepatitis carrier state by Regional Blood Transfusion Centres. This was based on follow-up of recipients of their previous donations of plasma or whole blood and by examination for the presence of the Australia antigen. Iodination was carried out at the Radiochemical Centre, Amersham, Bucks.

Counting was performed on the first, second, fourth, and sixth postoperative days, and beyond this period if there was any evidence of deep-vein thrombosis. A Pitman Isotope Localization Counter, Model 235, was used to count the medial surface of each thigh and calf at 10-cm. intervals with the legs elevated to 15° to obviate venous pooling.

The criteria for diagnosis of a deep-vein thrombus were those suggested by Negus, Pinto, Le Quesne, Brown, and Chapman (1968).

Measurement of Fibrinolytic Activity.—Blood-samples were taken from 27 patients, employing minimal haemostasis, within 30 minutes of the end of the operation. A second sample was taken from 25 patients on the first postoperative day. Fibrinolytic activity was measured by the whole-blood lysis time (WBLT) (Fearnley, Balmforth, and Fearnley, 1957), modified in that an acetate citrate diluent was used (Gallimore and Shaw, 1968), and each component of the test was increased by a factor of 2·5. Thus, each sample contained 0·5 ml. of blood diluted in 4·25 ml. of buffer and 0·25 ml. of thrombin solution. An acetate citrate diluent was used since it has been shown to increase the rate of *in vitro* fibrinolysis and is considered to enable greater accuracy in end-point determination (Gallimore, 1967). Individual samples were set up in triplicate and the mean lysis time was recorded.

RESULTS

Incidence of Deep-vein Thrombosis.—There was no significant difference between the two groups in the incidence of thrombo-embolic episodes (*Table I*). Of the 18 patients diagnosed as having deep-vein thrombosis, 16 had isotopic evidence of their thrombosis within 48 hours of operation and no thrombus was detected later than the fourth postoperative day. Two patients died: 1 in the treated group from massive pulmonary embolism, and 1 in the control group from myocardial infarction. The cause of death in each case was confirmed at post-mortem examination.

Fibrinolytic Activity.—The results of lysis-time estimations were plotted on a logarithmic scale (*Fig.* 1), in view of the known exponential relationship of the WBLT to fibrinolytic activity (Sherry and Alkjaersig, 1957; McNicol, Fletcher, Alkjaersig, and Sherry, 1961b). There was a relative inhibition of fibrinolytic activity within 30 minutes of operation in the treated group when compared with the control group and this was significant ($P<0{\cdot}005$). Even so, in the treated group the fibrinolytic activity was still significantly enhanced as compared with preoperative levels in resting patients of similar age (mean, 63·4 years, S.D. ± 7·3) and weight (mean, 65·4 kg., S.D. ± 15·4) ($P<0{\cdot}05$).

DISCUSSION

Various régimes have been suggested for the administration of EACA to patients undergoing prostatectomy (McNicol and others, 1961b; Andersson, 1962; Vinnicombe and Shuttleworth, 1966a; Kirkman, 1967). It has been demonstrated (McNicol and others, 1961b) that EACA is concentrated in the urine to levels up to a hundred times the concentration in the plasma. It is therefore theoretically possible to give a dose sufficient to inhibit urinary urokinase without inhibiting the fibrinolytic activity of

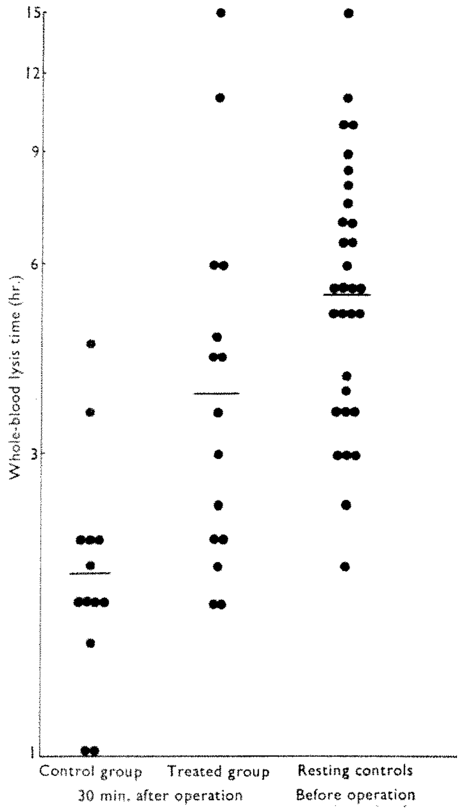

FIG. 1.—Fibrinolytic activity in the control and in the treated groups within 30 minutes of operation compared with that in resting preoperative patients. The treated group shows significantly less activity than the control group ($P<0{\cdot}005$) and significantly more activity than the preoperative levels ($P<0{\cdot}05$).

Table II.—RÉGIMES OF EACA ADMINISTRATION REPORTED IN THE LITERATURE

AUTHORS	EACA DOSE				
	Preoperative	During Operation	Postoperative	Perioperative*	Total Dose
Ladehof and others (1963)	6 g. i.v. in 30 min.	Nil	6 g. i.v. then 6 g. orally 6-hourly	18 g.	96 g.
Kirkman (1967)	5 g. orally then 6-hourly for 24 hours	Nil	5 g. orally 6-hourly	15 g.	80 g.
Vinnicombe and Shuttleworth (1966a)	Nil	0·5 g. i.v. per hour	0·5 g. i.v. hourly	6 g.	6 g.
Becker and others (1970)	Nil	5 g. i.v.	5 g. i.v. 6-hourly, then 3 g. orally 6-hourly	15 g.	148 g. (mean)
Andersson (1962)	Nil	0·1 g. per kg. i.v.	0·1 g. per kg. i.v. 6-hourly	21 g.	51 g. (mean)
McNicol and Douglas (1964)	Nil	Nil	1 g. per hr. for 4 hr, then 0·5 g. per hr. for 4 hr.	8 g.	8 g.
Present study	6 g. orally	6 g. i.v.	6 g. i.v.	18 g.	18 g.

* Total dose over 24 hours period commencing 6 hours before operation.

the blood. In fact many of the suggested régimes (Andersson, 1962; Ladehof and Otte, 1963; Kirkman, 1967) employ doses higher than is necessary solely to inhibit fibrinolysis in the urine. The aim of these régimes is to maintain a high urinary excretion of EACA and in some instances, actually to inhibit blood fibrinolytic activity as well (Ladehof and Otte, 1963). A review of some of the published dose régimes is given in *Table II*. The régime chosen in this study was of intermediate dosage, and administration was confined to the perioperative period, as it is during this time that the majority of deep-vein thrombi develop (Kakkar, 1969; Lambie, Mahaffy, Barber, Karmody, Scott, and Mathieson, 1970).

No significant increase in the incidence of deep-vein thrombosis was demonstrated in the group of patients which received EACA. This is in agreement with previous studies (Andersson, 1962; Vinnicombe and Shuttleworth, 1966b; Becker and others, 1970) in which the diagnosis of deep-vein thrombosis was based on less satisfactory criteria than the ^{125}I-fibrinogen technique employed here. This result does not support the argument that EACA should be withheld from routine use because of the risk of inducing intravascular thrombosis. However, it is possible that thrombi forming in the presence of circulating EACA would prove subsequently to be more resistant to lysis, and prone to propagation, than thrombi developing in untreated patients.

The effect of EACA on the fibrinolytic activity of blood is of interest in view of the possible relationship between the fibrinolytic system and venous thrombo-embolic disease. In the dosage used in this study EACA reduced significantly the marked enhancement of blood fibrinolytic activity which is the usual response to operation. Moreover this reduction in activity, which was demonstrated in samples taken within 30 minutes of operation, was present at a time when the majority of deep-vein thrombi are known to form. Despite this there was no increase in the incidence of deep-vein thrombosis, although it is true that the fibrinolytic activity of the treated group immediately after operation was still greater than that of preoperative resting patients. Therefore, having shown only a reduction in the enhanced activity induced by operation, it cannot necessarily be inferred that the fibrinolytic system is not involved in the pathogenesis of postoperative venous thrombosis. The precise relationship between fibrinolytic activity and venous thrombosis requires further evaluation by a specific study.

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REPAIR OF THE LARYNGOPHARYNX AND CERVICAL OESOPHAGUS AFTER IRRADIATION

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SUMMARY

The present situation regarding the nature and treatment of cancer in this area is given. Types of defect and methods of repair, their complications, and the choice of methods are described. Emphasis is laid on the increased hazards of surgery for the patient after full dosage of irradiation. Treatment should be based on surgical resection, usually preceded by a modified plan of irradiation often completed after surgery.

In conclusion the most valuable recent advances in the techniques of surgical repair of the laryngopharynx and cervical oesophagus after irradiation and resection for cancer are the use of large regional skin-flaps from outside irradiated areas, and total pharyngo-oesophageal replacement by means of vascular pedicled gut segments.

ABOUT 98 per cent of malignant tumours of the laryngopharynx and cervical oesophagus are squamous carcinomas and 90 per cent are locally advanced when first diagnosed. In addition about 50 per cent of patients have regional metastases to the neck lymph-nodes on first attendance at hospital. It follows that cure rates by conventional means are unlikely to be high and therefore treatment should interfere with essential function as little as possible.

After many years of reliance on external irradiation as a principal means of attempting a cure it is now mainly acknowledged that radical resection of the primary lesion must form the basis of curative therapy though often combined with irradiation. Coupled with this are the proved policy of in-continuity resection of the regional lymphatics which are palpably or probably involved by disease and the concept of rapid restoration of function made possible by modern reconstructive surgery.

The roles of radiotherapy and sometimes chemotherapy are now felt to be as adjuncts to surgery usually by means of preoperative treatment with a carefully planned dosage régime. It has lately been shown that such combined treatment can certainly decrease local recurrences and modestly increase the cure rates in cancer of the mouth, pharynx, and larynx (Strong, Henschke, Nickson, Frazell, Tollefsen, and Hilaris, 1966; Ogura and Biller, 1970). The surgeon practising in this field will be constantly faced with the hazard of tissue devitalization added to the inevitable problems of healing of potentially infected wounds, the situation being frequently aggravated by the poor general medical status of these patients.

In fairness it must now be added that modern supervoltage or telecobalt irradiation does not damage normal tissues in the neck to anything like the degree that has been a constant feature with older methods and higher total doses, often through incorrectly planned fields. It should also be remembered that a properly modified preoperative course of about 4000 rad telecobalt therapy usually has little damaging effect on healing potential by itself, although the individual effects are often quite variable. However, the time interval is important; the greater the time between irradiation and surgery the greater are the probable healing difficulties.

Because of these factors weighing against the rapid healing of neck tissues undergoing surgery, the use of local flaps is restricted and the whole basis of repair is of necessity conservative and greatly dependent upon a good blood-supply imported with distant flaps or pedicled gut segments.

Despite such problems, the aim of repair for the cervical gullet remains early restoration of function with minimum of risk and hospitalization. Today the patient should be given this assurance.

TYPES OF DEFECT

Both primary and secondary defects must be considered; the majority are in the first group and quite simply may be small or large. Examples of the former include defects following lateral pharyngotomy for the uncommon small cancer of the lateral or posterior wall or the epilaryngeal region. Larger primary defects are usually created by total removal of the larynx with or without part of the pharyngeal wall. The largest defects are created by the total excision of the larynx, laryngopharynx, and part or all of the oesophagus. They are treated by immediate closure when possible; otherwise by secondary closure at an interval.

Most secondary defects are not inevitably caused by surgery but occur as a result of poor healing, usually with fistula formation and generally in the second or third week after resection with primary closure. They may be large or small and occur most frequently following a previous course of irradiation. Later secondary defects are generally due to the growth of residual primary tumour causing fistulous breakdown.

METHODS OF REPAIR

There are four main types of lining repair:—

1. Primary closure using local mucosa.
2. Reconstruction with pedicled skin-flaps.
3. Replacement with free skin-grafts or free gut transplants.
4. Replacement with vascular pedicled gut segments.

Primary Closure.—The majority of primary surgical defects in the wall of the pharynx or cervical oesophagus can be repaired satisfactorily by immediate suture at the time of resection. This method can be used successfully with all such defects, provided at least one-third of the circumference of the pharyngeal mucosa remains available for tubing. Where a defect exceeds this size or where it is judged that the tissues have been greatly devitalized by irradiation it will be necessary to create a temporary skin mucosal stoma for secondary closure.

Pedicled Skin-flaps.—Three tissue components are needed for secure closure of all fistulous defects in the gullet wall: lining, support, and cover. These can easily be provided by the use of pedicled flaps of local or distant skin. Sometimes the latter are backed on their deep surface with split-skin grafts as a lining to save time, or a local flap may be turned inwards to provide a lining and then receives split skin on the raw outer surface for cover. However, pedicled skin of local origin is more often used to provide a lining and cover, as in the Marion-Duplay technique adapted by Lewis (1965) or in the original method of Wookey (1942). Still more frequently used today if the local skin is in good condition are inturned adjacent 'trap-door' flaps for lining, while support and cover importing a good blood-supply are provided by means of large pectoral or shoulder transposition flaps (Gillies, 1957; Conley, 1960). Such a technique is certainly wiser and more effective after full therapeutic courses of irradiation. When correctly planned it does not require any delay and can give excellent functional results with rapid healing in two or three stages (Shaw, 1962). Any raw donor areas are immediately covered with split-skin grafts if the defect cannot be closed by direct suture (*Figs.* 1, 2).

Where the neck tissues are scarred and grossly devitalized it may be impossible to rely upon local skin as a 'trap-door' turnover for lining. In such a case distant pedicle skin, usually tubed, will be needed to provide all the anterior components (*Fig.* 3). Alternatively, with only slight risk, the damaged neck skin can be used for cover and a large deltopectoral skin-flap is then used for the lining, as in the two-stage Bakamjian (1965) technique (*Fig.* 4). However, in the former case, where complete resurfacing and anterior lining with distant skin and subcutaneous tissue is essential, one or two fully tubed acromiothoracic chest pedicles may be used. This is a lengthy procedure requiring four stages, though it can give excellent results for large defects (*Fig.* 5).

Free Skin-grafts.—Following Rob and Bateman's (1949) original report on the use of free split-skin grafting for the reconstruction of the trachea, a number of workers (Edgerton, 1952; Conley, 1953; Negus, 1953) developed a similar method using a primary split-thickness skin-graft carefully positioned around a hollow latex or wire mesh stent to replace the pharynx and cervical oesophagus (*Fig.* 6 A).

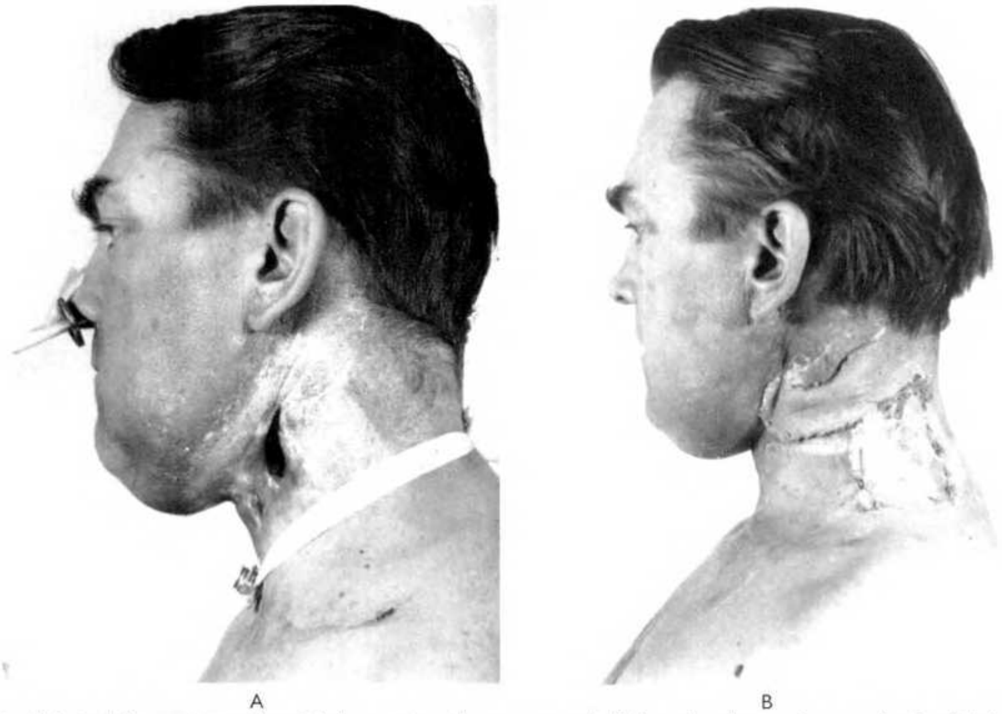


FIG. 1.—A, Lateral pharyngotomy with partial pharyngectomy (larynx conserved). B, Secondary closure using nape of neck pedicle for cover

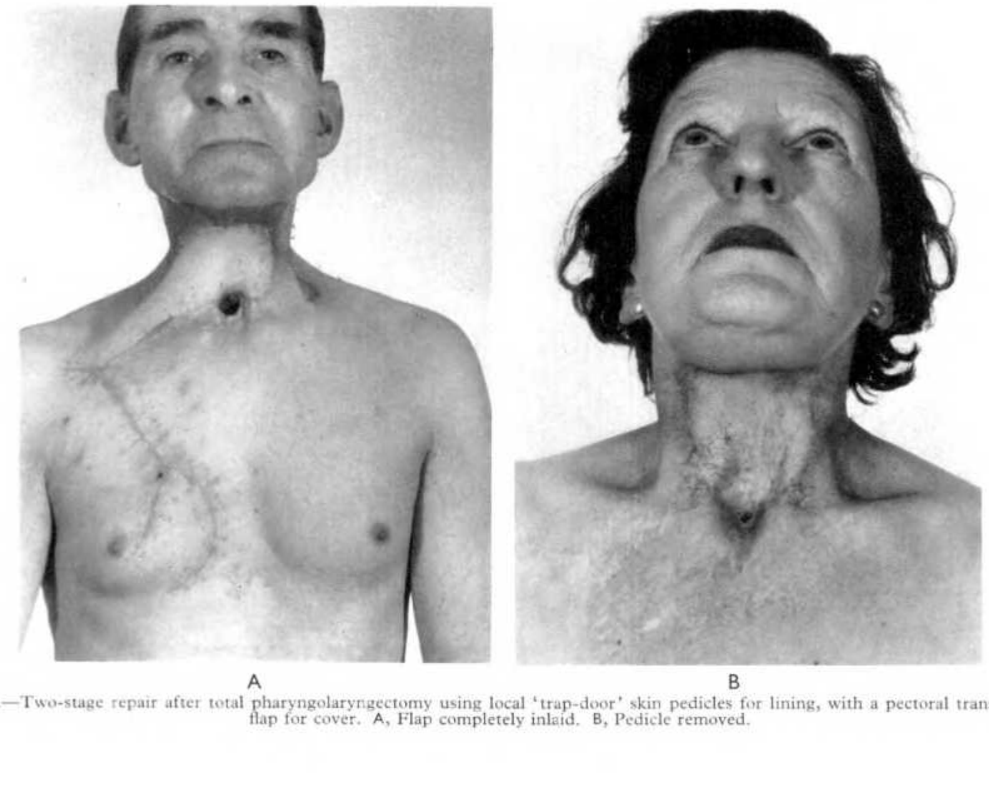
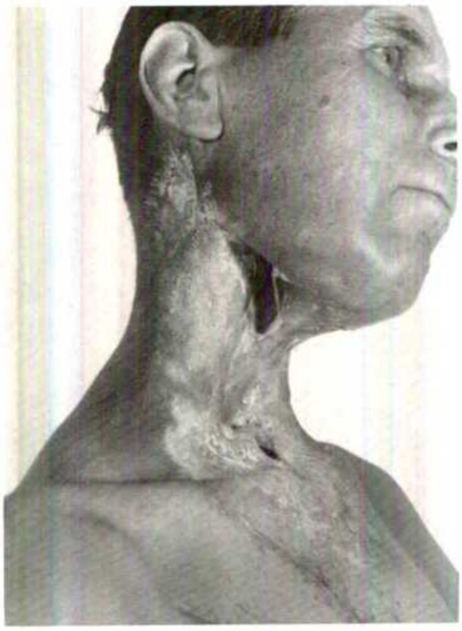


FIG. 2.—Two-stage repair after total pharyngolaryngectomy using local 'trap-door' skin pedicles for lining, with a pectoral transposition flap for cover. A, Flap completely inlaid. B, Pedicle removed.

Neck skin-flaps were used for cover and the stent was withdrawn through the mouth about 3 months later. The writer had personal experience of using this technique when it was first introduced. Providing the free skin-graft is carefully taken, followed by meticulous placement and suturing around the stent, it is possible to get good early functional results, the patients being permitted to swallow through the stent within 2 weeks of operation and often being out of hospital within 3 weeks. Despite such care, poor initial healing may occur and cause serious early complications in a small proportion of cases.



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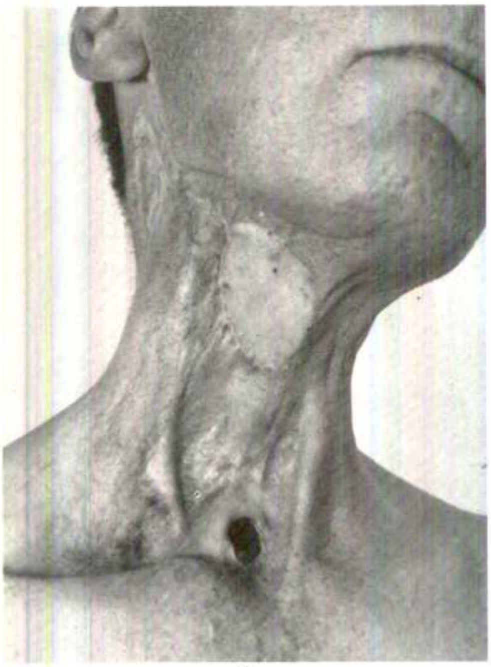

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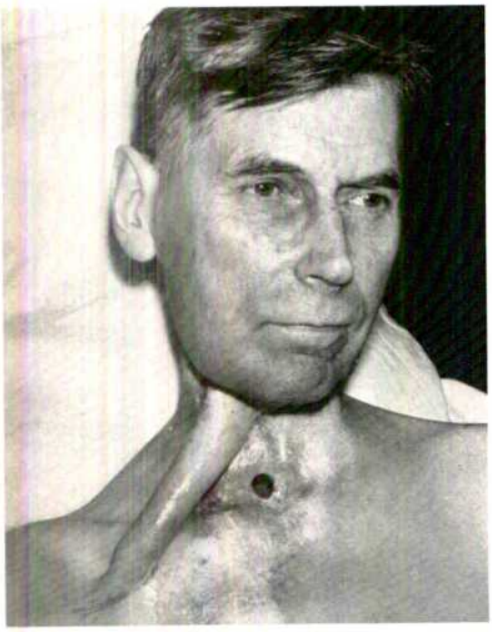


B

FIG. 3.—Partial pharyngectomy with total laryngectomy. Secondary closure using pectoral tubed pedicle flap for lining and cover.

However, the worse problem of intractable late stenosis of the graft usually at or close to the lower skin–mucosa junction in about one-half of the patients has caused the method to be abandoned (Shaw and Ormerod, 1957) (*Fig.* 6 B).

Kaplan and Markowicz (1964) and others have described the successful use in a few cases of a tube of whole-thickness penile skin, raw surface outwards, inserted as a free graft. Although intriguing, this has obvious sexual limitations and postoperatively is perhaps more hazardous than a split-thickness graft.

Free Gut Transplants.—The Nakayama technique of stapling small blood-vessels which was introduced in 1962 (Nakayama, Tamiya, Yamamoto, and Akimoto, 1962) has greatly aided the experimental work devoted to establishing a reliable means of grafting a completely excised segment of large or small bowel into the neck to replace a pharyngo-oesophageal defect (Seidenberg, Rosenak, Hurwitt, and Som, 1959; McKelvie, 1964; Jurkiewicz, 1965). Although some successful results have been reported in dogs and sheep, it has nevertheless proved extremely difficult to translate the method using the blood-vessels of middle-aged and elderly humans. Many practical problems have been reported; also it still involves anastomoses within the abdomen as well as in the neck.

Vascular Pedicled Gut Segments.—For the past 10 years adaptations of essentially old techniques (Kelling, 1911; Turner, 1936), using a fully vascularized pedicle to carry a segment of colon or stomach through the mediastinum and up into the neck, have been used with increasing success by a number of centres (Fairman, Hadley, and John, 1964; Le Quesne and Ranger, 1966; Harrison, 1969). The main reason for their revival has been dissatisfaction with the functional problems resulting from the delayed completion of skin-flap procedures coupled with new skill and knowledge in the use of transthoracic routes for the gut segments and vascular pedicles. Despite the fact that this is a serious operation by any standards, carrying at times a high, though falling, mortality, it has now become an

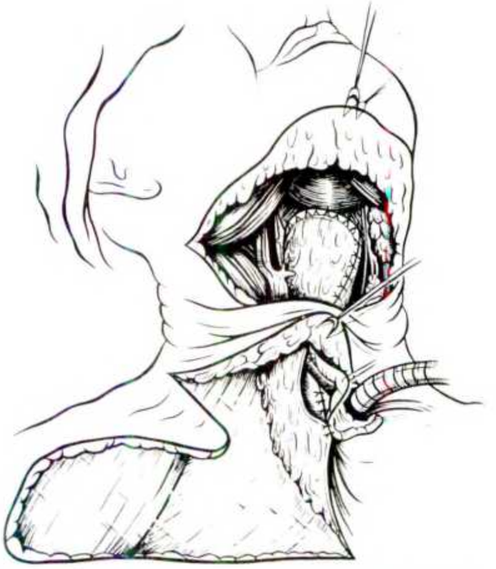
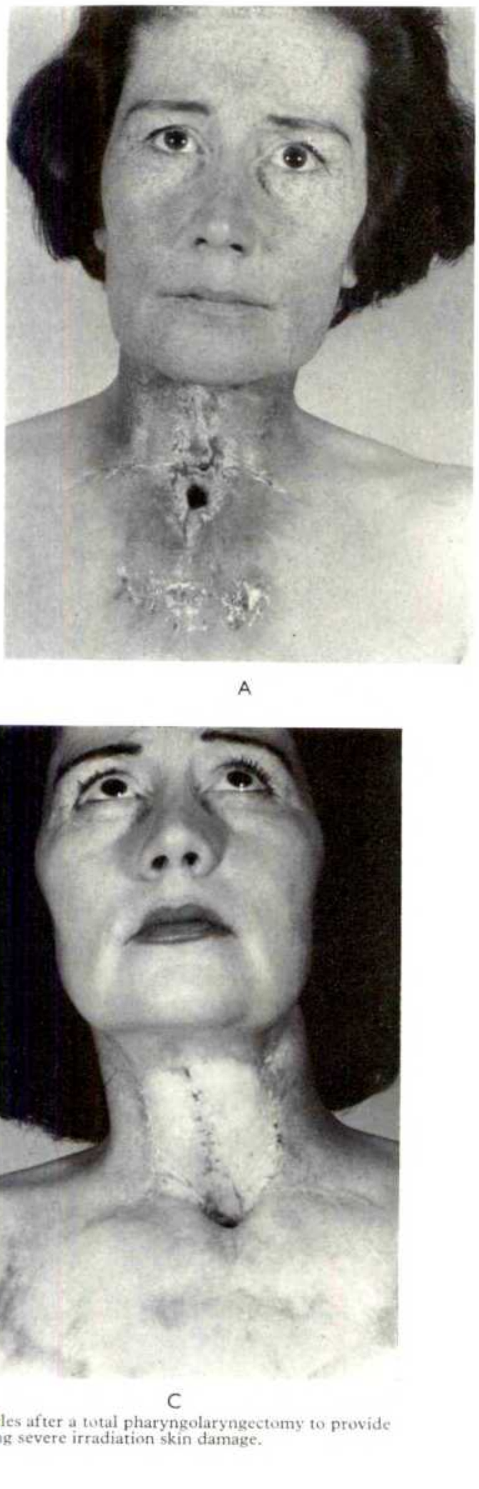


FIG. 4.—Use of medially based deltopectoral skin pedicle for immediate repair after a total pharyngolaryngectomy.

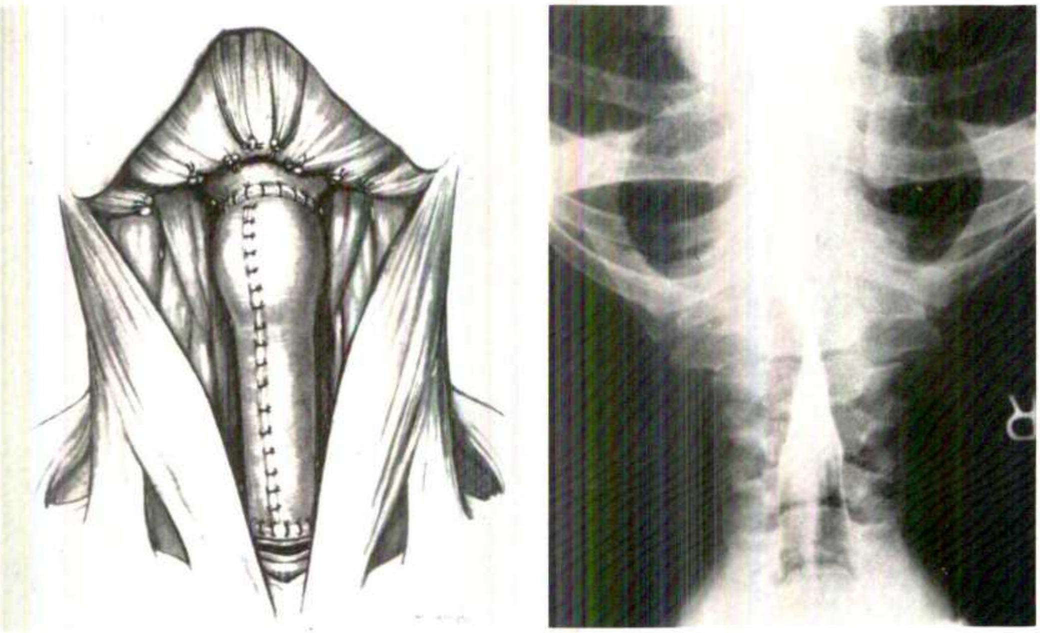


A

B

C

FIG. 5.—Four-stage repair using twin pectoral tubed pedicles after a total pharyngolaryngectomy to provide anterior lining, support, and cover following severe irradiation skin damage.



A B

FIG. 6.—Total pharyngolaryngectomy with immediate reconstruction using a free split-skin graft on a shaped latex mould. A, Diagram of free graft in place. B, Barium-meal film to show late stenosis.

established method of treatment for extensive tumours of the cervical oesophagus, and gives good results if used in selected cases by a skilled team. Debate continues regarding the precise indications for its use; whether it is preferable to use stomach or colon, and which route should be used (anterior or posterior mediastinal or presternal subcutaneous). Patients are generally able to leave hospital 3–4 weeks following successful surgery, with a satisfactory swallow as well as having a fair chance of regaining some useful speech (*Fig.* 7).

AIDS TO HEALING

General Condition of Patient.—The majority are in middle age and are often in poor general health for a variety of reasons some of which it is not possible to improve in the short time available before surgery. However, in consultation with a physician or the anaesthetist in charge a vigorous attempt should be made to overcome any chest infection, circulatory defect, or anaemia that is present. Diabetes must be corrected and sinusitis or dental sepsis must be cleared. The patient should be started on regular physiotherapy and introduced early to the speech therapist. It is also essential to carry out detailed preoperative nutritional studies on patients likely to undergo gut-transplant repairs together with routine checks of liver and renal function. Any drug sensitivities, especially to antibiotics, must be known. Chronological age is certainly no bar to surgery unless extreme, but physical condition and psychology must be taken into account when deciding the type of operation. These points again have much greater significance in the irradiated patient.

Planning and Technique.—Ideally all planning must be experienced, sometimes requiring consultation with other colleagues or the collaboration of two or more surgeons. The technique of repair must be meticulous with after-care by a skilled team of nurses and medical staff, preferably in special units.

Some years ago it was often said that tumour surgery in the head and neck required two teams: one to resect and the other to reconstruct—the Halstead concept Another cliché of the time supporting this argument was that if resection is carried out by the surgeon responsible for reconstruction inevitably there is a risk that the resection will be inadequate. Certainly this is no longer true today, the main reasons being, first, that reconstructive techniques are much more effective for all situations both in restoration of function, and in regaining the ability to speak, and, secondly, it has been clearly recognized that surgeons working in this field must themselves have experience in modern reconstructive surgery. In fact the reverse may therefore now hold more truth; that the surgeon trained in reconstructive techniques is best able to cope with any type of resectional defect that he may create.

Haemostasis, Sutures, Drains, and Dressings.—In recent years a wide variety of suture material has become available and it is felt that the less chromic catgut and diathermy are used the better is the result especially when working with irradiated tissues. Linen thread or silk for the largest vessels and 00 or 000 monofilament nylon on atraumatic needles for backing up defects closed with a single continuous extramucosal 00 atraumatic chromic catgut suture for the inner layer appear to give the best results.

Care in achieving haemostasis before closure together with the elimination of as much dead space as possible by the incorporation of muscle and connective tissue in mucosal suture lines and accurate tacking down of flaps will greatly help to reduce the amount of drainage required and will promote early healing.

The use of Haemovac-type continuous underflap suction drainage is certainly valuable and more comfortable for the patient, but in the heavily irradiated neck it is felt that there is still a good case for the use of additional bulky neck dressings as they do achieve an important and useful degree of immobility with adherence of the tissues during the first 3–4 days after surgery.

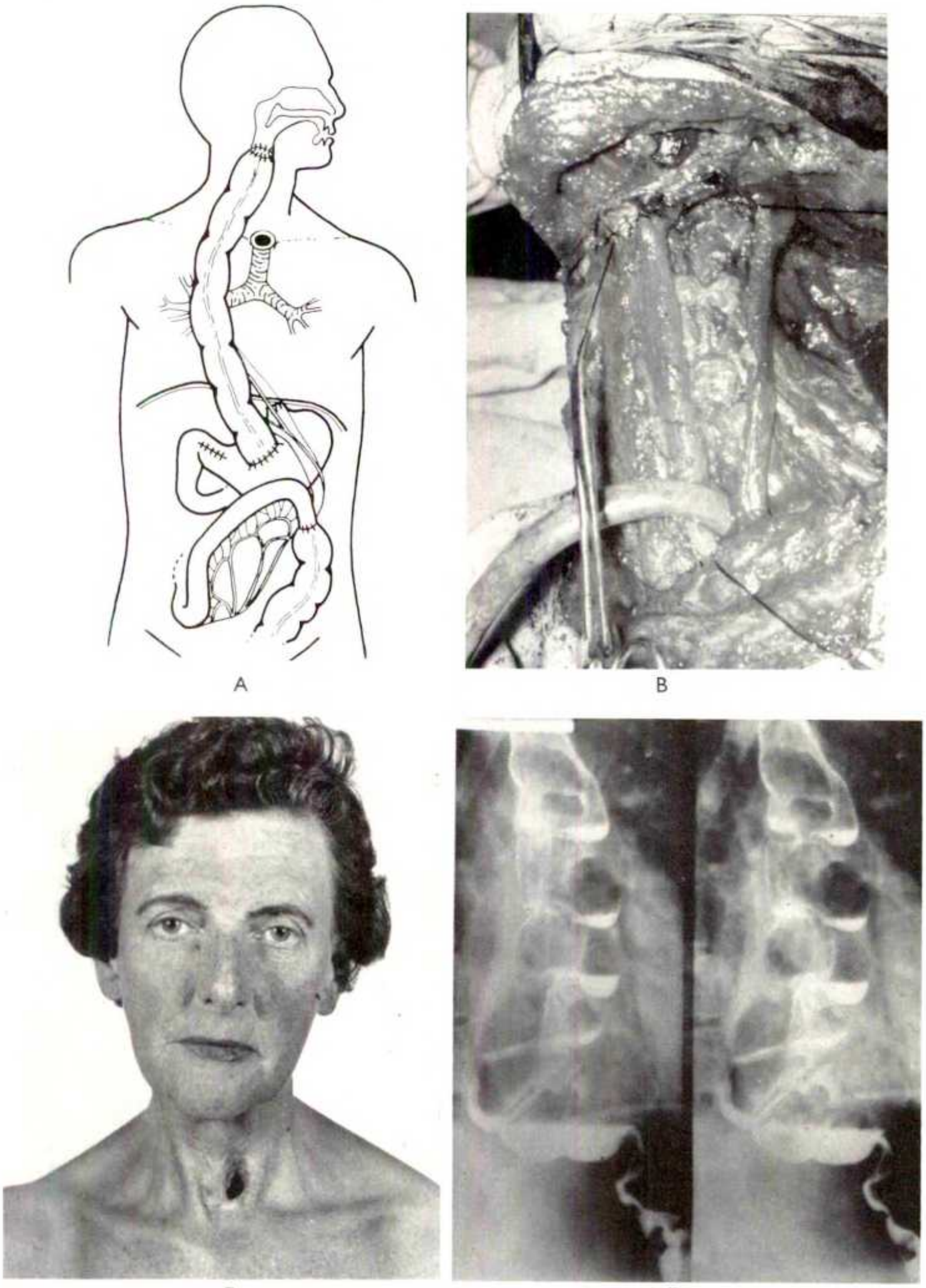


FIG. 7.—Total pharyngolaryngo-oesophagectomy with immediate reconstruction using a vascular pedicled segment of colon brought through the anterior mediastinum. A, Diagrammatic representation. B, Cervical anastomosis. C, Patient and D, barium-meal films 3 years after operation.

Feeding, Fluid, and Electrolytes.—Accurate maintenance of fluid and electrolyte balance is essential after all major surgical operations and is no less important in these patients, especially in view of their frequently complex medical problems.

Adequate nutritional intake when swallowing is in abeyance can certainly be maintained for several weeks by intravenous dextrose, aminosol, and lipid therapy, but over a long period this has obvious problems and reliance on nasogastric tube feeding, gastrostomy, or jejunostomy is both more effective and convenient, especially for protein supplements.

After reconstructive techniques likely to exceed 4 weeks to completion or where the abdomen must be opened as part of the procedure, experience shows that a feeding gastrostomy or jejunostomy is usually preferable to nasal tube feeding.

Antibiotics, Vitamins, and Hormone Replacement.—The use of a suitable wide-spectrum systemic antibiotic such as ampicillin or tetracycline is mandatory and must be continued in large doses throughout the period of initial healing after any reconstructive procedure—usually at least 2 weeks and often 3 weeks in irradiated patients. Vigilance to detect any overgrowth of pathogenic Gram-negative or other resistant organisms is always required.

The addition of vitamin supplements, especially vitamins B, C, and D, to the diet is helpful and the use of adequate hormone and calcium replacement after the total or even partial removal of the thyroid or parathyroid glands is essential.

COMPLICATIONS

There would seem to be little need to describe in detail the many possible complications relevant to the procedures described. However, certain problems are likely to be encountered more frequently after surgery in irradiated subjects. Fistula formation with a tissue defect following primary mucosal closure or secondary skin closure is common. The fistula is usually small in size and has been estimated to occur in 30–40 per cent of all suture lines following total laryngectomy. About 90 per cent of these close in a few weeks with simple measures to reduce infection. A small number will require plastic closure if no great improvement is noted after 8–10 weeks. If drainage from the fistula directly involves an exposed main vessel such as the common carotid artery, early intervention will be required at least to cover and protect the vessel with a suitable skin-flap.

There is no certain way to avoid fistula formation, which is often quite unpredictable in its occurrence, but a strict observance of surgical principles, meticulous technique at operation, and expert post-operative attention to drainage and dressings are essential. It is also very important to ensure the best possible local blood-supply without tension on the tissues in the design of the flaps and suture lines and to see that the normal circulating blood-volume and a normal haemoglobin level are well maintained after surgery. The use of some form of tube feeding is essential, preferably nasogastric, during the main healing period. Dressings bulky enough to secure some reduced mobility of the head and neck have a distinct advantage whether or not underflap suction drainage is employed. The value of systemic antibiotics has also been mentioned and is a practical necessity for at least 2 weeks following surgery.

Necrosis of the flap margins may occur unpredictably after irradiation despite good planning of the incisions. Usually the necrosis is small and of little consequence, but if major blood-vessels are exposed early cover by a well-vascularized skin-flap is again necessary.

With regard to pedicled gut transplants, most complications concern the anastomotic suture line to the pharynx and also may result from the surgical interventions within the mediastinum. The intra-abdominal anastomoses usually give little trouble. The most serious problem is partial or complete necrosis of the transplant. This, fortunately, is a rare event with proper planning and technique. Secondly, severe haemorrhage at operation within the thorax or later haemorrhage from the neck or thoracic vessels is often a serious risk. Gross superior mediastinal infection and necrosis can also follow this type of surgery in irradiated cases, particularly where there is pre- or postoperative chest infection. It is especially important in all these patients to spend at least 2 weeks preceding surgery in improving their general medical state and making good any nutritional defects, in addition to thorough bowel preparation.

Stenosis at anastomotic suture lines in the neck is not uncommon at skin–mucosa junctions, especially at the oesophageal end of a skin-tube repair if the technique has not been meticulous or if any local necrosis or infection has occurred. It seldom leads to severe dysphagia and can usually be overcome by repeated dilatation. Occasionally reoperation is necessary. When reconstruction has been by means of a free split-skin graft a complete stenosis of the graft may occur, requiring its total removal and a fresh reconstruction. In the author's experience mucosa–mucosa junctions have not given rise to any serious degree of stenosis requiring additional treatment.

Local recurrence of the tumour at or adjacent to the site of reconstruction is always an anxiety, especially if the repair is in any way difficult or prolonged. It is generally evidence of incomplete resection due to lymphatic permeation and by the time it becomes clinically apparent there is little chance of eradication by further surgery. Patients must then be treated by other means and are unlikely to be cured. A virtue of complete oesophagectomy followed by a pedicled gut transplant is that local lymphatic recurrence will be extramural and will not therefore cause undue dysphagia until a late stage, if at all.

CHOICE OF METHOD

The choice of the method of repair will depend chiefly on (*a*) the extent of the defect, (*b*) the details of previous irradiation or other treatment, (*c*) the general health of the patient, and (*d*) the surgical and nursing facilities available.

Although plans for repair should always be ready to meet unexpected contingencies at operation, it is preferable to obtain a precise knowledge of the extent of the lesion and thereby of the resection and defect created, as well as the other factors outlined earlier, before surgery. A suitable plan can then be prepared, followed through, and any required assistance anticipated.

In general, where the defect is small and can be closed without tension and with adequate cover, or where at least one-third of the mucosal circumference is intact, primary closure should be carried out unless the normal tissues have been excessively damaged by irradiation. In the latter case a simple stoma must be created by accurate skin/mucosa suturing, allowed to heal, and then closed secondarily with a transposed non-irradiated pedicle skin-flap.

When less than one-third of the mucosal circumference remains at any point so that tubing it and primary closure is impossible, either a stoma must be created again with secondary closure or a total excision completed and one of the described procedures used.

A special situation arises with the uncommon tumours arising on the posterior pharyngeal wall. If the bare area remaining after resection is less than 2 cm. in its greatest diameter either it may be left to heal by granulation and epithelial overgrowth or a local mucosal flap may be used to reduce or close the defect. If the area to be repaired is greater than 2 cm. in diameter it is best to restore the defect using an inlay pedicle skin-flap previously planned and inserted via a lateral pharyngotomy approach. When prior irradiation has been given the creation of a temporary small lateral pharyngeal stoma is advisable together with the use of such a pedicle. This stoma can easily be closed using local skin or a transposed pectoral flap at a second stage.

It has already been stated that the great majority of these tumours are advanced when first diagnosed. This applies particularly to the cervical oesophagus and here two situations often arise. The first is where a post-cricoid or pyriform fossa tumour is extensive enough to require a complete segmental excision of the larynx and pharynx in the immediate vicinity but does not extend far down, if at all, into the cervical oesophagus. In this situation most of the cervical oesophagus can be safely retained and several choices are available for reconstruction. Many such cases can be repaired well with only slight risk by using a skin-pedicle method, and of these, the long deltopectoral flap method developed by Bakamjian (1965) is perhaps the most suitable. It has a number of virtues, possibly the greatest being the use of non-irradiated skin for the lining of the new gullet together with the importation of a good blood-supply from branches of the internal mammary vessels. An effective and well-tried alternative where the neck skin has not been seriously damaged by irradiation is to use the local skin for lining as inturned 'trap-door' flaps and to bring up a pectoral transposition skin-pedicle flap for cover, as has already been described.

In the second situation, regrettably the more common, the cervical oesophagus is widely involved, the disease perhaps extending into the upper thoracic oesophagus. Here there is little alternative but to carry out a total pharyngolaryngo-oesophagectomy with replacement by a transposed vascular pedicled gut segment, the author's choice being to use an isoperistaltic segment of ascending and transverse colon. This is now an operation of proved effectiveness and advantages. However, it is still an extensive and serious procedure carrying at all times a considerable risk of postoperative mortality—especially relevant in view of the poor general nutrition of many patients with oesophageal cancer. Because of this and considering the comparatively low risks of skin-pedicle operations it is felt that the latter type of repair, carefully planned for suitable defects, must still be performed when possible in cases which are bad surgical risks.

CONCLUSIONS

Although it is correct to say that there has been little further improvement in curative treatment for tumours of the laryngopharynx and cervical oesophagus over the past 10 years, except for a better use of combined methods, there has been a more complete understanding of their surgical pathology (Harrison, 1970) and a great improvement in the techniques of repair of surgical defects, with early restoration of function. The most notable of these new techniques are the more sophisticated use of large regional skin-flaps from outside the irradiated areas and the employment of vascular pedicled gut replacements. These have resulted in less morbidity, reducing the time spent in hospital, allowing a faster return of the normal swallow, and enabling speech therapy to be begun earlier. The choice of technique remains important and much work must continue to be done on diminishing the hazards of gut transposition, especially in irradiated and undernourished patients.

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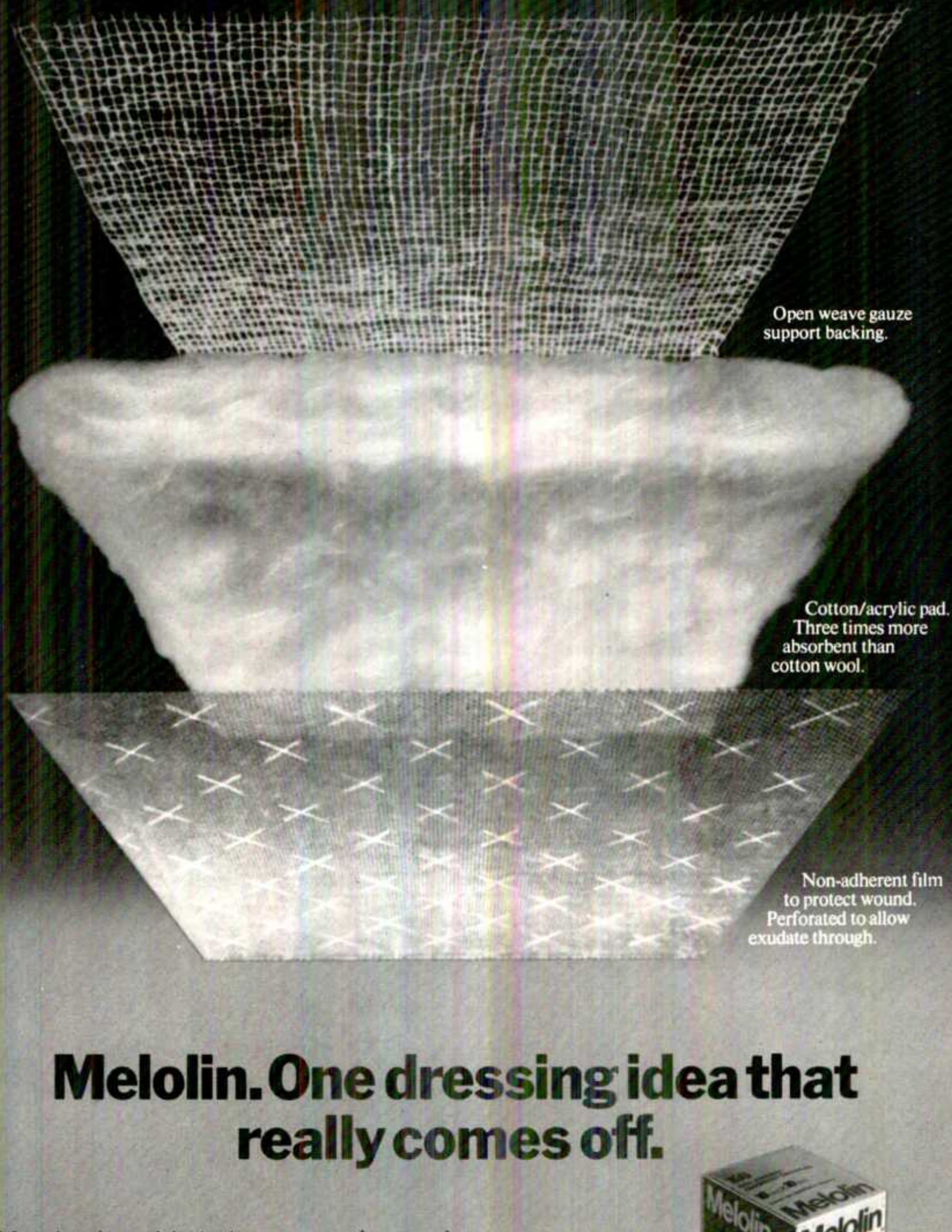
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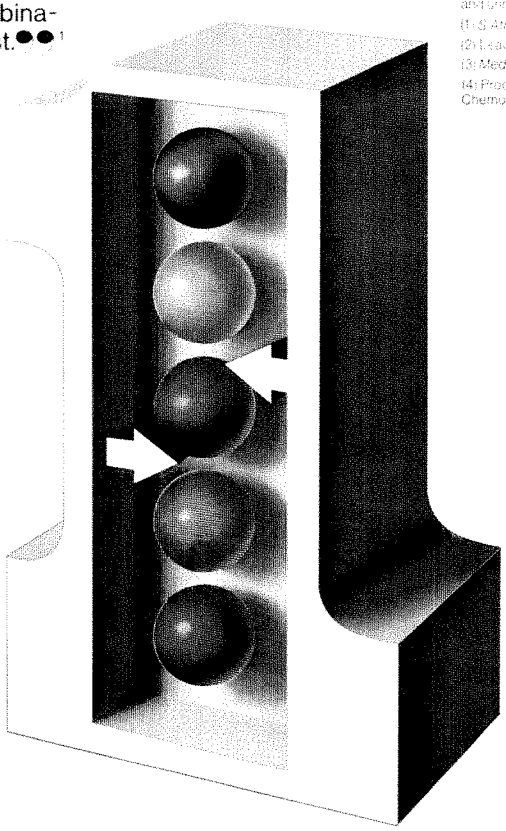

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THE ROLE OF RADIOTHERAPY IN THE MANAGEMENT OF MALIGNANT THYMOMA

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SUMMARY

A series of 18 cases of malignant thymoma referred for radiotherapy during a 21-year period is reviewed. The presentation, treatment policy, and results are examined. Of the 7 cases treated with a full radical dose all were alive at 3 years, all 4 cases followed for 5 years survived that period, and 3 of the 4 cases followed for 10 years were alive at that time. Of these, only 3 cases had had macroscopically complete excision of the tumour at thoracotomy. These findings suggest that postoperative radiotherapy should be of benefit in all cases of invasive thymoma whether operable or otherwise.

THE place of radiotherapy in the management of malignant thymoma is still a matter of some dispute. An editorial in the *British Medical Journal* (1969) on Hodgkin's disease of the thymus states: 'the lesion responded to radiotherapy, in contrast to those of true thymoma'. This would appear to imply that radiotherapy is not effective in the treatment of the latter condition. Holmes Sellors, Thackray, and Thomson (1967), however, state that radiotherapy plays an important part in the management of invasive thymoma, although they believe radiotherapy alone to be less effective than a combination of surgery and radiotherapy. Others, including Legg and Brady (1965), Piercy (1966), Wilkins, Edmunds, and Castleman (1966), and Hatcher, Exarhos, Logan, and Abbott (1967), also advocate a combination of surgery and radiotherapy. Sawyers (1968), however, suggests that postoperative radiotherapy is not needed if complete excision has been achieved.

The majority of these authors advocate postoperative rather than preoperative radiotherapy, although Holmes Sellors and others (1967) are of the opinion that the results of both approaches are equally satisfactory. One of the earliest advocates of combined surgery and radiotherapy was Keynes (1949), who suggested preoperative radiotherapy for thymomas with myasthenia. This approach has tended to continue to be used for such cases (Piercy, 1966), but even in this situation has been attacked by Henson, Stern, and Thompson (1965), who feel that preoperative radiotherapy has no value and is a contra-indication to surgery.

In the management of malignant thymoma surgery is nearly always attempted in the first instance, as, even if the lesion is inoperable, this may be the only way to establish a histological diagnosis. If complete removal is impossible or if local recurrence is feared following apparently complete removal, irradiation is usually given.

The use of radiotherapy alone meets with little support in the literature. However, many cases are inoperable (8 out of 15 cases in the present series) and it has been our policy to irradiate these patients unless they are hopelessly ill.

In this article we report the outcome of all the cases of malignant invasive thymoma receiving radiotherapy at the London Hospital from 1948 to 1968 inclusive.

MATERIAL

Eighteen cases were available for study, all of whom had histologically proved diagnoses of malignant thymoma, and all of whom had received radiotherapy.

In 15 cases radiotherapy was used as part of the original management of the condition. In 2 cases it was used for recurrence following surgery alone, and in 1 case the patient was watched for some years on the grounds of age and poor general condition before being referred for palliative irradiation.

Of the 15 patients who received radiotherapy as part of the primary management, all have been followed for 3 or more years, and 9 for 5 years or more.

Age at presentation ranged from 19 to 69 years, with an overall mean of 43 years. The population, however, fell into two age-groups: those below 30 years (6 patients, with an average age of 25 years) and those over 40 years (12 patients, with an average age of 52 years). The sexes were evenly distributed.

Three cases were asymptomatic, being detected on mass miniature radiography or 'routine' radiographs. The mean length of history for those with symptoms was 5½ months. The commonest thoracic symptom was left-sided chest and arm pain, although pain also occurred at other sites in the chest, arms, and neck. The association between myasthenia gravis and thymoma has long been established and 4 cases in the present series—2 lymphocytic thymomas and 2 'mixed' tumours—had symptoms of myasthenia at presentation. Other symptoms, each noted once only, were anorexia, vomiting, tiredness, chest-wall swelling, and hoarseness of voice.

In our series all the cases had lesions detectable on plain radiographs (*Figs.* 1 A, B). The commonest radiographic appearance was an anterior mediastinal mass. Four of the cases had palpable lymph-nodes. Three of these had small nodes in one or both axillae which were felt not to be significant and gave no rise to further trouble when left untreated. The fourth patient had a granulomatous lesion with involved nodes in both supraclavicular fossae.

Distant pulmonary metastases occurred in 1 patient, and a further patient developed multiple bony metastases 7½ years after presentation (*Fig.* 2). He was treated with preoperative radiotherapy, following which macroscopically complete excision of the tumour remnant was achieved, the histological appearance being that of a thymoma of mixed pathology with none of the features of a granulomatous lesion. At the time of the development of the bony metastases there was no clinical evidence of a new primary neoplasm elsewhere. A further patient with a proved lymphocytic lesion developed pelvic bone pain and tenderness 9 months after presentation, by which time pulmonary metastases had also developed. This pain responded well to radiotherapy and was felt to be due to metastases, although there were no conclusive changes on the radiographs.

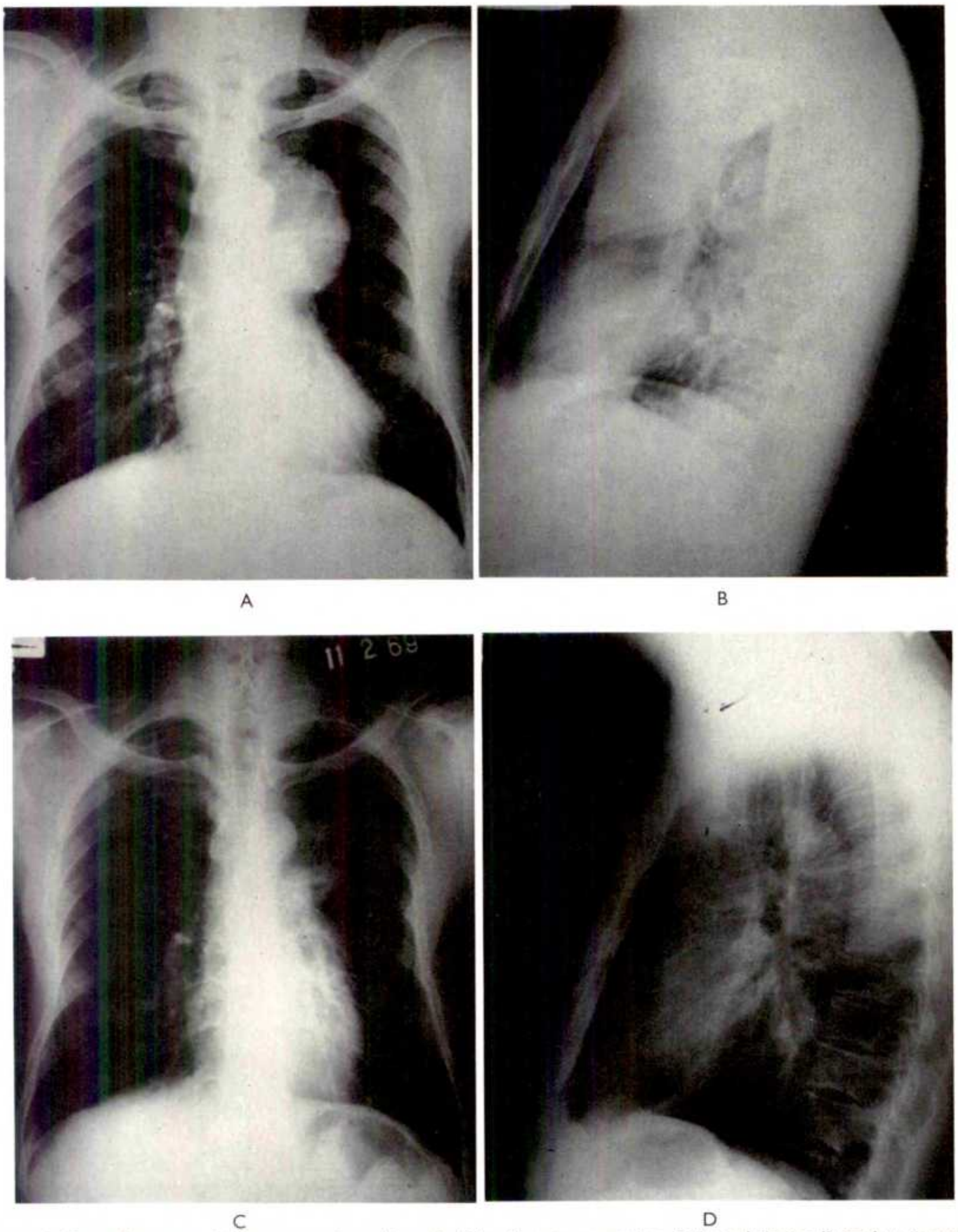

FIG. 1.—A. B., aged 50 years. A, Postero-anterior radiograph of the chest at presentation. B, Lateral chest radiograph at presentation. C, Postero-anterior chest radiograph 10 months after sternal split thoracotomy, biopsy, and radical radiotherapy. D, Lateral radiograph of the chest 10 months following treatment.

HISTOLOGY

Thomson and Thackray (1957) have suggested a basic classification in three groups: epithelial, lymphocytic, and teratomatous. The epithelial group, however, includes amongst others the lympho-epithelioma and the granulomatous thymoma, which are tumours of widely differing natural history. We have therefore used a slightly different classification in reviewing our cases, all of which have been histologically confirmed (*Table I*).

The 'benign' lympho-epithelioma is a small, well-circumscribed, well-differentiated lesion, most commonly associated with myasthenia. None of these has been referred to us for radiotherapy.

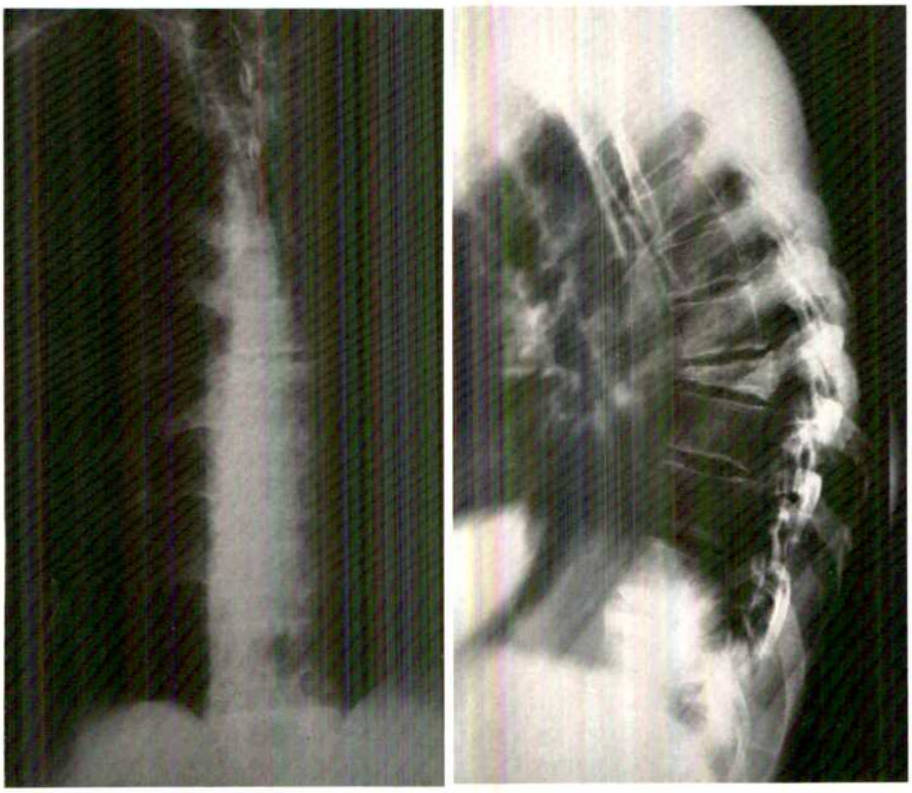

FIG. 2.—O. S., aged 51 years. A, View showing metastases in the dorsal spine. B, Lateral radiograph of the dorsal spine showing metastases. There were additional deposits in the cervical and lumbar spines, pelvis, and skull.

Table I

Classification	*No. of Cases*
'Benign' lympho-epithelioma	0 (in our series)
Invasive thymoma	
Epithelial	1 (no myasthenia)
Lymphocytic	6 (2 with myasthenia)
Mixed	6 (2 with myasthenia)
Granulomatous thymoma	2 (no myasthenia)
Teratoma	0 (in our series)

The invasive thymoma is a malignant lesion arising from the thymus. Since two elements—lymphoid and epithelial—occur in the thymus these are able to occur in varying proportions in the thymoma, providing a simple classification based on the predominating tissue type. A mixed lesion implies roughly equal proportions of epithelial and lymphocytic elements.

The granulomatous thymoma also contains mixed lymphoid and epithelial cells, but in addition it contains mononuclear cells, giant cells, and a fibrous stroma.

Teratoma is rare but does occur arising primarily in the thymus, although none was found in this series. Tissues representing all three germ layers are present.

SURGERY

Fifteen cases were submitted to thoracotomy, and in the majority a 'sternal split' approach was employed. In 8 of these cases macroscopically complete removal was achieved, and 7 of these, comprising 3 lymphocytic lesions and 4 tumours of mixed pathology, were referred for postoperative radiotherapy. The eighth was eventually irradiated for local recurrence.

In 2 of the 7 remaining cases removal was attempted but was known to be incomplete. The other 5 cases were regarded as inoperable and only a biopsy was performed.

RADIOTHERAPY TECHNIQUE

In this department we regard 4000 rad (megavoltage) in 20 treatments over 28 days as a radical tumour dose. Fifteen patients were irradiated as part of the primary management. Of these, 4 received this dose or a greater one on megavoltage. Three further cases were treated with conventional deep X-rays to an equivalent dose. The remaining 8 patients were treated palliatively on the grounds of widespread disease or poor general condition. Here the tumour dose varied from 2000 R (250 kV.) to 3500 rad on megavoltage.

If the tumour was relatively small a technique using two large anterior oblique wedge fields was used. Field size was of the order of 15 × 8 cm., wedge angle 45°, and hinge angle 90°. Tumour regression is shown in *Fig.* 1 C and D.

Table II.—SURVIVAL OF CASES RECEIVING RADICAL RADIOTHERAPY

CASES	TOTAL NO. OF CASES	3 YEARS		5 YEARS		10 YEARS	
		No. Followed	No. Alive	No. Followed	No. Alive	No. Followed	No. Alive
All cases	7	7	7	5	5	4	3
Patients under 30 years	2	2	2	1	1	1	0
Patients over 40 years	5	5	5	4	4	3	3

Table III.—EXTENT OF SURGERY AND THE SURVIVAL OF CASES RECEIVING RADICAL RADIOTHERAPY

EXTENT OF SURGERY	TOTAL NO. OF CASES	3 YEARS		5 YEARS		10 YEARS	
		No. Followed	No. Alive	No. Followed	No. Alive	No. Followed	No. Alive
All cases	7	7	7	5	5	4	3
Complete excision	3	3	3	3	3	2	2
Less than complete excision	4	4	4	2	2	2	1

Table IV.—SURVIVAL OF THE CASES RECEIVING RADIOTHERAPY IN THE PRIMARY MANAGEMENT OF MALIGNANT THYMOMA

CASES	TOTAL NO. OF CASES	3 YEARS		5 YEARS		10 YEARS	
		No. Followed	No. Alive	No. Followed	No. Alive	No. Followed	No. Alive
All cases	15	15*	10	9	6	9†	3
Patients under 30 years	6	6	2	4	1	4	0
Patients over 40 years	9	9*	8	5	5	5†	3

* Includes 1 case dying of myasthenia and lung abscess at 3 months. No evidence of recurrence.

† Includes 1 case dying of bronchopneumonia at 9 years. No evidence of recurrence.

More extensive lesions were treated with large parallel opposed fields or with parallel opposed fields supplemented with a wedge pair or additional direct anterior field. Field sizes were up to 20 × 15 cm. for the parallel opposed fields, and up to 20 × 8 cm. for the wedge fields. We believe these techniques yield an adequate dose to the anterior mediastinum without excessive exposure to the spinal cord. With conventional deep X-rays (250 kV.) parallel opposed fields and wedge pairs have been used.

SIDE-EFFECTS

In the present series 4 out of 10 cases treated with tumour doses ranging from 3500 rad in 20 treatments to 4500 rad over the same period showed evidence of pneumonitis. The classic presentation of this complication was a dry cough progressing to dyspnoea. There were low-grade fever and scattered coarse crepitations. Chest radiographs showed patchy mottling spreading from the treated area.

Although this problem reached serious proportions in 1 case, most patients were not badly affected and they responded to low doses of prednisone with the addition of antibiotics where there was evidence of superadded infection (Hope-Stone, 1967). In the severe case on such a régime immediate symptoms usually subside in 3 or 4 days, and complete resolution occurs within a month. If, however, fibrosis has developed steroids are less effective.

Mediastinitis, as shown by central chest pain and a rising pulse-rate, has not been observed in this series. Pericarditis has not occurred.

Meningitis was not seen but possible temporary spinal cord damage occurred in 1 case, who received a cord dose of 3000 rad with a 20-cm.-long field. This patient developed a transient radiation myelopathy associated with large-field irradiation to the thorax, which has been described by Jones (1964). This occurred 4 months after treatment and settled after 2 months with no residual neurological deficit. The highest dose received on the spinal cord in our series was 4000 rad in 20 treatments over 27 days. This is within the tolerance level suggested by Boden (1948) of 4000 rad in 15 treatments over 21 days for lengths of cord less than 15 cm.

RESULTS

Fifteen cases received radiotherapy as part of the primary treatment. Of these, 7 were treated with what we now regard as a radical dose, and the remaining 8 received palliative treatment only.

Table II shows survival figures for those treated radically, both for all the cases and for the two age-groups. These show satisfactory survival figures for up to 5 years after treatment. One patient, however, died of his disease at 6½ years. All the 10-year survivors are recurrence-free and no patient who was treated with a full radical dose and who was recurrence-free at 5 years has died.

Table V.—THE HISTOLOGY OF THE LESION AND THE SURVIVAL OF THE CASES RECEIVING RADIOTHERAPY IN THE PRIMARY MANAGEMENT OF MALIGNANT THYMOMA

HISTOLOGY	TOTAL NO. OF CASES	3 YEARS		5 YEARS		10 YEARS	
		No. Followed	No. Alive	No. Followed	No. Alive	No. Followed	No. Alive
All cases	15	15*	10	9	6	9†	3
Lymphocytic	6	6	4	3	1	3†	0
Epithelial	1	1	1	0	0	0	0
Mixed	6	6*	5	5	5	5	3
Granulomatous	2	2	0	1	0	1	0

* Includes 1 case dying of myasthenia and lung abscess at 3 months. No evidence of recurrence.

† Includes 1 case dying of bronchopneumonia at 9 years. No evidence of recurrence.

Table VI.—EXTENT OF SURGERY AND THE SURVIVAL OF CASES RECEIVING RADIOTHERAPY IN THE PRIMARY MANAGEMENT OF MALIGNANT THYMOMA

EXTENT OF SURGERY	TOTAL NO. OF CASES	3 YEARS		5 YEARS		10 YEARS	
		No. Followed	No. Alive	No. Followed	No. Alive	No. Followed	No. Alive
All cases	15	15*	10	9	6	9†	3
Complete excision	7	7*	6	4	4	4†	2
Less than complete excision	8	8	4	5	2	5	1

* Includes 1 case dying of myasthenia and lung abscess at 3 months. No evidence of recurrence.

† Includes 1 case dying of bronchopneumonia at 9 years. No evidence of recurrence.

Table III compares the results of those cases receiving a radical dose and complete surgical excision of the tumour with those who received similar radiotherapy but for whom the surgery was less than complete. These small numbers are not statistically significant but they do not demonstrate any great advantage of complete surgical excision in those cases who were subsequently irradiated radically.

Table IV shows the survival figures for all the cases receiving radiotherapy as part of their primary management. This series includes cases with extensive primary tumours, those with distant metastases, and those felt to be too frail for radical radiotherapy. *Table IV* shows how the overall figures are affected by the highly aggressive nature of the disease in the younger age-group. Only 2 out of the 6 cases in this age-group had sufficiently localized lesions to be treated radically, and these were the only survivors at 3 years. The only death occurring within 10 years among those receiving a full course of treatment was also in this age-group.

Table V attempts to show the effect of histology on the prognosis, but this is difficult in a small series. The apparently better prognosis for the 'mixed' tumours is more probably due to the earlier presentation in 4 out of 5 of these cases and the associated radical treatment. In the present series there was no demonstrable improvement in the response to radiotherapy with the lymphocytic lesions, as described by Holmes Sellors and others (1967).

Table VII.—THE RESULTS OF TREATMENT OF 7 CASES OF RECURRENCE OF MALIGNANT THYMOMA

Time after Treatment	*No. of Cases Alive and Well*	*No. of Cases Alive with a Recurrence*
3 months	5	1
6 months	2	2
1 year	2	2
2 years	0	1

The advantages of complete surgical removal shown in *Table VI* are probably more apparent than real. *Table III* has shown the nearly equal results with and without complete excision in those tumours which were irradiated radically, and undoubtedly an element of surgical discretion has improved the results for complete excision in the series as a whole by excluding poor-risk cases.

Table VII shows the results of treatment of recurrences. This, not surprisingly, indicates a very short period of survival after treatment and, in general, a short period of remission of symptoms. However, an occasional dramatic palliative result can be obtained, as in the case described by Roberts and Hope-Stone (1972), where palliative irradiation of the mediastinum caused regression, not only of the mediastinal mass, but also of the associated red-cell aplasia and a neuropathy.

DISCUSSION

The presentation of our cases was essentially similar to that in previously reported series, although in our series the mean age at presentation was slightly lower than the 54 years reported by Legg and Brady (1965).

Our patients' symptoms were also similar, although we have not noted the 'hiccups' reported by Wilkins and others (1966). However, 58 per cent (15 out of 26 cases) of the patients in the series of Wilkins and others (1966) were asymptomatic at presentation against 36 per cent in the series of Hatcher and others (1967), 20 per cent in that of Legg and Brady (1965), and 18 per cent in our own series.

The radiology of these tumours has been widely reviewed. Holmes Sellors and others (1967), discussing the radiological diagnosis, mention the sail-like shadows seen on plain radiographs, which they state is pathognomonic. These authors also advocate apical views, lateral tomography, angiocardiography, and pneumomediastinography. The radiological diagnosis has been further discussed by Jones (1955), who regards fluoroscopy and tomography in several planes as essential.

In the present series, however, the initial diagnosis was made without special radiographic procedures, although in 3 cases tomography was later carried out to determine more fully the extent of the lesion. This would suggest that for the invasive lesion giving rise to local symptoms, special radiographs are seldom vital in diagnosis. For the smaller lesions associated with myasthenia and of the type which have not been referred to us for radiotherapy the technique of selective thymic venography described by Kreel (1967) appears attractive and is described as less distressing to the patient than the other radiological contrast procedures.

All authorities are agreed that metastases outside the thorax are excessively rare except with the granulomatous lesion. Rachmaninoff and Fentres, reviewing the world literature in 1964, reported only 10 acceptable cases of distant metastases from these tumours. In 8 cases the tumour had spread to lymph-nodes: 4 each to the kidney, liver, and bones, and 3 to the spleen. In 2 cases there were metastases to the cranial nerves and there was 1 each to the skin, choroid plexus, spinal nerve-roots, brain, and dura mater. We feel that at least 1 of our cases can definitely be added to this series.

The association between red-cell aplasia and thymic tumours has been discussed by Havard and Scott (1960). This condition is felt to represent an autoimmune phenomenon and progresses later to a pancytopenia.

Two of our cases developed refractory anaemia late in their disease and in 1 a definite red-cell aplasia was demonstrated (Roberts and Hope-Stone, 1972).

Side-effects of radiotherapy in this condition have been discussed fully by Williams (1951), Jones (1960), and Skeggs (1968). The special problems reported are pneumonitis, mediastinitis, pericarditis, and meningitis and spinal cord damage. In our series, the only one of these side-effects to occur was pneumonitis. This can be expected in 40 per cent of the cases which are treated radically and occasionally leads to lung fibrosis but it usually resolves completely. Mediastinitis, which we have not encountered, represents a greater risk to life than pneumonitis, and we have no experience of its response, if any, to steroids. Pericarditis has been avoided, and Skeggs (1968) only reports it in cases treated with tumour doses of 5000–6000 rad in 5–6 weeks. Permanent spinal cord damage was avoided by our cord dose being within the limits of tolerance.

In assessing results the rarity of malignant thymoma makes the preparation of any series from a single centre difficult, and one is forced to attempt to draw conclusions from relatively few cases. It is also difficult to compare these figures for radiotherapy with those for surgery alone, where the majority of cases will have small localized tumours, and a few will be of the infiltrating type which tends to be referred to the radiotherapist. Having recognized this, however, it seems clear that our 5-year survival figures for radical radiotherapy (100 per cent), and the 65 per cent 10-year survival in cases treated by radical irradiation, with or without complete surgical excision, are unlikely to be much improved by surgery alone.

Since the response of late recurrence after radical surgery to irradiation is so poor it would seem reasonable to suggest that all cases of infiltrating tumours could with advantage be referred for postoperative radiotherapy, even if surgery is macroscopically complete. In addition, all locally inoperable cases should perhaps be given a chance to respond to a course of radical irradiation. Palliative treatment in widespread disease is sometimes rewarding. This should also be considered where appropriate.

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BRACHIAL PLEXUS LESIONS ASSOCIATED WITH TRAUMATIC ASPHYXIA

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SUMMARY

Among 19 patients admitted to hospital following a major disaster it was noted that 15 showed evidence of traumatic asphyxia and 7 had sustained brachial plexus injury. Three such cases are presented, the possible pathogenesis of the brachial plexus lesions is discussed, and the diagnostic difficulty presented by unconscious traumatically asphyxiated patients with monoparesis is highlighted.

THE syndrome of traumatic asphyxia is well documented (Bonnin, 1941.) First described by Ollivier in 1837 when the findings in 23 patients fatally crushed in a rioting crowd in a Paris street were presented, most of the cases reported in recent years have been of single individuals crushed in road-traffic, industrial, or agricultural accidents (Fred and Chandler, 1960). The Ibrox Football Stadium disaster of 2 Jan., 1971, in which 66 people were killed on an exit stairway as the crowd left the stadium is one of the few modern disasters where loss of life has been predominantly due to traumatic asphyxia and it is noteworthy for this reason alone. That 7 of the cases involved in the incident should have sustained brachial plexus lesions is believed to be unique in the tragic history of crowd-crush disasters.

CLINICAL MATERIAL

Of the 97 patients who attended the Casualty Department of the Southern General Hospital, Glasgow, immediately after the disaster, 15 were admitted with evidence of traumatic asphyxia. Six of these 15 patients were found to have associated brachial plexus injuries (1 further case of brachial plexus injury was admitted to hospital but showed no signs of traumatic asphyxia), and 3 of these patients are reported in detail here.

CASE REPORTS

Case 1.—The patient, a 19-year-old boy, arrived at the hospital about 30 minutes after injury. He was unresponsive to spoken commands but was able to move all his limbs except his right arm. He had striking bilateral subconjunctival haemorrhages (*Fig.* 1), his upper thorax and face were covered with small petechiae, and a linear abrasion was noted on the right side of his neck (*Fig.* 2). It was felt that a significant intracranial lesion could not be excluded and he was transferred to a neurosurgical unit. Twelve hours after injury, however, when the patient was alert and fully orientated, it was confirmed that the monoparesis was due to a right brachial plexus lesion involving predominantly the upper roots, and the following muscle strengths were recorded using the M.R.C. scale (Medical Research Council, 1965): biceps, 1; deltoid, 0; supinator, 1; triceps, 4. There was sensory impairment of the 5th, 6th, and 7th cervical roots, and the biceps and supinator tendon reflexes were absent. During the ensuing 48 hours the sensory loss recovered completely and the muscle strengths improved. Two months after injury motor recovery was almost complete.

Case 2.—A 14-year-old boy, who was not responsive to spoken commands on arrival from the disaster, was noted to be unable to move his left arm. Stigmata of traumatic asphyxia were limited to scattered petechiae on the face and bilateral subconjunctival haemorrhages. He had a linear abrasion on the left side of his neck (*Fig.* 3). During the 12 hours following admission to hospital his conscious level returned to normal but he remained disorientated in time and place. His increased co-operation at this time, however, allowed a more detailed examination of his left arm which showed an upper brachial plexus lesion with sensory loss over the dermatomes of the 5th and 6th cervical roots and grade-1 power in the biceps, supinator, and deltoid muscles. The biceps and supinator tendon reflexes were absent. The patient gradually improved, both in regard to his conscious state and in muscle power in his paretic limb, but although he was completely orientated without sensory loss 3 days after the disaster the motor loss was still detectable 2 months later, at which time some wasting in the deltoid was noted. Electromyograms performed 1 week and 5 weeks after the accident confirmed lower motor neuron damage.

Case 3.—A 32-year-old man, who was seen about 1 hour after the disaster, was found to be unresponsive to painful stimuli. His face and upper trunk were deeply cyanosed and he had marked bilateral subconjunctival haemorrhages. He was bleeding from both external auditory meati and he had marked dyspnoea due to multiple fractured ribs with a flail segment on the right side. As a basal skull fracture was suspected he was transferred to the neurosurgical unit for observation but subsequent skull radiographs were normal. Examination following recovery from his respiratory distress showed a paresis of the left biceps, deltoid, and supinator muscles and of the right anterior serratus muscle with some sensory loss over the dermatome of the 5th cervical root. He made rapid progress and when examined 2 months after injury the muscle groups in the left arm had almost returned to normal although there was still considerable weakness of the right anterior serratus muscle.

Cases 4–7.—These cases, 3 of which were fully conscious on arrival at hospital, were found to have minor unilateral paresis involving the myotomes of the 5th and 6th cervical roots. All of them made a complete recovery within 2 months. One case in this group showed no signs of traumatic asphyxia.

REVIEW OF EARLIER CASES

Following a similar incident at the Ibrox Stadium on 16 Sept., 1961, 12 cases of traumatic asphyxia were admitted to the Southern General Hospital, Glasgow. The case records of these patients were examined, but no evidence of a brachial plexus lesion had been documented and of the 6 patients who responded to a request for long-term follow-up, none could remember sustaining any weakness or sensory changes in the upper limbs at the time of their injury.

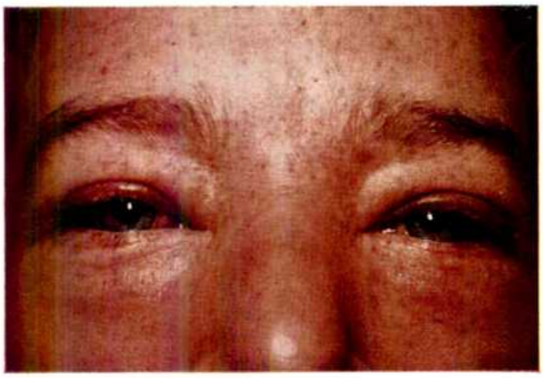
FIG. 1.—*Case* 1, showing bilateral subconjunctival haemorrhages and scattered petechiae.

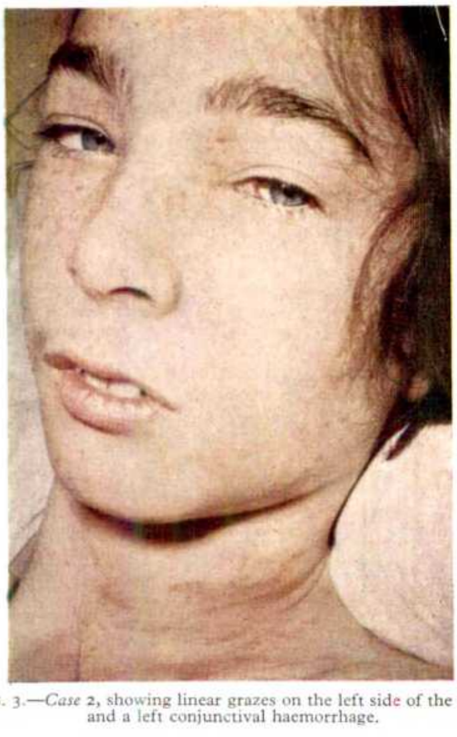
FIG. 3.—*Case* 2, showing linear grazes on the left side of the neck and a left conjunctival haemorrhage.

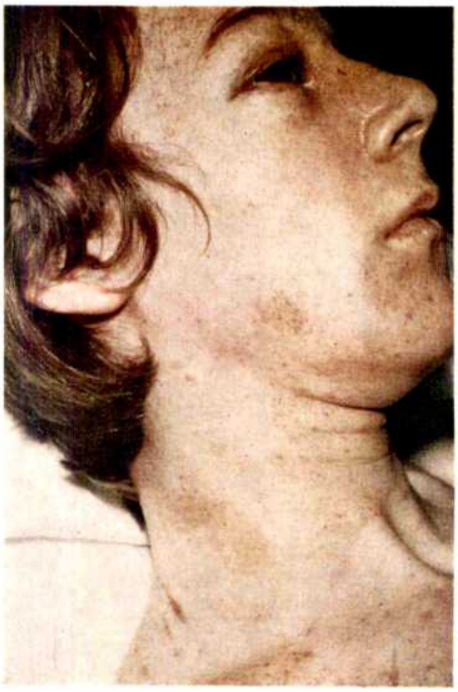
FIG. 2.—*Case* 1, showing scattered petechiae and linear abrasions on the neck.

DISCUSSION

Although many cases of traumatic asphyxia have been recorded (Shamblin and McGoon, 1963; Carveth and Mathews, 1967; Williams, Minken, and Adams, 1968; Feldman, 1969), little mention is made in the literature of the occurrence of simultaneous branchial plexus injury. That it may occur owing to direct trauma has been indicated (Fred and Chandler, 1960) but such a high incidence as occurred in this series has not been noted previously. Among 12 cases of traumatic asphyxia seen following a similar incident at the Ibrox Stadium in 1961, no cases of brachial plexus injury were noted, and in 1 case of traumatic asphyxia sustained at Ibrox in 1901 no brachial plexus injury was documented (Beatson, 1907).

Paraparesis has been recorded in 1 case of traumatic asphyxia (Heuer, 1923), and concomitant paraplegia has been reported but no obvious cause was found when the cord was explored and it was attributed to ischaemia (Reichart and Martin, 1951).

It is recognized that lesions of the upper roots of the brachial plexus may occur when the head and the ipsilateral shoulder are distracted (Barnes, 1949; Sunderland, 1968), and as the observed lesions were predominantly of the upper roots and primarily of a neuropractic nature their pathogenesis may be surmised to be as follows:—

1. During crushing by the crowd forceful lateral flexion of the neck may have occurred.

2. The patient's neck may have been pushed against the tubular steel railings which collapsed during the tragedy in the centre of the crowd. Abrasions of the lateral aspects of the necks of 2 of the cases with ipsilateral monoparesis would appear to support this view.
3. During the rescue of the trapped men it may be surmised that efforts to extricate the victims by traction on their arms while their heads were still not freed may again have resulted in extreme lateral flexion of the neck.

The high incidence of brachial plexus lesions in this tragedy prompts us to emphasize the diagnostic difficulty presented by a patient who is deeply unconscious with traumatic asphyxia and with a monoparesis; such a patient may be considered to be suffering from a serious head injury with a lateralizing sign warranting urgent neurosurgical investigation.

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A COMPARISON OF PORTAL AND SYSTEMIC VENOUS DRAINAGE IN PORCINE RENAL ALLOGRAFTS*

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SUMMARY

The results obtained when both kidneys were allografted in the pig are described. The experiments were performed in two groups of animals. In one group both kidneys were transplanted with portal venous drainage and in the other group caval drainage was used. Animals with portal venous drainage of the renal grafts survived for more than 4 months whereas those with caval drainage died within 15 days.

THE prolonged survival of an allogenic tissue in a 'privileged' zone is probably due to a barrier to the transport of transplantation antigens from the transplant into the lymphatic system of the host (May, Bauer, Leddy, Parmer, Vaugham, and Russel, 1969). The routes by which the antigens reach the host tissue from the transplanted organ have not been defined. The venous blood may be the main transport system for transplantation antigens. After transplantation in man and in experimental animals the caval and the portal venous systems are both potential routes for venous drainage; the latter offers the possible advantage of antigens passing directly into the liver. If this organ modifies transplantation antigens then the response of the host to the transplant should be altered. In the pig a kidney allograft with portal venous drainage is tolerated for several months with a mild rejection reaction (Mazzoni, Melis, Demofonti, Valli, Constantini, Francesconi, and Armisi, 1968). The pig liver can modify transplantation antigens coming directly into it through the portal vein. This effect undoubtedly depends on either the quantity of transplantation antigens or the length of time they remain in the liver (May and others, 1969). In order to clarify the influence of one of these factors (quantity of antigens) on the capacity of the pig liver to metabolize such antigens both kidneys (from the same donor) were allografted and anastomosed with portal venous drainage.

MATERIALS AND METHODS

Unselected pigs of different races and of either sex but with erythrocyte compatibility, weighing between 12 and 25 kg., were used. No food was given for 24 hours before the operation. The animals were premedicated with atropine and anaesthetized with halothane. Each pig received 500 ml. of normal saline intravenously. No immunosuppressive therapy or antibiotics were used and blood transfusion was avoided. The animals were given a routine diet 24 hours after receiving the allografts.

The left and right kidneys of the donor animals were isolated. The renal artery was prepared to its origin from the aorta, which was exposed above and below the renal artery. The inferior vena cava was exposed above and below the origins of the renal veins. The ureters were mobilized, paying attention to the arterial blood-supply. Heparin was given during the procedure (2000–3000 U.) Double renal allografts were performed in unselected pigs divided into two groups:—

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* Based on a paper read to the Surgical Research Society, in January, 1971.

1. **Allografts with Portal Venous Drainage.**— Both kidneys were removed from the recipient and the aorta was prepared from just above the renal arteries. The portal vein was dissected clear, removing any surrounding lymph-nodes. An end-to-side anastomosis was made between the portion of aorta removed with the allograft and the aorta of the recipient. An end-to-side anastomosis was made between the vena cava of the allograft and the recipient's portal vein. The average ischaemic time was 22 minutes. The kidneys were not perfused prior to reimplantation. The corresponding allograft and recipient ureters were anastomosed end to end, bringing the left ureter under the sigmoid colon (*Fig.* 1).

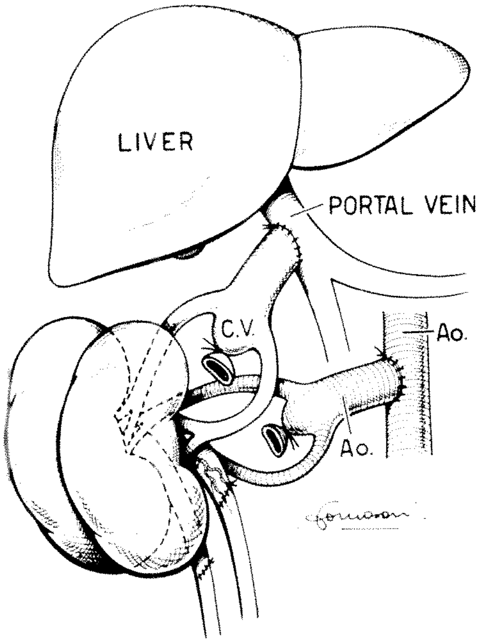

FIG. 1.—Bilateral renal allograft with portal venous drainage.

2. **Allografts with Caval Venous Drainage.**— A similar technique was used, differing only in that the venous anastomosis was made between the vena cava of the allograft and the vena cava of the recipient.

RESULTS

Animals which survived less than 5 days after the operation, dying because of anaesthetic or technical problems, were excluded.

1. **Allografts with Portal Venous Drainage** (10 animals).—Six animals survived more than 30 days and 4 were still alive at 120, 72, 105, 56 days, respectively, after transplantation (*Table I*). Intravenous pyelograms were performed in 4 animals and in 1 (No. 705) an intravenous pyelogram on the fifteenth day showed hydronephrosis in both kidneys. The picture was similar on the thirtieth day. The following day the animal died with a ureteral fistula and peritonitis. In a second animal (No. 706) intravenous pyelograms 15 and 60 days after transplantation showed that one kidney was not functioning while the other appeared to be quite normal. The kidney was explored and found to have a poor blood-supply, probably due to a spasm or torsion of the renal artery. In the other 2 animals (Nos. 707 and 709), which are still alive, intravenous pyelograms carried out 15 and 52 days after transplantation showed both kidneys to be functioning normally. Histological examination was performed in 6 animals. A glomerulitis of an inflammatory type was evident in 1 pig (No. 705) with no signs of rejection. In 4 animals (Nos. 706, 708, 715, and 718) the histological responses were similar, consisting of a very mild mononuclear cell infiltrate with a typical constant distribution around

Table I.—RESULTS OF RENAL TRANSPLANTATION IN THE PIG WITH PORTAL VENOUS DRAINAGE

EXPERIMENT No.	LENGTH OF SURVIVAL (days)	AUTOPSY	HISTOLOGY
705	32	Pyelonephritis (ureteral fistula)	Pyelonephritis
706	65	Intestinal obstruction	Mild mononuclear cell infiltration
707	120	—*	Biopsy: mild perivascular mononuclear cell infiltration
708	25	Portal thrombosis	Mild mononuclear infiltration
709	105	—*	—
713	72	—*	—
715	10	Bronchopneumonia	Mild perivascular infiltration
716	7	Portal thrombosis	No signs of rejection
717	56	—*	—
718	17	Intestinal obstruction	Mild mononuclear cell infiltration

Mean survival time, 50·9 days.

* Still living.

Table II.—RESULTS OF RENAL TRANSPLANTATION IN THE PIG WITH CAVAL VENOUS DRAINAGE

EXPERIMENT No.	LENGTH OF SURVIVAL (days)	HISTOLOGY
696	6	Rejection
697	4	Rejection
698	5	Rejection
699	9	Rejection
710	5	Rejection
711	12	Rejection
712	35	Rejection
719	5	Rejection
720	12	Rejection
721	15	Rejection

Mean survival time, 10·8 days.

the small vessels. There was no tubular necrosis or glomerular lesions. In 1 animal (No. 709) a biopsy taken on the sixtieth day showed only a partial and mild perivascular mononuclear cell infiltrate (*Fig.* 2). This animal was still alive 200 days after transplantation.

2. Allografts with Caval Venous Drainage (10 animals).—All the animals in this group died within 15 days of allografting with the exception of 1 which survived for 35 days (*Table II*). Histological examination of the kidneys of these animals showed a massive mononuclear cell infiltrate in the interstitial connective tissue with tubular necrosis. In the single long-term survivor (No. 711) there was a mononuclear cell perivascular infiltrate and glomerular lesions with periglomerular fibrin deposition (*Fig.* 3).

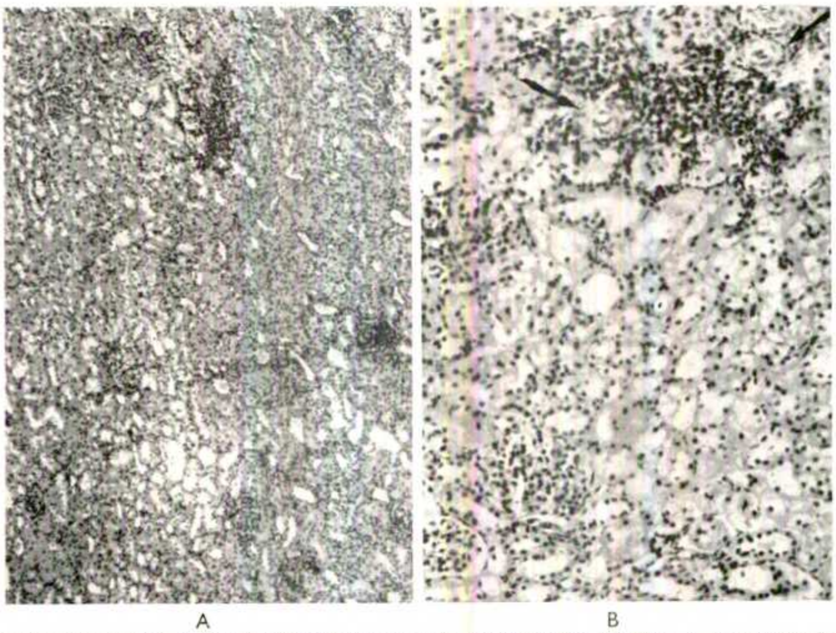

FIG. 2.—Bilateral renal allograft in the pig with portal venous drainage. Kidney biopsy at 60 days. A, Low-power view shows partial mild mononuclear cell infiltration. B, High-power view shows the typical disposition of the infiltration around the vessels. This animal was alive 200 days after transplantation.

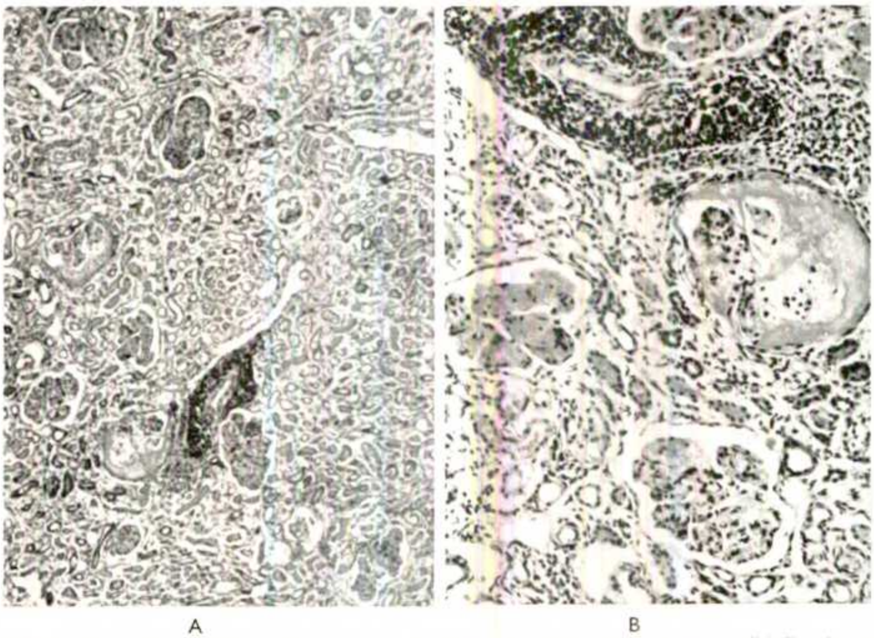

FIG. 3.—Bilateral renal allograft in the pig with caval venous drainage. A, Low-power view showing cell infiltration and glomerular lesions with intracapsular fibrin deposition. B, High-power view. This animal survived for 35 days.

DISCUSSION

The results demonstrate that tolerance is much more prolonged, not only in the case of a single-kidney allograft (Mazzoni and others, 1968; Mazzoni and Melis, 1969; Mazzoni, Di Martino, Melis, Demofonti, Valli, Francesconi, and Pellegrini, 1971), but also when both kidneys are allografted, with portal venous drainage. The average survival time of pigs with portal venous drainage of the renal allograft was 50·9 days, compared with an average survival time with caval drainage of 10 days. This suggests that even a double quantity of transplantation antigens carried directly into the portal vein is degraded so that rejection appears to be prolonged and perhaps abolished. Moreover, histological examination showed the presence of a partial lymphocyte infiltrate in most animals; even in those which survived with good renal function. Some of these animals are still living with no signs of rejection. These results were achieved with no immunosuppressive therapy. It is suggested that such histological responses may be due to processes of a different nature or to quite temporary and reversible immunological processes. This applies only to organs transplanted with portal venous drainage. As far as allografts with caval drainage are concerned, similar but more intensive histological lesions were evident in the grafts and were sufficient to explain death due to rejection. Kidneys allografted with portal venous drainage are tolerated for a long time in the pig but not in other animals. In the mouse and in the dog the same experiment does not prolong the survival time and rejection occurs in a few days (Barker and Corrier, 1967; Fukuda, Hanaoka, Solowey, and Rapaport, 1969; May and others, 1969). The pig is unique in its immunological reactions; for instance, it is the only animal (among those used in experimental surgery) that does not reject the liver allograft, though it does reject other organs (Calne, Davis, Hebertson, Millard, Pena, Salaman, and Sells, 1969). The porcine liver allograft even protects other organs, such as the kidney or the skin, when they are transplanted simultaneously (Calne, Sells, Pena, Davis, Millard, Hebertson, Binns, and Davis, 1969; Calne, Davis, Hadjiyannakis, Sells, Wite, Hebertson, Millard, Joysey, Davis, Binns, and Festenstein, 1970). It has been suggested that the pig may be different from other species and may share similar histocompatibility antigens due to the effect of controlled breeding. Certain strong transplantation antigens present in some strains of pigs are absent in the breeds normally used for transplantation experiments (Calne, Sells, and others, 1969). It has been shown that, using different breeds, and in animals with positive mixed lymphocyte culture reactions, similar results are obtained (Calne, Sells, and others, 1969). Nevertheless, the pig rejects the kidney in the same way and at the same time as other animals (Calne, Davis, and others, 1969; Mazzoni and Melis, 1969; Perper, Gorder, and Bowersox, 1970; Mazzoni and others, 1971). Perper and others (1970) have demonstrated recently that vascularized grafts can survive long periods in moderately immunosuppressed pigs, suggesting that survival of the grafts is not due to enhancement of tolerance but to a low threshold for suppression of the thymus-dependent immune response. Studies on tissue typing are in progress and may give an answer to this question (Vainan, Renard, LaFage, Ameteau, and Nizza, 1970). Other studies on pigs in this laboratory indicate a different lymph-node structure, lack of lymphocytes in the thoracic duct in comparison with the peripheral blood (Binns and Hall, 1966), and a very abundant diuresis. These characteristics, we believe, may explain the results obtained in the present series of experiments.

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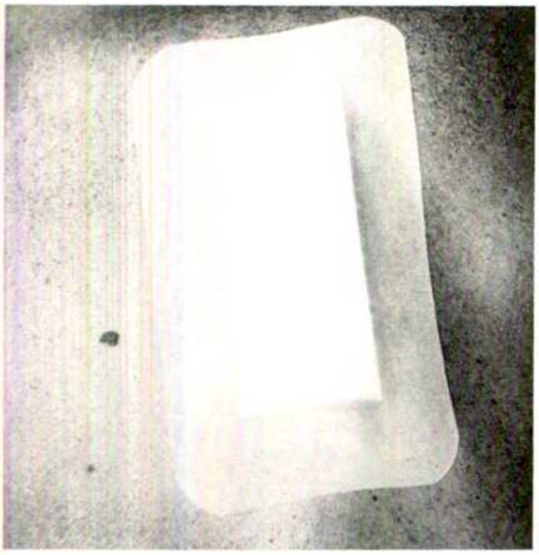

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THE SINGLE THYROID NODULE

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SUMMARY

Between November, 1966, and March, 1970, 2736 patients with single thyroid nodules were investigated at the Alexandra Hospital. Females were more frequently affected than males, with a ratio of females to males of about 7 : 1. The right lobe was one and a half times more frequently involved than the left. In both lobes the lower pole was six to eight times more commonly involved than the upper pole. Pathological data after surgical excision were available in 692 of these patients. Malignancy was proved in 81 cases. The overall incidence of carcinoma was 11·7 per cent. Malignant nodules were two to three times more frequent in persons aged below 20 and over 60 and in males than in females. The incidence of carcinoma in cold and warm nodules was 12·8 and 6·6 per cent respectively. No malignancy was found in a hot nodule or in a toxic adenoma. The location of the nodule was not helpful in predicting malignancy. It is concluded that the incidence of malignancy in cold and warm single thyroid nodules is high, and for this reason surgical removal supplemented with replacement therapy is recommended.

THE single thyroid nodule is of special interest to both physicians and surgeons responsible for the clinical management of patients with thyroid disease. This interest arises from the now well-documented risk of malignancy in such cases (Miller, Hamburger, and Mellinger, 1965; Taylor and Psarras, 1967; Koutras, Livadas, Sfontouris, Messaris, and Statherou, 1968).

In the present paper the clinical and isotopic findings in 2736 patients with single thyroid nodules are described. Pathological results are also included when available. It is hoped that this may be helpful in planning the management of patients with single thyroid nodules.

MATERIALS AND METHODS

The case material of the present study consists of 2736 patients with single thyroid nodules who were investigated at the Thyroid Clinic of the Alexandra Hospital in the period between November, 1966, and March, 1970. These cases have been selected from a total of 12,000 patients who were studied with ^{131}I for possible thyroid disease in the same period. A single thyroid nodule was accepted as being any localized enlargement of the gland without an obvious increase in the size of the remaining thyroid tissue.

All the patients were assessed clinically by the criteria of Crooks, Murray, and Wayne (1959), and in all of them the radio-isotope tests previously described by Malamos, Daikos, Samara, and Koutras (1959) were performed. These tests include measurement of the uptake of ^{131}I by the thyroid at 2, 4, 10, and 24 hours, of the $PB^{131}I$ at 48 hours and the performance simultaneously of a dot scan and a photoscan by a Baird Atomic, type 500, apparatus. The position of the nodule on examination and on the scan was recorded. The single thyroid nodules were described as 'hot', 'warm', or 'cold' according to whether the concentration of dots and/or the density in the photoscan showed a higher, an equal, or a lower concentration of radio-iodide compared with the surrounding parenchyma (Koutras and others, 1968). Of these 2736 patients with single thyroid nodules, pathological data after surgical excision were available in 692. The remaining 2044 patients

Table I.—DISTRIBUTION OF 2736 SINGLE NODULES ACCORDING TO AGE AND SEX

AGE (years)	MALES		FEMALES		TOTAL	
	No.	Per cent	No.	Per cent	No.	Per cent
Under 20	12	3·7	148	6·1	160	5·8
21–40	144	43·9	1040	43·2	1184	43·3
41–60	136	41·5	972	40·4	1108	40·5
61 +	36	10·9	248	10·3	284	10·4
Total	328	12·0	2408	88·0	2736	100·0

Table II.—LOCATION OF 2736 SINGLE THYROID NODULES

LOCATION	NO.		PER CENT	
Right lobe	1459		53·3	
Upper pole		129		4·7
Lower pole		747		27·3
Other		583		21·3
Left lobe	1038		37·9	
Upper pole		65		2·3
Lower pole		519		19·0
Other		454		16·6
Isthmus	231		8·5	
Bilateral	8		0·3	

Table III.—RESULTS OF SCANNING IN 2736 SINGLE NODULES IN RELATION TO AGE AND SEX

AGE (years)	NODULES				
	Cold	Warm	Hot	Toxic Adenomas	Total
Under 20	105	23	22	10	160
21–40	897	124	82	81	1184
41–60	741	83	138	146	1108
61 +	212	14	32	26	284
Total	1955	244	274	263	2736
SEX					
Male	235	42	22	29	328
Female	1720	202	252	234	2408
Total	1955	244	274	263	2736

have not been operated on or have been lost to follow-up.

RESULTS

Patients with a single thyroid nodule constituted 22·8 per cent of the total number of patients investigated for thyroid disease during the period from November, 1966, to March, 1970. This percentage is higher than that obtained in areas of the United States where thyroid disease is not endemic (Vander, Gaston, and Dawber, 1953; Slater, 1956).

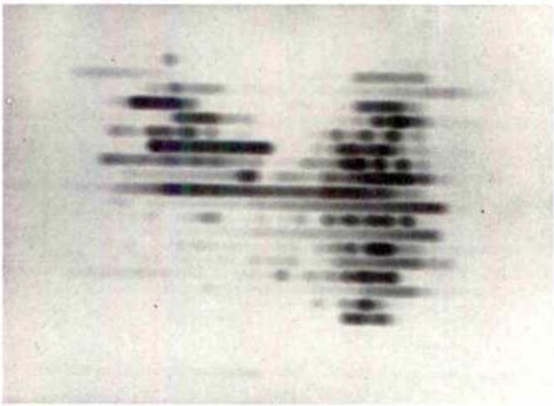

FIG. 1.—Scintiscan showing a cold nodule in the right lower lobe. Histology: nodular colloid goitre.

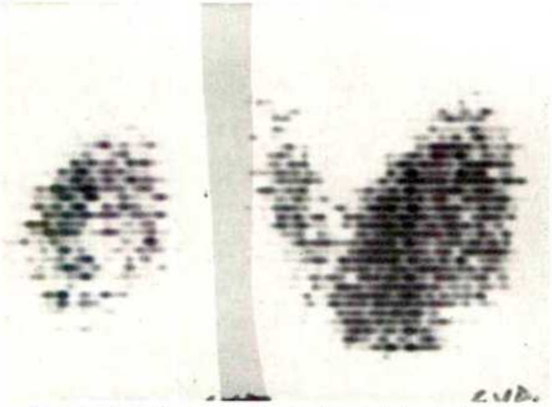

FIG. 3.—*Left*, Scintiscan of a single nodule in the left lobe. Only the nodule takes up iodine whereas the surrounding parenchyma is functionally inert (toxic adenoma). A cold area within the nodule should be noted and was probably due to colloid degeneration. *Right*, After the administration of thyroid-stimulating hormone to the hot nodule, the right lobe and the 'healthy' parts of the left lobe are shown. This confirms the diagnosis of toxic adenoma of the thyroid.

The distribution of the nodules according to the age and sex of the patients is shown in *Table I*, while the distribution according to the location in the thyroid is given in *Table II*.

It can be seen from *Table I* that single thyroid nodules are more frequent in the age-group of 21–40 years, while they are less common at the extreme ages. A high preponderance of females over males in a ratio of about 7 : 1 is evident. The higher incidence of single nodules in females is more or less constant for all age-groups. On the other hand, endemic diffuse goitre affects equally male and female prepubertal children, and it is only after puberty that the female preponderance appears (Malamos, Koutras, Kostamis, Kralios, Rigopoulos, and Zerefos, 1966).

From *Table II* it is clear that the right lobe is more frequently affected than the left one or the isthmus. In both lobes the lower pole is much more commonly involved than the upper pole, which is in agreement with a previous report by Kamba (1970).

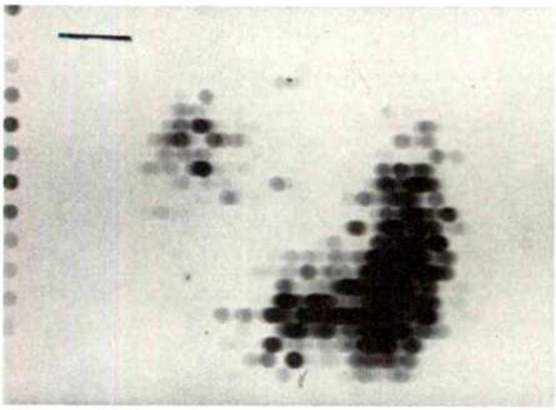

FIG. 2.—Scintiscan showing a cold nodule in the middle of the right lobe. Histology: papillary carcinoma.

Table IV.—HISTOLOGY RESULTS IN 692 SINGLE NODULES IN RELATION TO AGE AND SEX

AGE (years)	BENIGN		MALIGNANT		TOTAL
	No.	Per cent	No.	Per cent	
Below 20	29	76·3	9	23·7	38
21–40	294	90·5	31	9·5	325
41–60	250	90·3	27	9·7	277
61+	38	73·1	14	26·9	52
Total	611	88·3	81	11·7	692
SEX					
Male	78	74·3	27	25·7	105
Female	533	90·8	54	9·2	587

Table V.—HISTOLOGY RESULTS IN 692 SINGLE NODULES IN RELATION TO LOCATION

CLASSIFICATION	RIGHT LOBE		LEFT LOBE		ISTHMUS		BILATERAL		TOTAL
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	
Benign	313	87·9	236	88·7	57	90·5	5	71·4	611
Malignant	43	12·1	30	11·3	6	9·5	2	28·6	81
Total	356		266		63		7		692

The scintiscan results are shown in *Table III*, and representative examples are illustrated in *Figs*. 1–3. Cold nodules are about eight times more frequent than either warm, hot, or toxic adenomas. Cold and warm nodules together make up 80·4 per cent of the total. Analysis of these results according to the age of the patients shows the great preponderance of cold nodules in all age-groups and particularly between the ages of 21 and 60. Warm nodules are more frequent in patients in the 21–40 age-group, while hot nodules and toxic adenomas are more common in patients aged between 40 and 60.

The overall incidence of carcinoma was 11·7 per cent, i.e., 81 cases proved histologically out of 692 patients. The histology results in relation to age and sex, and location and function of the single nodules are shown in *Tables IV–VI*. Malignant nodules are two to three times more frequent in persons aged below 20 and over 60 and in males than in females. Fifty-four of the 81 patients with malignant disease were women and 27 were men, giving a sex ratio of 2 : 1 compared with more than 7 : 1 in the series as a whole. Forty-three (12·1 per cent) of the nodules in the right lobe were malignant compared with 30 (11·3 per cent) of those in the left lobe and 6 (9·5 per cent) of those in the isthmus. Seventy-eight of the 607 cold nodules and 3 of the 45 warm nodules were proved to be carcinomas, an incidence of 12·8 and 6·6 per cent respectively. No malignancy was found in a hot nodule or in a toxic adenoma.

Table VI.—HISTOLOGY RESULTS IN 692 SINGLE NODULES IN RELATION TO FUNCTIONAL CAPACITY

CLASSIFICATION	COLD		WARM		HOT	TOXIC ADENOMAS	TOTAL
	No.	Per cent	No.	Per cent			
Benign	529	87·2	42	93·4	27	13	611
Malignant	78	12·8	3	6·6	—	—	81
Total	607		45		27	13	692

DISCUSSION

A survey such as the present one would be of little use if it did not help in planning the management of the patient with the disease under discussion. The overall incidence of cancer of the thyroid found is high enough to justify a radical therapeutic approach. Looking through the figures of the present series, the high preponderance of cold nodules is impressive. Furthermore, 12·8 per cent of them were malignant. This figure agrees with previous results in a smaller series from this unit (Koutras and others, 1968). Although this percentage is not as high as in other selected series where figures between 20 and 58 per cent have been found (Saenger, Barrett, Passino, Seltzer, and Dooley, 1964; Miller and others, 1965), it is still considerable. In another large series of 607 cold nodules, Mellière, Massin, Calmettes, Chigot, Savoie, and Garnier (1970) found malignancy in 115, an overall incidence of 19 per cent. The incidence of malignancy in warm nodules in the present series was 6·6 per cent, and this figure questions the advisability of conservative treatment for such nodules which is advocated by some thyroidologists (Astwood, Cassidy, and Aurbach, 1960). No case of malignancy was detected histologically in 27 cases of toxic adenomas, in agreement with the results of others (Taylor and Psarras, 1967).

The preferential location of lesions in the right lobe is probably due to the fact that this lobe is a little larger than the left in 80 per cent of cases (Börner, Moll, and Heller, 1963; Keynes, 1966; Thompson and Jackson, 1969). Kamba (1970) also observed a greater incidence of nodules in the right lobe, but in his case material the difference from the left lobe was not as striking as in the present series. Regarding the isthmus, nodules in this part of the gland may well have arisen in one or other lobe and been forced to the midline by the action of the strap muscles. The slightly greater incidence of cancer in the right lobe does not seem, however, to be statistically significant. There is a slight discrepancy between the numbers of patients with single thyroid nodules who were investigated and those who were operated on, which is probably due to the fact that many of the patients treated surgically elsewhere were lost to follow-up. Since both groups seem to be identical, the results of the analysis of one group should also be applicable to the other.

It may be argued that the groups investigated are highly selected and do not represent the population as a whole. Although the figures of Sokal (1959) and Tellem, Shahl, and Meranze (1961) give a very low incidence of thyroid cancer in the general population, the more exhaustive study of excised thyroid glands such as that carried out at the Mayo Clinic by Mortensen, Bennett, and Woolner (1955) found many tumours which had not been detected during life. On the other hand, it is generally accepted that there has been an increase in the incidence of thyroid cancer in recent years (Colcock and Cattell, 1962; Veith, Brooks, Grigsby, and Selenkow, 1964; Wahner, Cuello, Correa, Uribe, and Gaitan, 1966; Weaver, Nishiyama, Burton, and Bitsakis, 1966). It is possible that many of the thyroid carcinomas which are removed surgically would, if they were not excised, remain clinically silent for the entire life-span of the patient. However, although thyroid cancer has a good prognosis in most of the cases which are treated, it still remains a potentially lethal disease if left untreated (Hirabayashi and Lindsay, 1961). It is generally accepted that the prognosis is closely related to early diagnosis (Woolner, Beahrs, Black, McConahey, and Keating, 1967, 1969). Thus, the problem is, when one is confronted with a patient with a single thyroid nodule, what is the best treatment for this particular case (Meachim and Stainsby, 1966; Taylor, 1968). Unfortunately, there is at present no practical technique for differentiating malignant nodules from benign ones before operation (Groesbeck, 1959; Attie, 1960; Greene, Piercy, and Singer, 1964). Radioactive iodine and scintiscanning give useful information and may make the clinician suspicious of malignancy, particularly in the case of cold and warm nodules, but they are in no way definitely diagnostic. There are a great many other lesions of the thyroid gland which do not take up radio-iodine or take it up to the same extent as the surrounding tissue. Hopefully, thyroid scans with isotopes other than iodine may provide in the future a simple technique for distinguishing between malignant tumours and benign structures, which are both 'cold' in the usual radio-iodine scans, but these techniques require further improvement before becoming generally applicable. Hot nodules and toxic adenomas are practically always benign, but they constitute only a small minority of the thyroid nodules.

Most surgeons prefer to avoid a needle biopsy since there is the real possibility that the tumour may be spread down the needle tract and the subsequent excision of the tumour made more difficult. Mellière and others (1970), however, stress that if aspiration in cystic nodules results in a complete disappearance of the nodule, then malignancy may be excluded, but if the nodule does not disappear completely after aspiration there is a 10 per cent chance of the lesion being malignant. In any case, the policy of this thyroid unit of the Alexandra Hospital, Athens, is to advise every individual with a single thyroid, particularly a cold, nodule to have it excised surgically, and in the case of the very young or the very old or in a male patient at the earliest possible date because the risk of malignancy is higher in these groups of patients (Taylor and Psarras, 1967; Koutras and others, 1968; Smith, 1969; Taylor, 1969).

It could be argued that since over 85 per cent of the thyroid nodules which are removed surgically are finally classified as benign these patients could have avoided an unnecessary operation. On the other hand, thyroid cancer is a slowly progressing diesase (Astwood and others, 1960). However, our policy seems justified in view of the extremely low morbidity with which this operation is accompanied. There have been no serious complications and no patient has died as a result of the operation. When the lesion appeared to be solitary, a complete lobectomy on the affected side was carried out together with the removal of the isthmus and a small slice of tissue from the apparently normal lobe of the opposite side (Crile, 1967; Taylor, 1968, 1969). In this way subsequent enlargement of the gland is made less noticeable. When the lesion proved to be malignant at operation, total thyroidectomy with preservation of at least two parathyroid glands and both recurrent nerves was carried out.

In all the patients in whom a partial or total thyroidectomy was performed replacement therapy was recommended in the form of thyroxine orally not only to provide the patient with an adequate level of thyroid hormone and thus a sense of well-being, but also to suppress the secretion of thyroid-stimulating hormone by the pituitary and thus prevent further growth of the thyroid gland or of any remaining nodular tissue.

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THE RELATIONSHIP BETWEEN BLOOD-FLOW AND FAILURE OF FEMOROPOPLITEAL RECONSTRUCTIVE ARTERIAL SURGERY

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SUMMARY

Blood-flow measured at operation in 80 limbs was found to be significantly related to the patency of the reconstruction 12 months later. The incidence of failure was 14 per cent when the flow exceeded 100 ml. per minute and was 54 per cent when the flow was less than this figure.

Although blood-flow was significantly lower in patients with obstructed distal arteries, there were wide variations in flow between limbs with similar degrees of obstruction. There was, however, a significant increase in the failure rate with increasing arterial obstruction, and where two or all three of the tibial arteries were obstructed the long-term failure rate was 48 per cent.

MOST early failures of reconstructive arterial operations occur at once, or within 24 hours of surgery, and it would seem likely that a high blood-flow through the reconstructed artery at the end of the operation would be associated with a low failure rate during the first year. Little has been published on this subject, and the conclusion of Mundth, Darling, Morow, Buckley, Linton, and Austen (1969) that there was no relationship between flow and failure rate conflicts with that of Cappelen and Hall (1967), who found that 4 out of 8 cases failed when the flow was less than 100 ml. per minute, but only 3 out of 33 failed at higher flow rates. This study was therefore undertaken to see whether the patency of the femoropopliteal segment 1 year after surgery was related to the arterial blood-flow on completion of the reconstruction and also whether these two factors were related to the degree of distal arterial disease indicated by arteriography.

Table I.—ANALYSIS OF 80 OPERATIONS (76 PATIENTS) ACCORDING TO TYPE OF OPERATION AND LENGTH OF SUBSEQUENT FOLLOW-UP

DURATION OF FOLLOW-UP	TYPE OF OPERATION			
	Femoral Rebore	Femoro-popliteal Vein-graft	Vein-graft for Popliteal Aneurysm	Femorotibial Vein-graft
12 months	14	43	4	7
Less than 12 months	1	7	0	4
Total	15	50*	4	11*

* One patient died before discharge from hospital.

PATIENTS STUDIED

Eighty limbs from 76 patients were studied. The type of operation is shown in *Table I.*

All patients suffered from atherosclerosis, and in 13 patients there was associated diabetes mellitus. The average age was 59 years. Two-thirds of the patients had ischaemic ulceration or impending gangrene of the extremity concerned. Femoral disobliterations were performed for short occlusions above the adductor hiatus with a minimally diseased popliteal artery, or in more severe disease when no suitable vein was available for a by-pass. In 50 out of the 80 limbs long autogenous vein-grafts were used because of the extensive degenerative arterial disease. Five of the femorotibial and 7 of the femoropopliteal by-pass vein-grafts were of the in situ type with the valves destroyed by retrograde passage of a Foley catheter introducer. In 3 patients the cephalic or basilic vein was used instead of, or in addition to, part of the long saphenous vein. Seventy-two of the limbs studied were sympathectomized. If this had not been done previously, ipsilateral sympathetic ablation was performed at the time of arterial surgery (Terry, Allan, and Taylor, 1970).

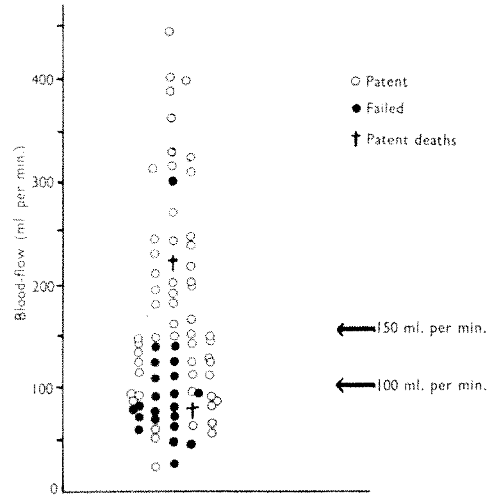

FIG. 1.—Blood-flow through the reconstructed artery (superficial femoral or popliteal artery or vein-graft) measured at operation in 80 patients.

METHODS

Blood-flow was measured at operation after the reconstructed segment was opened and a steady flow was obtained. With vein-grafts the probe was applied to the graft itself and with rebores it was placed below the distal arteriotomy whenever possible. A square-wave electromagnetic flowmeter* was used with cuff probes of type PM. Measurements were continued until the probe was removed just before skin closure.

Arteriographic Appearance.—Most systems for grading the distal arteries according to the degree of obstruction use only three categories. In this study

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* Type 372, Nycotron, Oslo, Norway.

40 per cent of the limbs would have been placed in the third group—having only one patent tibial vessel or diffuse blocks of all three vessels. In order to evaluate more precisely the relationship of blood-flow to the severity of distal arterial obstruction each limb was placed in one of eight groups, which are listed in *Table II*. Groups 4–8 would all be described as having a poor run-off.

Follow-up.—Two patients with patent grafts died postoperatively. Sixty-six of the limbs have been followed for 12 months, and the remaining 12 for 5–11 months. The average follow-up for all surviving cases was 11·7 months. When there was clinical doubt about patency, ankle and calf pressures were measured using the Parks 801 Doppler flow-detector, as previously described (Allan and Terry, 1969).

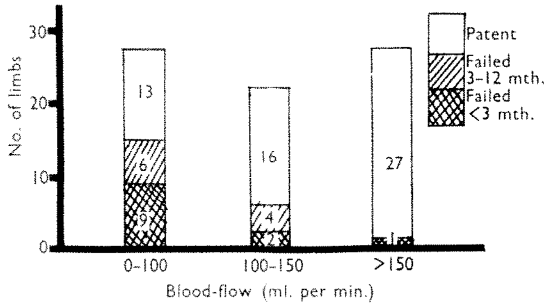

FIG. 2.—The 78 limbs are grouped according to the post-reconstruction blood-flow to show the incidence of failure within 3 and 12 months.

Table II.—BLOOD-FLOW AT OPERATION RELATED TO THE DEGREE OF PATENCY OF THE DISTAL TIBIAL VESSELS AS INDICATED BY ARTERIOGRAPHY IN 78 LIMBS

	GROUP							
	1. All Three Tibial Arteries Patent	2. Posterior Tibial and Peroneal Arteries Patent	3. Anterior Tibial and Peroneal Arteries Patent	4. Posterior Tibial Artery alone Patent	5. Anterior Tibial Artery alone Patent	6. Peroneal Artery alone Patent	7. Free Popliteal Segment only Patent	8. Diffuse Distal Disease
No. of limbs	27	11	9	6	5	10	4	6
Mean blood-flow (ml. per min. ± S.D.)	239 ± 109	158 ± 93	114 ± 79	96 ± 40	103 ± 32	107 ± 50	98 ± 30	81 ± 44
Percentage patency	92·6	72·7	77·7	66·6	60·0	50·0	25·0	50·0

RESULTS

1. Blood-flow and Failure.—*Fig.* 1 shows the blood-flow measured in the superficial femoral or popliteal artery or in the vein-graft of 80 limbs. There were 22 failures within the follow-up period and 2 patients with patent grafts died within 3 months of surgery. Twelve of the failures occurred within 3 months; in 9 of these cases the flow at operation was 100 ml. per minute or less. In *Fig.* 2 the limbs have been divided into three groups according to the flow, and it can be seen that the incidence of failure within 3 months was 3 out of 50 (6 per cent) if the flow exceeded 100 ml. per minute, and 9 out of 28 (32 per cent) if it was less than 100 ml. per minute ($\chi^2 = 6·3$, $0·02 > P > 0·01$).

There were 10 failures between 3 and 12 months after surgery, and the incidence of failure within 12 months was 7 out of 50 (14 per cent) when the flow exceeded 100 ml. per minute and 15 out of 28 (54 per cent) at lower flows ($\chi^2 = 8·6$, $0·01 > P > 0·001$). If one excludes 12 limbs which were followed for less than 12 months (10 patent and 2 failed) the incidence of failure at high flows was 14 per cent and at low flows 58 per cent ($\chi^2 = 8·3$, $0·01 > P > 0·001$).

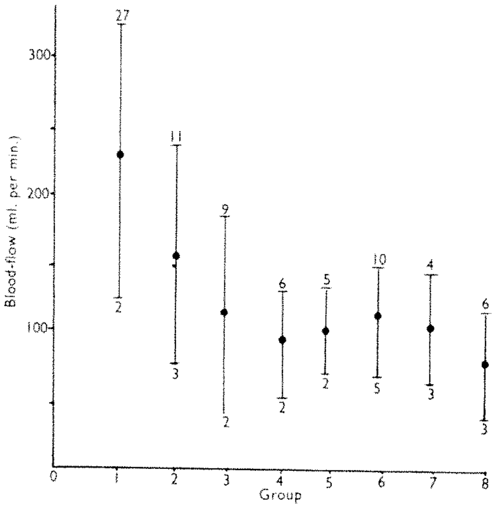

FIG. 3.—Mean blood-flow and standard deviation (S.D.) for the limbs in each group of run-off. For each group the upper figure is the number of limbs in that group and the lower figure is the number of failures within the follow-up period.

2. Arteriographic Appearance and Failure.—After allocating each limb to one of eight groups according to the state of the distal arterial tree the mean flow in each group and the standard deviation (S.D.) were calculated. The results are shown in *Table II* and *Fig.* 3. The fall in mean flow with increasing arterial obstruction is apparent in *Fig.* 3 and is found to be significant (Spearman's rank correlation coefficient, $r = 0·87$, $0·01 > P > 0·001$). In groups 1–3, which had anatomically good run-offs, flow exceeded 150 ml. per minute in 75 per cent of the limbs and 200 ml. per minute in 55 per cent. There was little difference in flow in groups 4–8.

The increasing rate of failure within 12 months as the run-off became worse (*Table II*) is also significant ($r = 0·92$, $P < 0·001$). In groups 1–3 85 per cent of the vessels remained patent, whereas only 52 per cent remained patent in groups 4–8.

DISCUSSION

Cappelen and Hall (1967) claimed that failure within 1 month after in situ femoropopliteal grafts was greater with blood-flows less than 100 ml. per minute. The flows they measured appear to have a similar distribution to those in the present report, although the majority of their cases had excellent or good run-offs. Sako (1967) felt that early failure was more common with flows in the region of 30 ml. per minute, and Mannick, Jackson, Coffman, and Hume (1967), in a study of 14 limb-salvage cases, reported that a critical level for failure could not be given as 1 case with a flow of 15 ml. per minute had remained patent. Little, Sheil, Loewenthal, and Goodman (1968) found in 40 vein-grafts that 80 per cent of those with a flow less than 60 ml. per minute thrombosed within 3 months. However, Mundth and others (1969) found no relationship between flow and failure, peripheral resistance, and the arteriographic run-off in 19 grafts. Some of their cases were followed for less than 3 months and in only 3 limbs did flow exceed 100 ml. per minute.

Table III.—CONTRIBUTING FACTORS IN THE FAILURE OF ARTERIAL RECONSTRUCTIVE SURGERY

Cause of Failure	*No. of Limbs*	*Time of Failure*
3-mm. vein-grafts	2	1 early, 1 late
Vein necrosis at upper anastomosis (3-mm. vein)	1	Early
Patent cusp, in situ vein	1	Primary failure
Vein-graft fistula, in situ vein	1	Late
Intimal dissection	1	Primary failure
Residual shelf after rebore	2	1 primary failure, 1 late
Cardiac failure	1	Primary failure

Selection of cases and operative techniques differ from centre to centre, and it is therefore difficult, in terms of blood-flow, to compare one series with another. Many factors influence the flow during an operation, in particular anaesthetic agents, systemic blood-pressure, the degree of hypo- or hypercapnia, circulating vasopressor agents, and regional or general hypothermia. It is our policy to reduce the physiological component of the peripheral resistance by generous fluid replacement, keeping the limb and body warm with a heated water-filled mattress and, usually, by lumbar sympathectomy. Where this is not done one would expect the immediate post-reconstruction flow to be influenced significantly by the degree of vasoconstriction obtaining in the distal vascular bed.

While the chances of failure with flows less than 100 ml. per minute are undoubtedly high, we would agree with Mannick and others (1967) that one critical value below which a reconstruction must fail cannot be given, as one of our reconstructions with a flow of 20 ml. per minute was patent 2 years after surgery. Some of these grafts will undoubtedly remain patent owing to the head of pressure opening up the distal arterial tree or new collaterals. On serial arteriograms taken at intervals in the postoperative follow-up period progessive dilatation of the tibial vessels may be seen, and in the early postoperative period the systolic ankle pressure may show gradual improvement over 48 hours.

Darling, Linton, and Razzuk (1967), in a study of 295 vein-grafts, felt that the commonest cause of failure related to technical problems at the time of operation, namely a vein-graft less than 4 mm. in diameter, a kinked graft, a difficult distal anastomosis due to a sclerotic popliteal artery, or a poor take-off from the common femoral artery. Baddeley, Ashton, Slaney, and Barnes (1970) were unable to support this view, the commonest cause of failure in their series being progression of atherosclerosis distally. The present study confirms the finding that failure rates are much higher in the presence of advanced atherosclerosis of the distal arterial tree, but other factors are also involved. These are set out in *Table III.* In only 1 of these cases did the flow exceed 100 ml. per minute.

It remains to be explained why primary failure, that is, failure of the reconstruction within the hospital admission period, may still occur when flows in excess of 100 ml. per minute have been recorded. In 1 of 3 such cases in the present series the cause was a technical fault, but in 2 cases no obvious reason was apparent. In our more recent experience primary failure has occurred in 2 vein-grafts where initially a flow in excess of 150 ml. per minute was measured. Both grafts were less than 4 mm. in diameter at the upper anastomosis. One failed as a result of a period of postoperative hypotension and was salvaged by thrombectomy. In the other the graft was inserted at too great a tension and became occluded when the limb was straightened.

After 12 months progression of atherosclerosis may play a part in failure caused by either inflow- or outflow-tract obstruction. However, many grafts will remain patent in the presence of a completely occluded main vessel outflow, and it would appear that a graft becomes more resistant to thrombosis once re-endothelialization of the intima and anastomotic suture lines has occurred. Restenosis of a rebored segment may occur within 12 months, and strictures of vein-grafts at the site of valve remnants have also been recorded; in these situations it is unlikely that peroperative flow measurements bear any relationship to later failure.

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THE EFFECTS OF POSTURE, EXERCISE, AND BANDAGE PRESSURE ON THE CLEARANCE OF ^{24}Na FROM THE SUBCUTANEOUS TISSUES OF THE FOOT*

By A. D. B. CHANT†

VEIN CLINIC, CARDIFF ROYAL INFIRMARY

SUMMARY

The effects of posture, exercise, and bandage compression on the clearance of ^{24}Na from the subcutaneous tissues of the foot in 12 control subjects and in 32 patients with venous abnormalities have been investigated. Lowering the foot slowed clearance in the control subjects and in the patients with varicose veins, but no slowing occurred in patients with chronic deep venous thrombosis (D.V.T.). Exercise increased the clearance in the controls but this increase was less in the varicose vein and D.V.T. groups and absent in the group with venous ulcers. Treatment of the patients with varicose veins by sclerotherapy returned their exercise increment in clearance of ^{24}Na to control levels. Bandage compression increased clearance until a maximum was reached at approximately the intravascular hydrostatic pressure. Thereafter it declined. A significantly higher bandage compression was required to produce maximum clearance of ^{24}Na in patients with D.V.T. In two further experiments when bandage compression was maintained at intravascular hydrostatic pressure the effect of posture on clearance was abolished.

These observations indicate that ^{24}Na clearance may be of value in the investigation of patients with venous abnormalities.

THE original study by Kety (1949) on the relationship between the clearance of ^{24}Na and blood-flow led to the use of ^{24}Na clearance in the assessment of peripheral arterial disease. Little has been written concerning the possible use of this technique to assess patients with venous disease. Cooper, Elkin, Shea, and Dennis (1949) and McInally (1952) suggested that a relationship existed between ^{24}Na clearance and the venous system. Their findings were supported subsequently by the studies of Chant (1968).

This paper extends these original observations by studying the influence of posture, exercise, and bandage compression on the clearance of ^{24}Na from the subcutaneous tissues of the foot. The subjects investigated comprised the following groups: (1) Patients with varicose veins, (2) Patients with treated varicose veins, (3) Patients with deep venous thrombosis, (4) Patients with venous ulcers, and (5) Control subjects.

MATERIALS AND METHODS

The mean age and sex ratio of the subjects were similar in all the groups apart from a slight male predominance in the control group. The diagnostic criteria for deep venous thrombosis (D.V.T.) are set out in *Table I*. No D.V.T. was acute. No patient had clinical evidence of arterial disease. The patients in the varicose-vein group had no evidence to suggest deep venous disease but all had incompetent communicating perforating veins.

Table I.—THE DIAGNOSTIC CRITERIA IN THE PATIENTS WITH DEEP VENOUS THROMBOSIS

Experiment No.	*Age* (years)	*Criteria for Venous Obstruction*
13	34	Clinical
14	38	Radiological
15	56	Clinical
34	65	Operative and histological
35	50	Clinical
37	54	Clinical
46	41	Radiological
52	60	Radiological and operative
63	26	Radiological
66	68	Radiological
80	40	Radiological
92	36	Radiological

Investigations were performed in a temperature-controlled room ($27 \pm \frac{1}{2}°$ C.). The patient lay on a tilt table at the bottom end of which was a treadle ergometer. Following a period of acclimatization a subcutaneous injection of 0·1 ml. normal saline containing 3–5 μc. of ^{24}Na was given in the dorsal aspect of the first metatarsal space. Clearance was measured in a horizontal position (k_1) and in a sitting position with the legs supported by the treadle ergometer but sloping downwards at 45° (k_2). Exercise was also performed in this latter position, the patient moving the ergometer for 10 minutes at a work rate of 40 ft. per lb. per minute (k_e). Radioactivity was measured by a scintillation counter (Isotope Development Ltd., Type 7070) and the count rate was recorded on a chart (Elliott Automation Emrec Mk. II). The clearance of the isotope was measured for approximately 10–15 minutes in each position.

The methods of extraction of the clearance constant (k) and interpretation of the exercise are described below.

In 6 subjects (3 in the control group and 3 in the D.V.T. group) after injection of the isotope a sphygmomanometer cuff was used to simulate bandage compression. It was applied to the foot, centred over the site of the injection in order to maintain an even cuff pressure. The cuff was connected to a mercury manometer and inflated stepwise while measurements of radioactivity were taken with the subjects first in position 1 and then in position 2.

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* Based on a paper read to the Surgical Research Society at Leeds in July, 1968.

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In 2 further subjects the sphygmomanometer cuff was connected to a saline reservoir with the meniscus kept at heart level whatever the subject's posture. The patient's position was then varied from horizontal to vertical in stages whilst the clearance estimations were made.

Extraction of the Clearance Constant (k) **from the Radioactivity Record.**—Count rates per minute, C (expressed as a percentage of an arbitrary chosen maximal rate), were taken from the radioactivity record at 1-minute intervals. A computer was used to calculate the regression of $\log_e C$ upon times for all experimental periods and subjects. This was done to see whether the disappearance of radioactivity from the site of injection followed an exponential course. The correlation coefficients for these regression lines did not differ significantly from 1. It was concluded that the decline of radioactivity was mono-exponential and that the slope of the regression line represented the clearance constant (k) as defined by Kety (1949).

An interpolation method was used for the measurement of radioactivity during the exercise period. The curve showing the decline of radioactivity during the post-exercise period was extrapolated backwards to the time of termination of the exercise. It was assumed that the decline in local radioactivity from the level at the start to the level at the end of the exercise period had likewise followed a mono-exponential course, and the slope of the semi-logarithmic plot of C against time interpolated as the (k) value for the exercise period. For simplification in the presentation of these results two definitions are made. The term 'postural decrement' is defined as the decrease of ^{24}Na clearance found when the limb is lowered from the horizontal to the vertical position ($k_1 - k_2$), and 'exercise increment' is defined as the increase in ^{24}Na clearance caused by exercise ($k_e - k_2$).

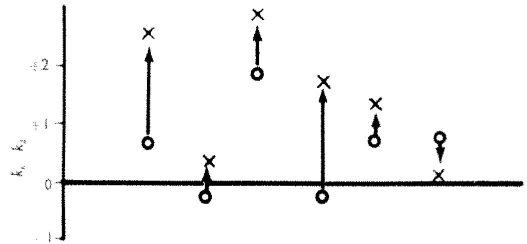

FIG. 1.—Treatment of varicose veins has improved the ability of 5 out of 6 patients to increase clearance on exercise. In the sixth, treatment produced a D.V.T. and no improvement was therefore noted. ○, Pre-treatment. ×, Post-treatment.

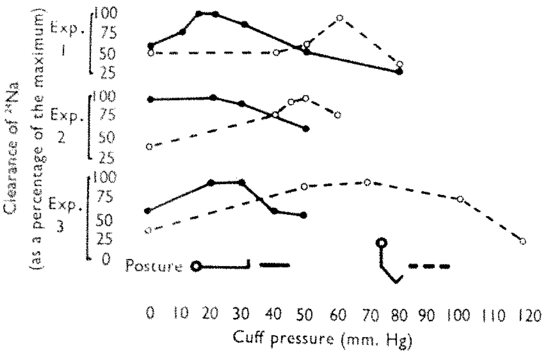

FIG. 2.—Showing the increase in clearance with increased cuff pressure until when cuff pressure exceeds intravascular pressure clearance decreases.

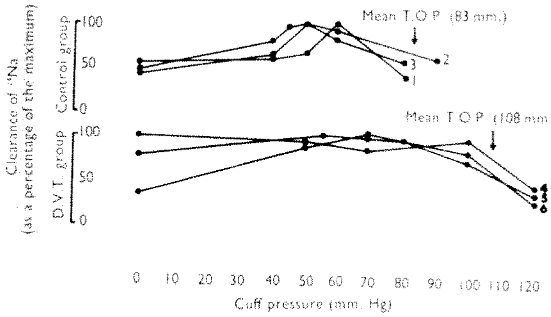

FIG. 3.—Clearance/cuff pressure curve in the vertical position. Note the significantly higher tail-off point (T.O.P.) in patients with diseased veins.

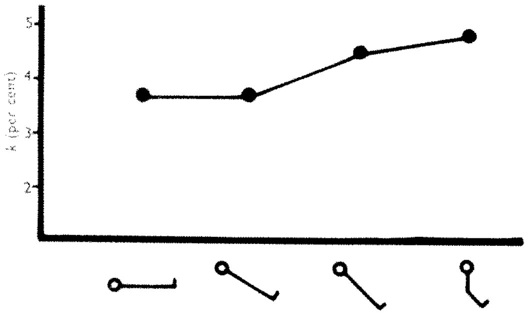

FIG. 4.—The effect on clearance of keeping the cuff pressure equal to the intravascular hydrostatic pressure by means of a saline reservoir. The usual slowing in clearance in the vertical position no longer occurs.

RESULTS

1. Influence of Posture on the Rate of Clearance of ^{24}Na.—The slowing of clearance ($k_1 - k_2$) with dependent posture is shown in *Table II*. In the control subjects there was a marked decrease in ^{24}Na clearance when the leg was lowered. In patients with varicose veins the decrease was similar, and statistically there was no difference between the groups. There is, however, a very marked difference both in the variance ($P < 0.05$) and the mean ($P < 0.001$) when these groups are compared with the D.V.T. group. In the patients with D.V.T. lowering the limb had little effect on the clearance rate. The ulcer patients included cases of D.V.T. and varicose veins. The postural decrement in their case fell midway between these groups.

2. Influence of Exercise on the Clearance of ^{24}Na.—Exercise increased clearance in both the control and the varicose vein groups (*Table II*). In the D.V.T. group, however, this effect was less and in the ulcer group it was absent altogether. The means of the control and the ulcer groups differed significantly ($P < 0.01$).

A trend is apparent from the controls with good veins to the ulcer patients whose exercise increment did not differ significantly from zero. Six patients were investigated before and after treatment of their varicose veins which were mostly confined to the calf. Treatment consisted of injection sclerotherapy to the incompetent perforating veins. Five of the 6 patients showed an increase in exercise increment (*Fig.* 1); the sixth developed a D.V.T. and his exercise increment was reduced.

Table II.—CLEARANCE CONSTANTS IN POSITIONS 1 AND 2 AND ON EXERCISE

GROUP	NO. OF PATIENTS	k_1	k_2	k_e	$k_1 - k_2 \pm$ S.D.	$k_e - k_2 \pm$ S.D.
Control	12	4·1	2·0	3·1	2·0 ± 1·0	1·1 ± 0·4
Varicose veins	12	3·8	1·6	2·3	2·2 ± 1·3	0·8 ± 1·2
D.V.T.	12	2·1	1·7	1·8	0·3 ± 0·5	0·1 ± 0·7
Ulcers	8	3·8	2·2	2·2	1·7 ± 1·7	0·0 ± 0·7

3. Influence of External Cuff Pressure on Clearance of ^{24}Na.—The result of increasing the cuff pressure was to increase clearance up to the point when the cuff pressure approximately equalled the intravascular hydrostatic pressure, when the rate of clearance fell (*Fig.* 2). The cuff pressure at which definite evidence of a fall in clearance (20 per cent maximum) had been obtained was called the 'tail-off point'. It can be seen from *Fig.* 3 that the average tail-off point for the disease group in the vertical (2) position occurred at a significantly higher value ($P < 0\cdot05$) than in the controls. In the final group of experiments the cuff pressure was maintained at the hydrostatic pressure within the vessels by means of a saline reservoir. The effect of this was to abolish the usual slowing in clearance found in dependent postures. If anything a slight increase occurred (*Fig.* 4).

DISCUSSION

The association of peripheral oedema with venous disease is well recognized. Indeed the various treatments of venous disease, for example, injection of incompetent perforating veins and bandaging, are often directed towards relieving oedema. It would seem likely therefore that if the movement of oedema or tissue fluid could be traced this measurement might form a rational basis for an objective assessment of venous disease and its treatment. It would appear from the present studies that this is now possible. Thus, in the posture experiments clearance slows when the limb is lowered; this corresponds to the pooling noted both clinically in the form of oedema and by previous plethysmographic studies (Mellander, Oberg, and Odelram, 1964). During exercise the clearance rate of ^{24}Na increases in the same way that oedema decreases.

This analogy is supported further by the results demonstrated between clearance and bandage pressure. Although similar experiments have been performed using Xe (Campion, Hoffman, and Jepson, 1968) the initial increase in clearance with pressure has not been demonstrated previously. This increase in clearance coincides with an increase in femoral vein blood-flow (Spiro, Roberts, and Richards, 1970). Doubt was cast on the interpretation of these experiments (Chant, 1970). It is interesting to note that subsequent experiments (Sabri, Roberts, and Cotton, 1971) showed this increase in flow to be time-dependent and probably due in part to the emptying of the veins on compression and partly to the removal of tissue fluid by pressure. Provided, therefore, that bandage pressure never exceeds intravascular hydrostatic pressure, then bandaging limits the formation of oedema but does not increase the vascular resistance to the detriment of blood-flow. It also appears from the sphygmomanometer cuff experiments that in patients with D.V.T., higher bandaging pressures are necessary than in control subjects. Accurate bandaging, however, presents problems. Intracapillary pressure varies with posture and exercise; it is also graded from the toe to the right atrium. A conventional bandage, therefore, to produce maximal clearance should be applied with 'tight turns at the bottom, loose turns at the top'. This type of bandage works loose and in any case is relevant only to the posture in which it is applied. The theoretically perfect hydrostatic stocking described by Wood (1968) would seem to provide an answer from the tissue perfusion viewpoint, and this is substantiated by the present experiments (*Fig.* 4).

So far the results are compatible with the concept that changes in ^{24}Na clearance parallel the movement of tissue fluid. However, the difference found in the postural response to the lowering of the limb between the control and the D.V.T. groups would on preliminary examination appear to be against this interpretation. If, as was previously supposed, the clearance of an isotope reflects blood-flow, then the decrease in clearance demonstrated in the control subjects is due to a vascular postural reflex such as the one postulated by Gaskell and Burton (1953). If this is correct then in the D.V.T. group one must assume that the disease process has in some way interfered with the reflex. There is, however, an alternative explanation which once more fits in with the concept of tissue-fluid pooling. It is likely that in cases of D.V.T. the consequent venous hypertension has led to the formation of oedema. It is probable that the oedema forms a sheath around the veins and acts in a manner similar to the hydrostatic stocking demonstrated in *Fig.* 4, thus limiting changes in clearance.

The relationship between the clearance of ^{24}Na, posture, and exercise has been shown to differ in health and disease. To assess the possible clinical application of this finding in diagnosing chronic deep venous obstruction a prospective study involving larger numbers of patients is indicated; the significant difference in the postural decrement between healthy subjects and patients with obstructed veins suggests that this is practicable, and this is supported by the findings in 1 patient in whom a diminished postural decrement predicted previously unsuspected deep-vein disease (*Table I*, experiment 52). Similarly, the exercise increment also seems to relate to the patient's venous state. The patients with the lowest exercise increment values were those with venous ulcers, while those with the highest were the control subjects. It seems likely therefore that this relationship provides the basis for the objective evaluation of treatment in venous disease. The assessment of varicose veins before and after treatment (*Fig.* 1) illustrates the potential use of the method; here the incompetent perforating veins which contribute to the inefficiency of the calf pump in such cases have been sealed by sclerosant and the exercise increment in clearance improved.

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PERSISTENT AND RECURRENT HYPERPARATHYROIDISM

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SUMMARY

During the past 11 years at Hammersmith Hospital 11 patients have had parathyroid operations following a previous neck exploration. Six had persistent hyperparathyroidism and 5 had recurrent hyperparathyroidism with a 'lucid interval' of biochemical normality of from 5 months to 11 years. Successful results were obtained in 9 of the 11 patients after a total of 29 operations, 4 of which were combined with sternotomy. The reasons for failure at operation and the medical and surgical management of these patients are reviewed.

EVER since Mandl (1926), a Viennese, performed the first successful parathyroidectomy on 30 June, 1925, surgery has been the accepted mode of therapy for hyperparathyroidism, with excellent results. Indeed, Black and Ackerman (1950) claimed that the surgical treatment of this condition was more certain and satisfactory than that of any other surgical endocrinopathy, including disease of the thyroid. Despite this assertion, there are still unsuccessful parathyroid operations even in expert hands. Probably the most famous of these was Charles Martel, a sea-captain, whose history was so graphically told by Fuller Albright in his Presidential address to the American Endocrine Society in 1948. Captain Martel had 7 operations over a period of 6 years, with the removal of two normal parathyroids and a total thyroidectomy before the offending parathyroid adenoma was removed from the anterior mediastinum by Edward D. Churchill.

The incidence of unsuccessful or 'failed' first operations for hyperparathyroidism varies. Unsuccessful or 'failed' in this context means that the condition is not permanently cured following operation. Failure may occur despite the removal of one or more tumours if there is primary chief-cell hyperplasia or there are multiple parathyroid adenomas. In contrast, 'some cures' occur when no parathyroid tissue has been removed.

Hellstrom and Ivemark (1962) reported 25 failures in 138 patients, Chamberlin, Nicholas, and Hanka (1963) 11 in 48, and we have had 6 in 99 patients. Cope, Barnes, Castleman, Mueller, and Roth (1961) reported 51 failures in 299 patients, but many of their operations were performed for diagnostic reasons.

During the past 11 years at Hammersmith Hospital 11 patients have required parathyroid operations following previously unsuccessful exploration. Five of these patients had recurrent hyperparathyroidism after a definite lucid interval and 6 had persistent hyperparathyroidism. Nine of the 11 patients were referred after unsuccessful operations elsewhere. The problems which these 11 patients presented and their management are discussed here.

The patients presented here compare in age and sex distribution with those of most other reported series. There were 7 women and 4 men with a mean age of 40 years. Two patients had a family history of endocrine disease. *Table I* lists the primary clinical manifestations which brought the patients to seek advice. In contrast to most reviews and our own total series of 99 patients with hyperparathyroidism, where the majority of symptoms related to renal involvement, 4 of the 11 patients presented with bony lesions of the jaw. Three patients complained of renal colic, 1 had painless haematuria, and 1 was found to have nephrocalcinosis. Two patients presented with dyspepsia; 1 had a duodenal ulcer and Zollinger-Ellison syndrome, while the other had developed an anastomotic ulcer 2 years following a partial gastrectomy for duodenal ulcer. Depression, accompanied by anorexia, nausea, and vomiting, was the diagnostic lead in another patient.

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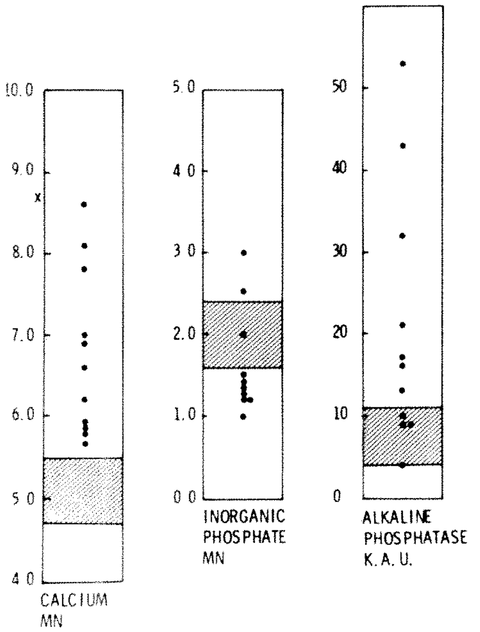

FIG. 1.—The results of the biochemical tests carried out in 11 patients.

Table I.—THE MAIN PRESENTING COMPLAINTS IN 11 PATIENTS

Clinical Complaint	*No. of Patients*	
Skeletal	4	
Jaw lesions		4
Renal	4	
Colic		3
Haematuria		1
Peptic ulcer	2	
Duodenal ulcer		1
Anastomotic ulcer		1
Mental	1	
Depression		1

Many of the patients had associated conditions which are listed in *Table II*. Hypertension, with a mean diastolic blood-pressure greater than 90 mm. Hg, was present in 6 patients and tended to be labile. Its onset was usually within 1 year of the diagnosis of hyperparathyroidism. Two were treated with antihypertensive drugs prior to parathyroidectomy. Following successful operation the blood-pressure returned to normal in 2 patients, but remained elevated in the others. Following unsuccessful parathyroid operations there was no permanent change in blood-pressure although in 1 patient it decreased for several days. During this time her serum calcium was also normal.

Radiological evidence of hyperparathyroidism was present in 8 patients when they were admitted for persistent or recurrent hyperparathyroidism. Four of these 8 patients had cystic lesions without evidence of subperiosteal resorption in their phalanges. The skeletal changes of osteitis fibrosa cystica recurred in 6 patients and in all of them the jaw was affected, being the only bone affected in 2 cases. Two patients had associated pathological jaw fractures, two of the lesions were excised radically and irradiated, and 1 of these patients also received chemotherapeutic drugs. It is of note that of the 4 patients with cystic bone changes but no subperiosteal resorption 3 had normal alkaline phosphatase and the fourth, in whom the alkaline phosphatase was elevated, had associated Paget's disease. Two of the patients with normal alkaline phosphatase, previously had typical subperiosteal resorption which disappeared following the first parathyroid exploration. The patient with Paget's disease and hyperparathyroidism had an invasive tumour which threatened breakdown of the overlying skin, necessitating surgical intervention. It seems that the combination of hyperparathyroidism and Paget's disease may present a more aggressive situation, and Jaffe (1958) reported that osteoclastoma unassociated with hyperparathyroidism is rare in the jaw except in Paget's disease. An interesting finding was profound muscular weakness in 3 patients; it involved all the muscle groups without any associated atrophy or tenderness but improved following successful parathyroidectomy.

Table II.—THE PHYSICAL SIGNS AND ASSOCIATED CONDITIONS IN 11 PATIENTS

Signs and Conditions	*No. of Patients*	
Hypertension	6	
Osteitis fibrosa cystica	6	
General		4
Local		2
Corneal calcification	5	
Renal involvement	6	
Nephrocalcinosis		2
Nephrocalcinosis + calculi		1
Nephrocalcinosis + renal tubular acidosis		1
Renal calculi		2
Muscular weakness	3	
Peptic ulcer	3	
Pluriglandular syndrome	1	
Paget's disease	1	
Carcinoma of the breast (resected)	1	
Abnormal sella turcica	1	

DIAGNOSTIC TECHNIQUES

The results of the biochemical tests are shown in *Fig.* 1. All the patients had hypercalcaemia, 8 had a low serum phosphate, and 7 had an elevated alkaline phosphatase.

It was particularly important to confirm the diagnosis of hyperparathyroidism and the tests which were most valuable in this respect included the phosphate excretion index, which was increased in all 8 patients in whom it was performed, and the cortisone-suppression test, which showed no suppression in the 5 patients in whom it was done. The cortisone-suppression test was useful in eliminating sarcoidosis and vitamin-D intoxication (Dent, 1956). Other tests included calcium-turnover studies (^{45}Ca/^{47}Ca), parathyroid-hormone immuno-assay, urinary calcium and hydroxyproline levels, and the histoloy of bone biopsy.

Table III.—PARATHYROID SIZE, WEIGHT, NUMBER, AND HISTOLOGY IN 11 PATIENTS

PATIENT	AGE AND SEX	WEIGHT AND SIZE	POSITION	HISTOLOGY	TOTAL REMOVED (NORMAL AND TUMOUR)
1. W. M.	37 F.	*a.* 3 normal		Chief-cell adenoma	4
		* *b.* 2·1 g. 3·7 × 2 cm.	Right lower		
2. G. D.	57 F.	*a.* 3 adenomatous		Hyperplasia	8
		* *b.* 1·0 × 1·0 cm.	Behind left sterno-clavicular joint		
		* *c.* 2 pieces	Right side		
		* *d.* 2 pieces	Right side		
3. T. R.	25 M.	*a.* 3·0 × 1·0 × 0·5 cm.	Left	Parathyroid adenoma	3
		* *b.* 3·0 × 2·0 × 1·0 cm.	Above aortic arch on left		
4. A. L.	44 M.	* *a.* —	Right and left lower	Hyperplasia	4
		* *b.* 1·5 × 1·0 cm.	Right and left upper		
5. B. E.	45 M.	*a.* —	Left lower (normal)		3
		* *b.* —	Right upper (normal)		
			Right lower (normal)		
6. L. V.	18 F.	*a.* —	Right lower	Adenoma	2
		b. —	Left intrathyroid (normal)		
		* *c.* —	—		
7. M. C.	41 F.	*a.* —	—	Transitional-cell adenoma	3
		* *b.* 2·0 × 1·3 × 0·8 cm.	Right lower		
8. S. J.	35 F.	* *a.* 1·5 g.	Right upper	Adenoma	2
		* *b.* 4·35 g. 1·7 × 1·7 × 1·1 cm.	Left upper		
9. G. E.	54 F.	*a.* 1·0 × 0·75 × 0·25 cm.	Right and left lower	Hyperplasia	5
		b. —	In thymus		
		c. —	Left upper		
		* *d.* 700 mg. 1·5 cm.	Right upper		
10. J. S.	58 F.	*a.* 10 × 0·75 × 0·5 cm.	Left upper	Hyperplasia	1
		b. —	—		
		* *c.* —	—		
11. D. R.	24 M.	*a.* 'Walnut size'	Right lower	Mixed-type adenoma	3
		b. —	—		
		* *c.* 4·5 g. 2·0 × 3·0 × 2·0 cm.	Right lower		

* Operation at Hammersmith Hospital.

Localizing procedures are useful in patients who have had previous parathyroid explorations, not only because extensive adhesions are encountered, but also because of the greater possibility that the parathyroid tumour is in an unusual position. Procedures used to localize the parathyroid tumours at Hammersmith Hospital were barium swallow, thyroid scanning, thermography, selenomethionine-75 scanning, arteriography, blue dye, and selective venous catheterization with parathyroid hormone immuno-assay. Barium swallow was of value in 2 patients and in 10 of the 99 of the entire series. It is probably the most useful of the non-specific tests. It was misleading in 6 patients, usually because of coexisting thyroid nodules. Thyroid scanning was of value in 1 patient in whom the normal outline of the thyroid was distorted. Thermography has only been used recently and has so far been disappointing. 'Hot spots' have frequently been seen on the thermogram preoperatively, but have not corresponded with the position of the tumour at operation. Of interest, however, is that the 'hot spot' has disappeared when tests have been repeated after parathyroidectomy. Selective arteriography has been performed in 4 patients and was successful in suggesting the position of the tumour in 2 but was misleading in 1. Three of the studies were percutaneous retrograde catheterizations and 1 patient had an unsuccessful operative left inferior thyroid arteriogram. In 1 of the 2 successful arteriograms there was vessel deviation and in the other there was a suggestion of a tumour blush. Although more specific than either barium swallow or thyroid scanning, arteriography has a definite morbidity and is time consuming. Ortho-toluidine blue has been used on four occasions, but was not helpful.

Selective venous catheterization and parathyroid hormone immuno-assay was performed in 3 patients and was successful in 1. The procedure has the advantage of being specific and of localizing even small hyperfunctioning tumours. In 2 patients it was not helpful because there was very little difference in the concentration of parathyroid hormone at the various assay sites. Certainly patients with multiple hyperplastic glands and those who have had previous neck operations present difficult problems in the interpretation of this procedure. Barium swallow has been used in almost all of the 99 patients in the series, whereas the other tests have been employed selectively and especially in those who have had previous neck surgery.

RESULTS OF SURGERY

The 11 patients have had 29 neck explorations, 4 of which were combined with sternotomy. Fifteen operations were performed prior to transfer to Hammersmith Hospital and 14 were carried out at this hospital. Successful results were ultimately obtained in 9 of the 11 patients. Successful initial secondary operations occurred in 7 patients but 2 patients required two procedures and 1 patient needed three explorations. The term 'successful' is used if the serum calcium returns to normal. In 1 patient the serum calcium returned to normal despite the failure to demonstrate any parathyroid glands during the operation. Two other patients had an unsuccessful operation and their hyperparathyroidism continues.* Both patients are asymptomatic and are being treated with effervescent phosphate and a low-calcium diet.

The main reasons for an unsuccessful exploration include multiple tumours (adenomas or hyperplasia), ectopic position of the tumour, small size of the tumour, inadequate exposure, lack of meticulous dissection in a dry field, confusion with thyroid adenoma, contused tumour, and tumour spillage. Multiple parathyroid tumours were found in 10 patients, of whom 6 had multiple adenomas and 4 had primary hyperplasia of all four glands. Three of the patients with multiple adenomas had recurrent hyperparathyroidism after lucid intervals of 14 months, 23 months, and 11 years respectively. As stated by Kleinfeld (1959), it is impossible to know whether their recurrent hyperparathyroidism was due to a recurrent or a missed adenoma. Two other patients, 1 with primary nodular hyperplasia and another who had three normal glands removed, had recurrent hyperparathyroidism.

Although all the tumours in these 11 patients were greater than 1·1 cm., smaller ones are not uncommon and 6 patients in the entire series of 99 patients with hyperparathyroidism had tumours weighing less than 100 mg. and measuring 1 cm. in diameter. Inadequate exposure and lack of meticulous dissection in a dry field are important and were responsible for failure in at least 1 patient. Differentiation from thyroid adenomas is at times difficult and frozen sections are then essential. When parathyroids are manipulated they frequently change colour like a chameleon and may then resemble the thyroid. Therefore a careful look at the surface of the thyroid gland should always be carried out before any manipulation. The importance of resecting the parathyroid tumour without spillage was referred to by Black and Ackerman (1950). They report 1 case of their own and 1 other (de Wesselow and de Wardener, 1949) in whom recurrent hyperparathyroidism was due to the presence of multiple recurrent pieces of parathyroid tissue. One of the cases reported here may have a similar aetiology as eight pieces of parathyroid were removed before the serum calcium returned to normal. Gentle but complete removal of all parathyroid tumours is thus essential.

The histology of the parathyroid tumours as well as the dates of resection, size, weight, and position are listed in *Table III*. There were no deaths from the secondary operations but 4 complications occurred, the most significant being recurrent laryngeal nerve injury. In the primary operations there was 1 death in a 62-year-old man who was admitted in a comatose dehydrated state with azotaemia, pancreatitis, and ilio-femoral and renal vein thrombosis. He died of cardiac arrest 24 hours after successful removal of a parathyroid tumour.

There were 2 recurrent laryngeal nerve injuries in 88 patients having their first parathyroid operation. One was of a transient nature and first became noticeable 4 days following operation, and the other was due to a recurrent laryngeal nerve which traversed the capsule of a 28-g. parathyroid tumour. In the patients undergoing secondary operations there were 2 recurrent laryngeal nerve injuries. One followed total thyroidectomy and the other occurred after a combined neck and mediastinal exploration. One was bilateral and required tracheostomy for 4 years, and the other resulted in a right vocal cord paralysis which eventually resolved spontaneously.

As seen from this review, patients requiring secondary operations for hyperparathyroidism present formidable problems and an increased risk of surgical morbidity, but the overall results are very acceptable. Localizing procedures are helpful and worth while prior to secondary operations. The difficulties encountered in these secondary operations emphasize the importance of a thorough exploration at the first operation. The surgeon must be patient and prepared to give time to what may be a long and tedious dissection to find a very small adenoma which is occasionally not much larger than a normal parathyroid gland. Even following identification of an obvious tumour and three other normal parathyroids the problem may not be resolved and life-long follow-up is recommended.

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* One patient has now had a tumour removed following selective venous catheterization and hormone immuno-assay.

THE EFFECT OF REMNANT SIZE ON THE OUTCOME OF SUBTOTAL THYROIDECTOMY FOR THYROTOXICOSIS

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SUBTOTAL thyroidectomy is widely employed as a method of destructive therapy for thyrotoxicosis, especially in young patients in whom treatment with radio-iodine is usually avoided in this country. A review in 1967 (Leading article, *Lancet*, 1967) stated: 'subtotal thyroidectomy . . . offers the surest and most permanent relief . . . with a relapse rate of 8 per cent and an incidence of hypothyroidism around 5 per cent'. The writer did indicate, however, that our knowledge of the long-term results of surgical treatment is still incomplete. This view is confirmed by examining the reported morbidity figures from different centres for the past 10 years. The incidence of hypothyroidism varies from 3 to 28 per cent, recurrent hyperthyroidism from 1·2 to 22 per cent, and total morbidity from 4·8 per cent (Reeve, 1964) to over 30 per cent (Wilson, 1967). The great variation in these figures is difficult to explain and may reflect differences in the methods of assessing postoperative thyroid status as much as the type of surgery which has been performed.

The results of treatment of thyrotoxicosis with radio-iodine are more predictable in that there is only one major factor which determines the outcome. The effect of ionizing radiation on the replicative mechanism of thyroid follicular cells leads to hypothyroidism in a significant number of patients within their lifetime (Greig, 1965; Philp, 1966), and is probably not influenced in the long term by factors such as the presence of thyroiditis (Irvine, 1967) or modifications of dosage régimes (Philp, Harrison, Ridley, and Crooks, 1968). In contrast, there appear to be several factors which may markedly influence the response to surgical treatment, and their relative importance has still not been clearly defined. One of these is likely to be the size of the thyroid remnant, and this paper examines the relationship between this factor and the eventual thyroid status of patients treated by subtotal thyroidectomy.

PATIENTS AND METHODS

Retrospective Studies.—

a. In a retrospective study of 146 unselected patients who had been treated for thyrotoxicosis by subtotal thyroidectomy between 2 and 21 years (mean 9·4 years) previously in the same surgical unit postoperative thyroid status has been related to the remnant weight which was estimated at operation. In these patients the operative procedure was designed to leave a remnant of approximately 3–6 g. The methods used to define the thyroid status of the patients have already been reported (Hedley, Flemming, Chesters, Michie, and Crooks, 1970).

b. In a separate study the surgeon's estimate of remnant weight has been correlated with the incidence of hypothyroidism in 200 female and 38 male patients treated for thyrotoxicosis by subtotal thyroidectomy between 1965 and 1969 inclusive.

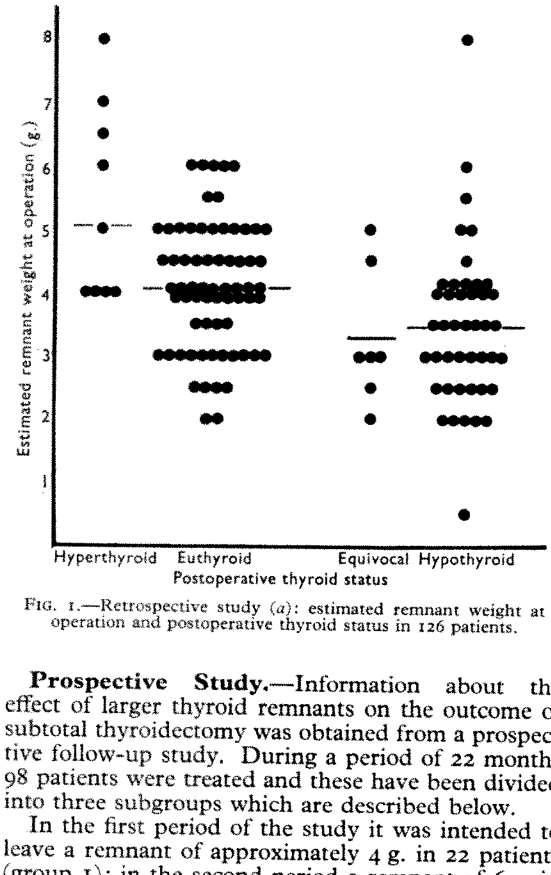

FIG. 1.—Retrospective study (*a*): estimated remnant weight at operation and postoperative thyroid status in 126 patients.

Prospective Study.—Information about the effect of larger thyroid remnants on the outcome of subtotal thyroidectomy was obtained from a prospective follow-up study. During a period of 22 months 98 patients were treated and these have been divided into three subgroups which are described below.

In the first period of the study it was intended to leave a remnant of approximately 4 g. in 22 patients (group 1); in the second period a remnant of 6 g. in 46 patients (group 2); and in the third period a remnant of 8 g. in 30 patients (group 3).

Cadaver Study.—The accuracy of subjective estimation of remnant weight by individual surgeons was assessed by experiments in cadavers. Two surgeons experienced in thyroid surgery (W. M. and T. D.) carried out subtotal thyroidectomy procedures in 19 cadavers. Estimates were made of the weight of each remnant in situ and also of the two portions of resected tissue. The remnants were then removed totally and the estimated weights of both parts of the gland were compared with the actual values obtained by weighing.

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RESULTS

Retrospective Studies.—

a. This retrospective study revealed that in the 146 patients successfully followed up 36 per cent were hypothyroid at the time of the review, and in a further 5 per cent (graded as 'equivocal') some evidence of thyroid insufficiency was revealed by a therapeutic trial with thyroxine but they were not classed as hypothyroid by the criteria that we employed. A total of 6 per cent had developed recurrent hyperthyroidism at some time since operation. The estimate of remnant weight made at operation was available for 126 of these patients (*Fig.* 1). The mean estimated remnant weight of the euthyroid patients was significantly greater than in those with hypothyroidism ($P < 0{\cdot}005$) and smaller than in those with recurrent hyperthyroidism ($P < 0{\cdot}05$). However, the differences between the means of these three groups were small, being less than 1 g. in either direction, and there was extensive overlap in the estimated remnant weight for all three thyroid status categories (*Table I*). Six patients had a second operation for recurrent hyperthyroidism and in each case the estimated size of the second remnant was comparable to the first but 5 of the 6 patients had a further recurrence of hyperthyroidism.

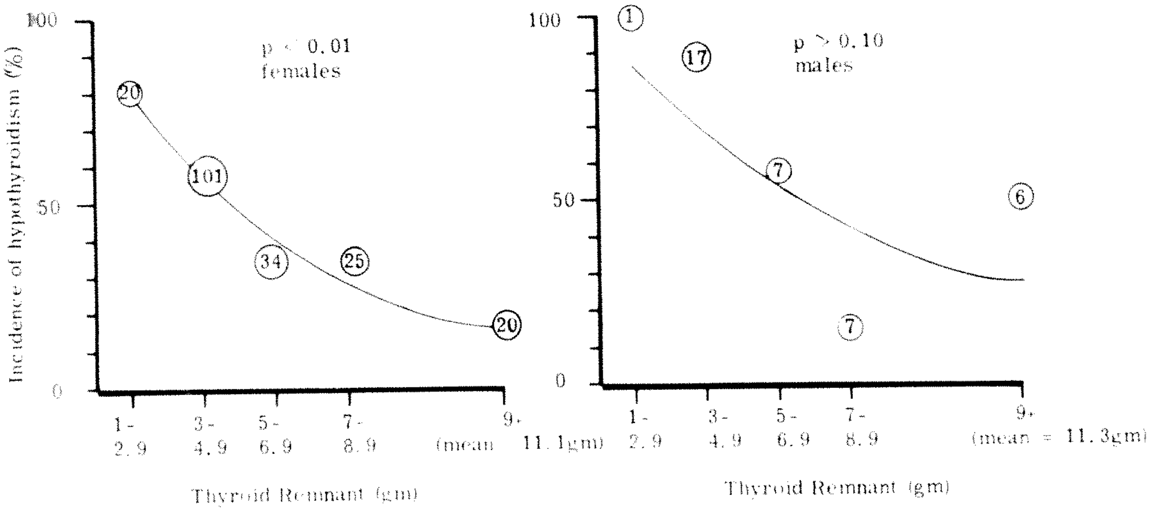

FIG. 2.—Retrospective study (*b*): relationship between the estimated remnant weight and postoperative hypothyroidism.

b. Estimated remnant weights for the 200 female and 38 male patients were divided into four categories covering the range from 1 to 9 g. or over. The proportion of patients with hypothyroidism in each remnant weight category is shown in *Fig.* 2. In the females the decrease in the incidence of hypothyroidism with increasing remnant size is highly significant ($P < 0{\cdot}01$), and a similar but less consistent trend was found in the small group of males ($P > 0{\cdot}1$). The data suggested a curvilinear relationship between the incidence of hypothyroidism and remnant weight, and the curves in *Fig.* 2 were fitted assuming a semilogarithmic relationship. Thus, as the remnant size increased the accompanying decrease in the incidence of hypothyroidism would become progressively smaller, suggesting that, in some patients, factors other than remnant size are more important causes of hypothyroidism.

Prospective Study.—The decision to leave a larger thyroid remnant at operation was followed, as would be expected, by an increase in the mean estimated remnant weight (*Table II*). The mean weight (4·19 g.) for group 1 was significantly ($P < 0{\cdot}001$) smaller than the means for group 2 (6·52 g.) and group 3 (7·33 g.). Mean remnant weights for groups 2 and 3 did not differ significantly. When, however, the thyroid status of each patient was defined at

Table I.—RETROSPECTIVE STUDY: NUMBER OF PATIENTS AND POSTOPERATIVE THYROID STATUS COMPARED WITH THE MEAN AND RANGE OF ESTIMATED REMNANT WEIGHTS AT OPERATION

THYROID STATUS	NO. OF PATIENTS	ESTIMATED REMNANT WEIGHTS (g.)	
		Mean ± S.E.M.	Range
Euthyroid	67	4·2 ± 0·14	2–6
Equivocal	7	3·3 ± 0·41	2–5
Hypothyroid	43	3·5 ± 0·18	0·5–8
Recurrence	9	5·1 ± 0·43	4–8
Total	126		

Table II.—PROSPECTIVE STUDY: NUMBER OF PATIENTS WITH THE MEAN AND RANGE OF ESTIMATED REMNANT WEIGHTS AT OPERATION

TREATMENT GROUP	NO. OF PATIENTS	ESTIMATED REMNANT WEIGHTS (g.)		DIFFERENCE BETWEEN GROUPS
		Mean ± S.E.M.	Range	
1	22	4·19 ± 0·299	2·0–7·0	1 and 2, $P < 0{\cdot}001$
2	46	6·52 ± 0·35	3·0–14·0	1 and 3, $P < 0{\cdot}001$
3	30	7·33 ± 0·34	3·5–12·0	2 and 3, $0{\cdot}1 > P > 0{\cdot}05$

12 months after operation it was found that the change in policy at operation had been accompanied by only a small and not significant ($\chi^2 = 0{\cdot}441$, d.f. $= 2$) decrease in the percentage of hypothyroid patients (*Table III*). The explanation is likely to be that although a new surgical policy was adopted there must necessarily be considerable variation in effective size of the remnant fashioned in individual patients because of such factors as initial size, consistency, vascularity, and the degree of thyroiditis in the gland.

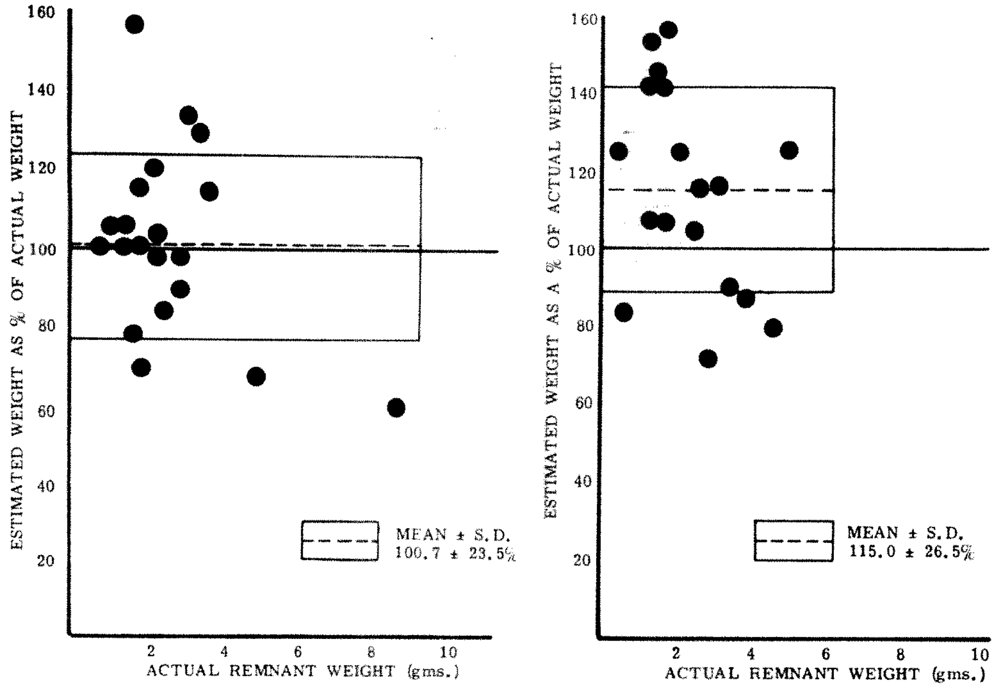

FIG. 3.—Cadaver study: distribution of the estimated remnant weights plotted against the actual weight with the mean value and standard deviation (S.D.) indicated for two surgeons.

Table III.—PROSPECTIVE STUDY: NUMBER OF PATIENTS AND POSTOPERATIVE THYROID STATUS AT 1 YEAR AFTER SUBTOTAL THYROIDECTOMY

TREATMENT GROUP	EUTHYROID	HYPOTHYROID		TOTAL
		No.	Per cent	
1	11	10	47·5	21
2	28	19	40·4	47
3	16	14	46·6	30
Total	55	43	43·8	98

$\chi^2 = 0{\cdot}441$; d.f. $= 2$

In group 1 there was no difference in the mean estimated remnant weight of the euthyroid and hypothyroid patients, while in group 2 the remnant of hypothyroid patients was in fact larger ($P < 0{\cdot}05$). In group 3 the remnant of the euthyroid patients was larger ($P < 0{\cdot}05$) and 1 of these patients developed recurrent hyperthyroidism 18 months after operation.

Cadaver Study.—This investigation was carried out to assess the extent to which variation in the surgeon's subjective assessment of remnant weight may influence the outcome of operation.

A total of 20 estimations by one surgeon and 18 by another was made on the weight of resected tissue and of the remnant in situ. Estimated weights were expressed as a percentage of the actual weights. Mean estimated remnant weights were 100·7 per cent by one surgeon and 103·3 per cent by the other (*Fig.* 3). Mean estimates of resected tissue were 123·8 and 115 per cent respectively. The standard deviations of the estimated remnant weights were 23·5 and 26·7 per cent, and using a rounded average of 25 per cent the distribution of estimated remnant weights would be as shown in *Table IV*. For instance, for 75 per cent of all the patients the estimated remnant weight would be within 63–127 per cent of the actual weight. Of the remaining 25 per cent of the patients, 20 per cent would have estimated remnants which fell within the ranges 54–63 per cent and 127–146 per cent of the actual weight and the remaining 5 per cent would differ by more extreme amounts

Table IV.—CADAVER STUDY: DISTRIBUTION OF ESTIMATED REMNANT WEIGHTS EXPRESSED AS A PERCENTAGE OF ACTUAL REMNANT WEIGHT

Percentage of All Patients	*Estimated Weight as a Percentage of Actual Weight* (g.)
10	± 2·9
25	± 7·5
50	± 15·9
75	± 27·1
80	± 30·1
90	± 38·7
95	± 46·1
99	± 60·5
99·8	± 75·0

from the actual remnant size (Yule and Kendall, 1958).

DISCUSSION

Several questions were raised by the first retrospective study (*a*) reported here. It shows that differences in estimated remnant weight between the groups with a different postoperative thyroid status were extremely small and almost the whole range of values for each group overlapped. These findings could be interpreted as an indication that in some patients small differences in remnant size are important, or, conversely, that remnant size has little influence on the outcome of operation. If small differences in remnant size were significant then it would be important to determine the accuracy with which remnant size can be controlled under the usual conditions of clinical surgery. The high incidence of hypothyroidism found in this part of the study could be ascribed to the radical type of resection with the implication that an improvement in the results of operation could be produced simply by increasing remnant size.

Table V.—ESTIMATED REMNANT SIZE AT OPERATION AND REPORTED MORBIDITY AFTER SUBTOTAL THYROIDECTOMY

AUTHORS	REMNANT SIZE	PERCENTAGE HYPOTHYROID	PERCENTAGE HYPERTHYROID	TOTAL MORBIDITY
Pemberton (1930)	4·5–10·5 g.	—	2·9	—
Thompson, Morris, and Thompson (1930)	2·0– 8·0 g.	—	19·5	—
Troell (1944)	3·0– 7·5 g.	—	6·0	—
Bertelsen (1947)	2·0 g.	—	4·9	—
Goldman (1948)	3·0– 4·0 g.	20·5	3·6	24·1
Cattell and Morgan (1939) and Cattell (1949)	2·0 g.	2·4	4·5	6·9
Cattell, Alford, and Bartels (1952)	4·0 g.	—	3·3	—
Szilagyi and others (1955)	0·4– 4·0 g.	27·2	—	—
Beahrs (1956)	5·0 g.	—	9·5	—
Blackburn (1962)	6·0– 8·0 g.	3·0	—	—
Roy, Allan, and Harden (1967)	16·6–30·5 g.*	5·0	11·0	16·0
Taylor and Painter (1962)	8·0 c.c.	9·3	4·6	13·9
Murley and Rigg (1968)	8·0 c.c.	7·5	0	7·5

* Deduced from authors' data.

A review of sixty-six reports published between 1925 and 1968 revealed only thirteen in which an attempt had been made to quantitate the remnant size (*Table V*). Estimates of remnant size varied between 0·4 and 30·5 g. but the values in ten reports lay between 2 and 10·5 g. This 'therapeutic range' has presumably been chosen on the assumption that it leads to a remission of the symptoms, and prevents recurrent hyperthyroidism, in the majority of patients. There is nevertheless great variation in the reported incidence of postoperative complications (Hedley and others, 1970). The present study, in which thyroid status has been carefully defined, suggests that postoperative morbidity may be much greater than previously supposed.

Some authors have expressed the view that there is an optimum remnant size which, in their centres, is associated with a low incidence of hypothyroidism and recurrent hyperthyroidism (Szilagyi, Barrett, and Preuss, 1955; Taylor and Painter, 1962; Murley and Rigg, 1968). The concept of a thyroid remnant of optimum size which would be associated with a low postoperative incidence of both recurrent hyperthyroidism and hypothyroidism was originally disputed by Bartlett (1951), and later studies have confirmed that régimes aiming to produce low levels of both these complications are mutually exclusive (Crile and McCullagh, 1951; Wilson, 1967).

In the second retrospective study (*b*) correlation of estimated remnant size with postoperative hypothyroidism indicated that, within the so-called therapeutic range, relatively small changes in remnant size have an important effect on the outcome of operation in some patients. The practical value of this finding is diminished because it is taken out of context and does not reflect the difficulties encountered in clinical practice when attempts are made to leave a 'standard' remnant. A group of patients treated by subtotal thyroidectomy will inevitably be heterogeneous with respect to remnant size. This is clearly shown by the prospective study in which increases in mean estimated remnant size between 4 and 8 g. did not diminish the overall incidence of apparently irreversible hypothyroidism in the group at 12 months after operation. This project was, however, associated with 1 early recurrence of hyperthyroidism and it seems inevitable that the incidence of this complication will be much higher in those patients with larger remnants. It is likely that, in comparison with the retrospective study, some reduction in the incidence of hypothyroidism was obscured because in this study thyroid status was defined at 12 months after operation using methods and criteria which detect even relatively minor abnormalities. In contrast, thyroid status was not defined in the retrospective studies until at least 2 years had elapsed after operation. Transient hypothyroidism is common after subtotal thyroidectomy and it is possible that more patients in the prospective study might have become euthyroid if thyroxine had been withheld. However, it is doubtful whether delaying treatment for an indeterminate period can be justified.

The studies on cadavers showed that the subjective assessment of remnant weight is open to considerable error. Although the overall performance is remarkably consistent, it appears that individual estimates of remnant size in 75 per cent of patients may vary by ± 27 per cent of the actual weight; for the remaining 25 per cent the variation will be much greater. In absolute terms this means that the actual weight of a remnant intended to be 8 g. might in fact lie between 4 and 12 g. Discrepancies of this order would explain the poor overall correlation of estimated remnant size and postoperative thyroid status in this and in other clinical surveys.

The information from the retrospective and prospective studies confirmed that remnant size is one of the important factors which determines thyroid status after thyroidectomy, but there is equally good evidence that the mass of the remnant as determined at operation is not always related to its functional capacity. In these patients other factors such as autoimmune thyroiditis are clearly important and hypothyroidism will not be prevented by conservative surgery.

One recent finding in our studies of thyroid remnant function is of fundamental importance when considering the influence of remnant size on the results of subtotal thyroidectomy. It is accepted that failure of the thyroid uptake of radio-iodine to suppress with the administration of exogenous triiodothyronine (T3 suppression test) is characteristic of the basic disease process in Graves' disease (Werner, 1956; Kendall-Taylor, 1972). Suppression of the uptake is evidence of a normal pituitary-thyroid axis. Recent studies (Hedley, Ross, Beck, Donald, Recht, Michie, and Crooks, 1971) using this technique in the early postoperative period have shown that a remission of Graves' disease occurs within 12 months of operation in 70–80 per cent of surgically treated patients irrespective of remnant size. Follow-up studies have shown that whereas this remission is permanent the basic disease process may persist in the remaining 20 per cent of patients for more than 20 years and it is in this group that recurrent hyperthyroidism may occur. It is likely, therefore, that modifications of the outcome of subtotal thyroidectomy will only be possible if those patients who will not enter a remission can be identified *before* operation. If they could be detected it is interesting to speculate that, while surgery remains one of the principal forms of treatment for thyrotoxicosis, morbidity might be reduced by leaving large remnants in those patients who will not remit and employing a radical resection or other forms of treatment in the group in whom the disease will persist and who might therefore develop a recurrence.

CONCLUSIONS

This study suggests that efforts to find an optimum remnant size are unlikely to be rewarding. In unselected patients with thyrotoxicosis the complications of hypothyroidism and recurrent hyperthyroidism will be inversely related and manipulation of remnant size will not be effective in reducing the total morbidity. At the present time the object of treatment should be to prevent persistent or recurrent hyperthyroidism; an appreciable incidence of hypothyroidism should be accepted as inevitable and treated promptly with replacement therapy.

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THE EFFECT OF EXPERIMENTAL BILE-DUCT OBSTRUCTION ON CRITICAL BIOSYNTHETIC FUNCTIONS OF THE LIVER

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SUMMARY

Using biosynthetic activities which have a maximum energy requirement, the effect of obstruction of the bile-duct has been studied in isolated perfused rat livers, and compared with controls undergoing 'sham' ligation and with normal animals. The maximum rate of gluconeogenesis from lactate was inhibited by 67 per cent after bile-duct ligation when compared with the normal value. The maximum rate of urea synthesis which occurred in the presence of ornithine was the same in the jaundiced and in the normal animals. 'Sham' operation, without ligation of the bile-duct, inhibited gluconeogenesis by less than 20 per cent but doubled the maximum rate of urea synthesis.

It is concluded that complete biliary obstruction seriously impairs gluconeogenesis and prevents the normal increase of urea synthesis which occurs in response to trauma and that these changes develop earlier than might be expected after the onset of obstruction.

Some possible mechanisms of these effects are discussed. If similar abnormalities of hepatocyte function are demonstrated in man it is suggested that surgical relief of obstructive jaundice is indicated at an early stage.

THE chemical changes observed in the blood of a patient or animal after the bile-duct becomes obstructed are due to retention of bile rather than to a direct effect of the obstruction on the cells of the liver. Abnormalities of clinical liver-function tests are not marked unless the obstructive jaundice has been present for some time, and it is usually considered that hepatocyte function remains normal during the first few weeks after obstruction has taken place. However, most biochemical activities of the liver take place at such a rate that the standard clinical tests of function, which are relatively insensitive, remain normal until gross hepatic damage has occurred.

Recently, perfusion techniques have been developed which allow a direct study of the biosynthetic reactions of the liver. The maximum rates of energy-requiring cellular activities are more sensitive tests of liver function than are the investigations usually employed. The synthesis of glucose from lactate (Meyerhof, 1930; Hems, Ross, Berry, and Krebs, 1966), of urea from ammonia (Cohen and Sallach, 1961), and possibly of protein, are the principal reactions which consume large quantities of ATP, and require the integrated action of both mitochondrial and cytoplasmic enzymes.

In the experiments recorded in this paper ligation of the bile-duct has been used to produce jaundice, and the maximum rates of gluconeogenesis and urea synthesis in the perfused livers of jaundiced animals were compared with those in both normal and control animals. A preliminary account of part of this work has been presented previously (Lee, Ross, and Haines, 1971).

MATERIALS AND METHODS

Male albino Wistar rats weighing between 150 and 200 g. were obtained from Messrs. Scientific Products Farm, Ash, Kent, and were fed on a standard 41B diet.

Bile-duct Ligation.—Three groups of rats were prepared for liver perfusion. Group 1 consisted of those animals which had had their bile-ducts ligated and divided using an ether anaesthetic administered by the 'open' method. A control group of animals (group 2) underwent a sham operation, using an exactly similar anaesthetic. Care was taken to anaesthetize the animals in both groups for the same length of time (12 minutes). The abdomen was opened through a midline supra-umbilical incision. The duodenal loop was located and delivered through the wound under sterile conditions. The bile-duct was dissected from the surrounding structures, avoiding damage to the peritoneum over the portal vein and thus preventing inflammation and adhesions which make subsequent cannulation of the portal vein difficult. Two silk ligatures were passed behind the common duct just distal to the junction of the hepatic ducts, care being taken not to damage the pancreas. In group 1 the ligatures were tied and then the duct was cut between them. In group 2 the ligatures were removed without being tied. The animals in group 3 underwent no surgery before perfusion.

Perfusion Experiments.—Subsequently the rats were anaesthetized with intraperitoneal pentabarbitone and their livers were perfused using the technique described by Hems and others (1966) and Ross (1972) (*Figs.* 1, 2). In order to reduce the liver glycogen content and to induce maximal rates of glucose and urea synthesis all the animals were starved for 48 hours before perfusion. The animals in groups 1 and 2 therefore received only water after operation. Substrates were added to the medium after 40 minutes of perfusion and samples of the medium were taken for analysis at 15-minute intervals over the period 40–130 minutes of perfusion. Time courses of glucose synthesis and lactate removal or of urea synthesis and ammonia removal were constructed from these data.

Expression of Results.—The results are expressed as μmol per minute per g. wet weight of liver, since the ratio of wet weight : dry weight and the total weight of the liver were not significantly different in the three groups of animals 2 days after bile-duct ligation. Figures are the mean ± standard error of the mean (S.E.M.) (*see* Results).

Chemical Analyses.—

Serum proteins were determined by the micro-Kjeldahl method.

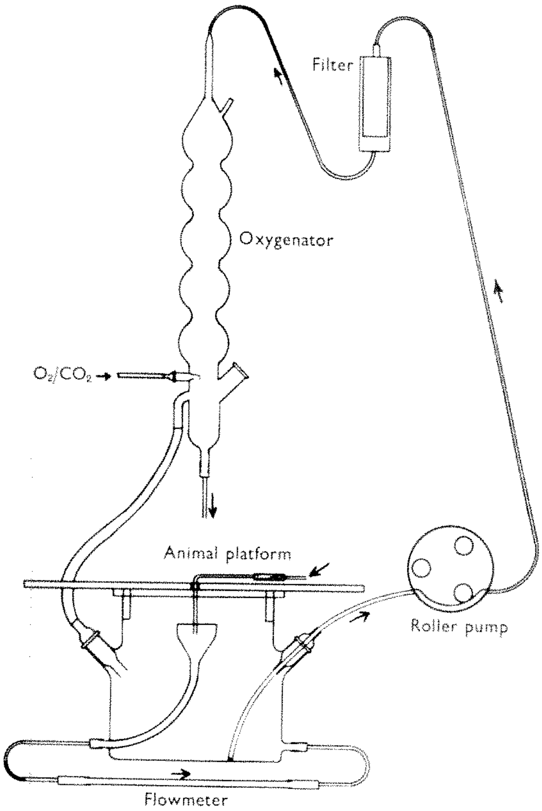

FIG. 1.—Diagram of the liver perfusion apparatus, showing the direction of circulation of the medium. The medium in the collecting vessel is lifted by the roller pump through the nylon-mesh filter to the top of the oxygenator. From there the medium passes to the reservoir whence it enters the liver via the portal vein. Excess medium leaves the reservoir by an overflow to the collecting vessel. Note the arrangement of the funnel to collect the venous outflow from the liver and to return it to the collecting vessel via a flowmeter. For clarity the animal is not shown.

Bilirubin was determined by the sulphanilic acid method in Biochemica test combination (Catalogue No. 15944 TBAA).

Lactate was determined with the Boehringer Biochemica test (ultra-violet method TC/B Catalogue No. 15972, TLAA) using a Boehringer Tecometer Photometer at 340 nm., and *glucose* was determined using the Boehringer Biochemica test combination (Catalogue No. 15754 TBAN).

Urea and *ammonia* were determined with Nessler reagent before and after treatment of the samples with urease.

Oxygen was determined in the inflowing and outflowing medium with the Scholander-Roughton apparatus. Oxygen consumption was calculated from this 'a – v' difference and the flow rates of medium through the liver determined with a siphon-flow meter.

RESULTS

Effects of Bile-duct Ligation.—

Serum Bilirubin.—The serum bilirubin of all the animals in group 1 rose significantly within 2 days of bile-duct ligation, reaching a value of 5·8 ± 1·8 mg. per cent (11 animals), compared with 0·45 ± 0·27 mg. per cent (9 animals) in the sham-operated control group and 0·72 ± 0·50 mg. per cent (10 animals) in the normal animals.

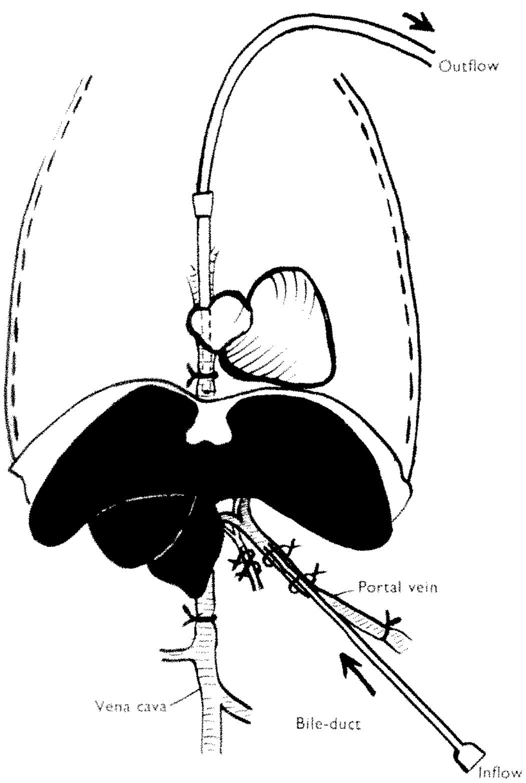

FIG. 2.—Diagram of the operative procedure for the in situ perfusion of the liver. The bile-duct and portal vein are cannulated; note that the portal vein is also tied distally. The inferior vena cava cannula is inserted through the wall of the right atrium and tied, as shown, in the vena cava above the diaphragm. Finally, the inferior cava is tied, as shown, below the liver, and the animal is connected to the perfusion apparatus via the portal cannula.

Weight Increase.—The livers of jaundiced rats were noted to enlarge about 1 week after obstructing the bile-duct. Histological examination showed that the enlargement resulted from the retention of bile in the dilated biliary tracts as well as from an increase in the number of cells in the liver, particularly in the ducts and periductal spaces. Similar changes have been reported in other animals and in man (Lieber and Stewart, 1934; Sherlock, 1963). The cellular proliferation is associated with an increase in the dry weight of the liver. No significant difference was found between the wet or dry liver weights of the 2-day jaundiced animals and the controls, the 2-day jaundiced animals and the normal animals, and the normal and control groups. However, the increase in both the wet and dry weights of the livers of jaundiced rats became significant 7 days after the ducts had been ligated (*Table I*). The wet weight increased by 34·6 per cent and the dry weight by 16·6 per cent of the control values, an alteration which correlates with the histological changes in the liver.

Serum Albumin.—The effect of ligation of the bile-duct was studied in a separate experiment in which animals were killed at 2 days and at weekly intervals up to 7 weeks after ligation of the bile-duct. No significant fall in serum albumin was observed (*Table II*) until the sixth week.

Table I.—EFFECT OF BILE-DUCT OBSTRUCTION ON THE WET AND DRY WEIGHTS OF THE LIVER

ANIMAL	NO. OF ANIMALS	WET WEIGHT (g. ± S.E.M.)	DRY WEIGHT (g. ± S.E.M.)	WET WEIGHT / DRY WEIGHT
Normal	3	6·59 ± 0·61	1·89 ± 0·17	3·48
Sham-operated (2 days)	2	6·29 ± 0·32	1·78 ± 0·01	3·51
Jaundiced (2 days)	3	6·87 ± 0·75	1·90 ± 0·13	3·61
Jaundiced (7 days)	3	8·89 ± 0·52	2·21 ± 0·16	4·20

Table II.—EFFECT OF BILE-DUCT OBSTRUCTION ON THE SERUM ALBUMIN OF RATS

Duration of Bile-duct Ligation (weeks)	*No. of Animals*	*Serum Albumin* (g. per 100 ml. of serum ± S.E.M.)
0	6	2·50 ± 0·18
1	4	2·38 ± 0·20
2	4	2·65 ± 0·30
3	4	2·40 ± 0·15
4	4	2·17 ± 0·45
5	4	2·47 ± 0·25
6	5	2·02 ± 0·18
7	4	2·05 ± 0·17

Perfusion Studies.—Perfusion of the liver by the in situ technique of Hems and others (1966) was not unduly affected soon after the operation of duct ligation, provided precautions were taken to avoid the formation of adhesions around the porta hepatis and portal vein. Two days after duct ligation perfusion proceeded normally. After a longer period, e.g., 7 days, there was an increasing incidence of complications, particularly of exudation from the surface of the liver, which made the technique of in situ perfusion less reliable. It is suggested, therefore, that the isolated perfusion technique of Schimassek (1963) may be more suitable for such delayed studies.

Flow Rate and Perfusion Pressure.—At 2 days after bile-duct ligation no increase in perfusion pressure was required. Flow-rates of 4·2 ± 1·1 ml. per minute per g. of liver in the duct-tied animals (11 animals), 3·8 ± 0·8 ml. per minute per g. in the sham-operated (3 animals), and 5·1 ± 1·1 ml. per minute per g. in the normal controls (4 animals) were observed. These flow rates adequately provided the expected oxygen requirement of the liver, and anoxia cannot therefore be suggested as an explanation for the abnormalities of the liver-function tests described below.

Glucose Synthesis from Lactate. — Addition of 1500 μmol Na-L-lactate (10 mM) to the perfusion medium results in a significant formation of glucose, which appears in the perfusion medium at a linear rate. In the present experiments the rate of glucose synthesis in the normal animals was the same as that observed by other workers (Strück, Ashmore, and Wieland, 1965; Hems and others, 1966; Exton and Park, 1967). The rate was suppressed by 67 per cent in the duct-tied animals and by 28 per cent in the sham-operated controls (*Table III*). Duct ligation therefore exerted a significant depressant effect upon the synthesis of glucose by the liver. Lactate was removed from the medium in parallel with the formation of glucose in all three groups. The ratio of lactate removed : glucose formed, which is expected to be 2, was 2·15 in the sham-operated controls, but it increased to 2·60 in the duct-ligated animals. An additional significant effect of duct ligation may therefore be the diversion of lactate to paths other than that of glucose synthesis, e.g., oxidation. Oxidation of lactate is minimal in the control animals which have been starved for 48 hours (Strück and others, 1965; Hems and others, 1966), and no increase in liver glycogen was found under these conditions of perfusion.

Table III.—THE EFFECT OF BILE-DUCT OBSTRUCTION ON THE SYNTHESIS OF GLUCOSE FROM LACTATE

ANIMAL	NO. OF ANIMALS	GLUCOSE FORMED	LACTATE USED	LACTATE USED / GLUCOSE FORMED
		(μmol per min. per g. wet weight of liver ± S.E.M.)		
Normal	7	0·97 ± 0·13	1·70 ± 0·33	1·75
Sham-operated (2 days)	7	0·70 ± 0·21	1·51 ± 0·25	2·15
Jaundiced (2 days)	5	0·32 ± 0·09	0·84 ± 0·30	2·60
Jaundiced (7 days)	3	0·36 ± 0·22	0·63 ± 0·38	1·75

Seven days after duct ligation the rate of glucose synthesis was still only 37 per cent of that in the controls (*Table III*), indicating that the animals had not adapted to the biliary obstruction within that time.

Urea Synthesis.—In the normal rat liver urea is synthesized at a high rate when ammonium salts are added to the perfusion medium (Trowell, 1942; Hems and others, 1966). The rate may be increased by up to three times by the addition of the catalyst ornithine (Krebs and Henseleit, 1932), and this yields the highest rates of urea synthesis yet observed *in vitro* (Hems and others, 1966). In the present experiments the rate of urea synthesis (expressed as μmol of ammonia removed) was lower than that observed by Hems and others (1966), possibly owing to differences in the strain of rat used. In the presence of 10 mM NH_4Cl, ammonia was removed at a rate of 1·25 ± 0·18 μmol per minute per g. (3 animals). With the addition of 400 μmol of ornithine (2·66 mM) to the medium the rate of ammonia removal was 1·68 ± 0·10 μmol per minute per g. (3 animals). The maximum rate of urea synthesis was compared for the three groups of animals. In each group the rate of urea formation was linear with time and accounted for 80–90 per cent of the ammonia removed. Duct ligation did not apparently alter the rate of urea synthesis when compared with the normal animals. However, when compared with the sham-operated controls an inhibition of 41 per cent was observed (*Table IV*). The sham operation itself resulted in a doubling of the rate of urea synthesis, and this increase was almost entirely prevented by duct ligation.

Oxygen Consumption.—Oxygen consumption by the liver has been determined in animals prepared as in Materials and Methods. The oxygen consumption of livers perfused under basal conditions without added substrate was not apparently affected by ligation of the bile-duct or by the sham operation (*Table V*). The figure of 2·11 ± 0·08 μmol O_2 per minute per g. (6 animals) for the liver perfused without substrate does not differ from that found by other workers (Schimassek, 1963; Forsander, Räihä, Salaspuro, and Maënpää, 1965; Hems and others, 1966).

Table IV.—Synthesis of Urea in the Perfused Liver of Rats with an Obstructed Bile-duct

Animal	No. of Animals	Ammonia removed	Urea formed
		(μmol per min. per g. wet weight of liver ± S.E.M.)	
Normal	3	1·68 ± 0·10	0·70 ± 0·21
Sham-operated (2 days)	4	2·83 ± 0·40	1·45 ± 0·20
Jaundiced (2 days)	4	1·87 ± 0·025	0·85 ± 0·15

Addition of 10 mM NH_4Cl and 2·66 mM ornithine to the medium resulted in a considerable increase of oxygen consumption in all three groups of animals. Assuming that $\frac{2}{3}$ mol of O_2 are required per mol of urea synthesized (Cohen and Sallach, 1961), in the normal control the extra oxygen consumption exceeded that expected (expected = 1·07 μmol per minute per g.; observed = 1·93 μmol per minute per g.), a finding which confirms that of Hems and others (1966). This difference between the expected and the observed oxygen consumption disappeared in the sham-operated animals (expected = 1·64 μmol per minute per g.; observed = 1·75 μmol per minute per g.).

The observed extra oxygen consumption in the duct-ligated animals was actually lower than that expected (observed 0·79 μmol per minute per g.; expected 1·17 μmol per minute per g.), but these figures do not represent a significant difference.

DISCUSSION

Control of Gluconeogenesis.—Inhibition of gluconeogenesis in the rat liver with an obstructed bile-duct must reflect some metabolic defect induced by the retention of a constituent of the bile or consequent upon the increased intraduct pressure. The factors which control the rate of glucose synthesis from lactate are the supply of the substrate, the transport of the substrate into the cell and between intracellular compartments, the availability of ATP, and the activity of specific rate-limiting enzymes, notably pyruvate carboxylase, phospho-enolpyruvate carboxykinase, and fructose diphosphatase (Krebs, 1964). In the present experiments there was no restriction of substrate supply nor is this likely to be a factor *in vivo*. In obstructive jaundice plasma levels of glucogenic amino-acids and of lactate and glycerol, the principal substrates of gluconeogenesis, are normal or raised (Record, Alberti, and Williamson, 1971; Record, 1972). Preliminary observations suggest that the ATP content of the liver is not abnormal during perfusion of the jaundiced rat liver (Lee and others, 1971). Furthermore the oxygen consumption of the liver with a ligated bile-duct remained normal and increased in response to the addition of substrates.

Table V.—Effect of Obstructive Jaundice on Urea Synthesis and Oxygen Consumption in the Perfused Rat Liver

Animal	No. of Animals	Time (min.)	Urea Synthesis*	Oxygen Uptake
			(μmol per min. per g. fresh weight of liver ± S.E.M.)	
Normal	1	30	—	2·0
		85	1·60	3·93
Sham-operated (2 days)	2	30	—	2·02 ± 0·05
		85	2·47 ± 0·35	3·77 ± 0·06
Jaundiced (2 days)	3	30	—	2·24 ± 0·13
		85	1·75 ± 0·17	3·03 ± 0·34

* Expressed as amount of ammonia removed.

The activity of the rate-limiting enzymes remains to be determined, but it is of some significance that the concentration of acetyl coenzyme A, the intracellular effector of pyruvate carboxylase, is decreased in the livers of rats 9 days after obstruction of the bile-duct (Record and others, 1971). Although there is no complete agreement (Krebs, Speake, and Hems, 1965; Menahan, Ross, and Wieland, 1968; Willms and Söling, 1968) concerning the physiological role of acetyl coenzyme A in controlling the rate of gluconeogenesis, a reduction in the activity of pyruvate carboxylase such as might result from lowered cellular acetyl coenzyme A levels is a likely explanation for the present results.

Control of Urea Synthesis.—The maximum rate of urea synthesis is controlled by the supply of substrate and catalyst (Krebs and Henseleit, 1932), by the activity of the rate-limiting enzymes (Schimke, 1963; McLean and Novello, 1965) and by the availability of ATP (Cohen and Sallach, 1961). In the present studies substrate and catalyst were provided in excess and there is evidence both from oxygen consumption and from direct measurement (Lee and others, 1971) that ATP was available. However, the extra oxygen consumption which accompanied the ammonium salts to the liver was less in the jaundiced liver than in the normal liver. It has been suggested that the excess oxygen consumption may be required for protein synthesis (Hems and others, 1966), and this apparent defect in the jaundiced rat liver may be a forerunner of the subsequent failure of albumin synthesis in protracted bile-duct obstruction.

Effect of Surgery on Liver Metabolism.—Gluconeogenesis and urea synthesis are considered to be increased in response to surgery; *in vivo* this may be a reflection of the extra substrate made available from tissue breakdown (Kinney, Long, and Duke, 1970). However, the present findings suggest that 2 days postoperatively the maximum rate of gluconeogenesis is not increased and may actually fall. On the other hand, the maximum rate of urea synthesis is increased by nearly 100 per cent. Under the conditions of the present experiment this observation is consistent with an increase in the activity of the enzymes of the urea cycle, since substrate and catalyst were present in excess. It may be that bile-duct obstruction inhibits urea synthesis by preventing the 'activation' or induction of the enzymes of the urea cycle which is the normal response to trauma.

CONCLUSION

Standard clinical tests of liver function are usually normal in patients (and animals) with early obstructive jaundice. The present study confirms what has been widely suspected: that the clinical tests may remain normal in the face of considerable disturbance of liver-cell metabolism. This has been revealed by the use of tests of maximal biosynthetic capacity in the isolated perfused liver, and it remains to be seen if such tests can be applied in the whole animal or in clinical practice. The results obtained support a case for the early surgical relief of obstructive jaundice.

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PERIPHERAL TUBERCULOUS LYMPHADENITIS IN THE ELDERLY

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Summary

1. Retrospective and current studies of peripheral tuberculous lymphadenitis in the elderly (over the age of 60 years) are described.

2. The efficacy and side-effects of standard antituberculous chemotherapy in this group of patients are analysed.

3. Simple excisional surgery with the local instillation of streptomycin is suggested as a rational and effective method of treatment of localized tuberculous lymphadenitis in the elderly.

THE PATIENTS

1. The Retrospective Study.—Sixty-two patients presented with peripheral tuberculous lymphadenitis at St. Thomas's Hospital, London, during the period from 1958 to 1967, and 8 (12 per cent) were over the age of 60. These 8 patients were all English and had lived the greater part of their life in South London. The diagnosis was confirmed by bacteriological culture in all cases. All the patients started a course of antituberculous chemotherapy, which, if completed, comprised parenteral streptomycin for 6 months and oral para-aminosalicylic acid and isoniazid for 18 months. Surgical treatment comprised either excision of the gland group or incision and drainage. Two patients had undergone surgery for involvement of the same gland group 10 or more years previously.

Three patients failed to take the oral drugs. Two patients developed irreversible auditory nerve damage as a result of taking streptomycin. Tuberculous lymphadenitis recurred in 4 patients during follow-up.

2. The Current Study.—Six elderly patients with tuberculous lymphadenitis were seen during a 10-month period at the Bolingbroke Hospital, London. All the patients were English and lived in South London. There was no evidence of tuberculosis elsewhere in any patient. Measurement of the sedimentation rate, a chest radiograph, and culture of the urine and sputum (if any) were performed in each case. Diagnosis was confirmed by culture and histological examination of the excised tissue. Three patients had had previous surgery for tuberculous lymphadenitis. Treatment comprised excision of the affected gland group, with instillation of 1 g. streptomycin powder into the wound. One declined surgery, and her collar-stud abscess was successfully treated by aspiration and instillation of 1 g. streptomycin at weekly intervals for 1 month.

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All the patients had primary healing of their wounds, and there was no evidence of recurrence or further tuberculous lymphadenitis during the follow-up period. No patient suffered any iatrogenic complications.

The methods and results of treatment in the retrospective and current series are summarized in *Tables I* and *II* respectively.

Table I.—THE RETROSPECTIVE STUDY OF PERIPHERAL TUBERCULOUS LYMPHADENITIS IN THE ELDERLY (1958–67)

AGE AND SEX	TREATMENT	LENGTH OF FOLLOW-UP	SIDE-EFFECTS OF CHEMOTHERAPY*	RESULTS
83 F.	Incision	18 months	Failed to take drugs	Healed
73 F.	Incision	4 years	Streptomycin deafness	Recurrent abscess at 3 years
76 F.	Excision	3 years	Never took drugs	Multiple recurrences at 6 months
60 M.	Excision	5 years	—	Persistent sinus for 18 months
77 F.	Excision	4 years	—	Healed
67 F.	Excision	5 years	Streptomycin deafness	Multiple recurrences within 1 year
63 F.	Incision	2 years	—	Healed
63 F.	Excision	9 months	Refused drugs after 4 months	Healed

* All patients started a course of anti-tuberculous chemotherapy.

Table II.—THE CURRENT SERIES OF PERIPHERAL TUBERCULOUS LYMPHADENITIS IN THE ELDERLY (1969)

AGE AND SEX	TREATMENT*	LENGTH OF FOLLOW-UP	SIDE-EFFECTS	RESULTS
81 F.	Excision of collar-stud abscess	10 months	None	Healed
64 M.	Wide excision	18 months	None	Healed
64 F.	Local excision	15 months	None	Healed
83 F.	Aspiration	16 months	None	Healed
85 F.	Excision	16 months	None	Healed
77 F.	Excision	12 months	None	Healed

* Streptomycin powder (1 g.) was instilled locally at the time of surgery.

DISCUSSION

Peripheral tuberculous lymphadenitis is becoming less common when all age-groups are considered, but an increasing percentage of elderly patients is found. Fraser (1965) found that 9 out of 18 women reviewed at the Southampton Chest Hospital with peripheral tuberculous lymphadenitis were over the age of 60.

Site.—Cervical lymph-glands are most commonly involved and although 2 cases of axillary lymph-gland involvement are recorded in the retrospective series the incidence of the latter ranges from 3 to 10 per cent, according to the series (Fraser, 1965; Kent, 1967).

A Localized or a Generalized Manifestation of Tuberculosis?—In neither the retrospective nor the current study was there any evidence of active tuberculosis elsewhere at the time of treatment or during the period of follow-up. In contrast, Fraser (1965) states that 15 of his 30 cases had active tuberculosis elsewhere at the time of presentation, or during the preceding 10 years, but he does not comment on the age of these patients. Miller and Cashman (1955) consider tuberculous lymphadenitis to be a localized disease in children.

Treatment.—Chemotherapy has not superseded surgery in the treatment of tuberculous lymphadenitis nor has it eliminated relapses (Fraser, 1965). In the retrospective study 3 patients (37 per cent) failed to take the drugs and 2 suffered permanent side-effects (deafness). Excision and local instillation of streptomycin have avoided these problems without impairment in the quality of the results.

Relapses.—Kilpatrick and Douglas (1957) state that 46 per cent of their cases, received from two Edinburgh hospitals, had previous lymphadenitis, and that 15 per cent of their personal cases relapsed despite full anti-tuberculous drug therapy. Gillam and Knowles (1963) found that there was a relapse rate of 25 per cent in patients studied from University College Hospital, but found complete excision under chemotherapeutic cover to be successful for disease localized to the upper cervical region. Cover was maintained until the skin had healed. The relapse rate in the present retrospective study was 4 cases (50 per cent), with 3 occurring in the first year. It seems that although the majority of relapses occur early the rate is, to a certain degree, proportional to the length of follow-up, but lack of relapse in the small current series is encouraging, and it is particularly satisfactory that this has been achieved with none of the side-effects seen in elderly patients on anti-tuberculous drugs.

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SHORT NOTES OF RARE OR OBSCURE CASES

TUMORAL CALCINOSIS

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SUMMARY

An extreme case of tumoral calcinosis is presented. This condition is common in the highland natives of New Guinea and is commonly referred to as 'hip stones'. The pathogenesis, clinical findings, and treatment are discussed and the relevant literature is reviewed.

TUMORAL calcinosis, which is locally referred to as 'hip stone', is not uncommon in the Eastern and Central Highlands regions of New Guinea. Found also in other areas of New Guinea as well as in South, Central, and East Africa, the condition has received little publicity in medical journals. It is, however, of clinical interest and presents a diagnostic problem to the uninitiated.

CASE REPORT

A female, aged 43 years, from the Chimbu district of the Central Highlands, was admitted to the Goroka Base Hospital complaining of hard and painful lumps over both greater trochanters, the lateral humeral condyles, and the left lateral ankle malleolus. There was an offensive, thick, whitish discharge from both trochanteric lumps, and old surgical scars were apparent over both hips and elbows. The patient was apyrexic, ambulatory, and in reasonable health. She complained of pain within both hip lumps and of the general inconvenience of all her lumps.

Owing both to language difficulties and to a general lack of appreciation of time and dates an accurate history was difficult to obtain from the patient. It would appear that the lumps had first appeared in the region of the elbows some 7 years previously and over both hip-joints 5 years previously. She had sought surgical relief 3 years previously and an attempt had been made at that time to remove the lumps. Recurrences had developed within a few months of surgical removal.

Radiographs of the hip, elbow, and ankle-joints revealed extensive but patchy calcification within the soft tissue near but not connected to these joints (*Figs.* 1, 2). Repeated serum calcium estimations were within normal limits and we were unable to culture organisms from the discharging sinuses. Radiographs of the chest and long bones failed to reveal any abnormality.

The patient requested surgical removal of her lumps, and this was carried out at two separate operations on 23 Feb. and 4 March, 1971. Very large, poorly circumscribed calcified masses were removed from both trochanteric regions, the elbows, and the left ankle. The specimens were sent to Dr. Wilkey, Pathologist at Port Moresby, who reported that the microscopic picture was typical of tumoral calcinosis and commented that he had not previously heard of a case with so many lesions.

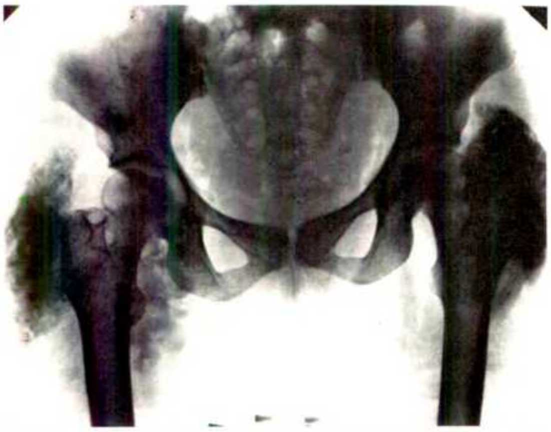

FIG. 1.—Radiograph showing calcified lumps over both greater trochanters.

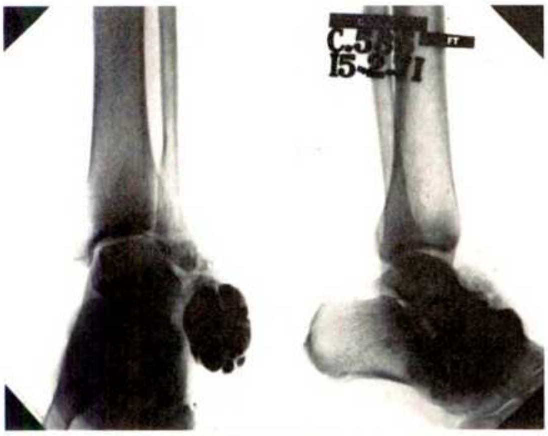

FIG. 2.—Radiograph showing calcified lumps over both ankle-joints.

The patient made an uneventful recovery and was subsequently discharged from hospital. Unfortunately follow-up studies will probably be impossible as these people for various reasons will not attend regularly at out-patients' clinics.

AETIOLOGY AND PATHOGENESIS

In the New Guinea Highlands, as no doubt in various other lands, the indigenous people frequently sleep on the bare ground or boards. This in many cases leads to prolonged intermittent ischaemia involving the subcutaneous tissue surrounding the pressure areas. Fat necrosis results with subsequent calcification. Once established, the area of necrosis and calcification seems to increase in size, frequently with a breakdown of the overlying skin and the discharge of a white chalky fluid through the resulting sinus. In some cases a secondary chronic infection develops.

Macroscopically the mass may be subcutaneous or intramuscular. It lies within a collection of thick fibrous tissue with which it blends and ramifies and from which it cannot be shelled out. This fibrous tissue does not easily separate out from the surrounding normal tissue and it may ramify deeply and extensively, as in the case presented here. The tumour is partially calcified and may be extremely hard and it frequently contains cystic areas with whitish chalky material. In the region of the greater trochanter the trochanteric bursa lies deep to the tumour and has to be removed with the tumour. The tumour does not appear to arise from or within the bursa although this has been suggested by Koten (1969). A secondary bursa may, however, be formed in association with the tumour.

CLINICAL FINDINGS

The clinical findings have been well described by McClatchie and Bremner (1969).

The condition occurs in adults of both sexes. There is usually a solitary, hard, and slow-growing tumour in the vicinity of a joint. Occasionally the lesions may be multiple. Some tumours contain softer cystic areas with a chronically discharging and sometimes secondarily infected sinus. Episodes of pain and tenderness punctuate the course of the condition, and are caused by the aseptic inflammatory reaction which accompanies episodes of necrosis within the mass (Smith, 1968). Secondary infection may cause further pain and discharge.

Once seen and recognized the condition is rarely misdiagnosed thereafter. The radiographic appearances are typical (*Figs.* 1, 2). These reveal radio-opaque areas of calcification throughout the mass which vary in density but do not involve the joint.

TREATMENT

It is generally agreed that only wide excision will cure the condition. This is achieved in most cases by simply removing a large block of tissue including the tumour. In the case of the true hip stone, excision will include removal of the trochanteric bursa. Primary closure and drainage are usually adequate and where secondary infection is present an antibiotic cover is a wise precaution.

Where the tumour is recurrent and has ramified widely, as in the case presented here, total surgical excision is a formidable procedure. There are no planes of demarcation between the tumour and normal tissue, and the anatomy in the vicinity is distorted; blood-loss may be considerable and the surgeon should be prepared for a major operation.

DISCUSSION

Tumoral calcinosis has been reported from Zambia, Rhodesia, Uganda, Kenya, and South Africa (McClatchie and Bremner, 1969; Sonnenfeld, 1970) as well as from numerous areas on the island of New Guinea.

The condition masquerades under many pseudonyms in different districts, being variously referred to as 'hip stone', 'ankle stone', 'calcified bursa', 'calcification of a lipoma', 'Kikuyu bursa', etc.

The size and multiplicity of the leasions make the case presented here a little unusual, but there is every reason to believe that it is nothing more than an extreme example of multiple tumoral calcinosis.

Pathological calcification is commonly classified as 'dystrophic calcification', 'metastatic calcification', and 'calcinosis'. Dystrophic calcification is the deposition of calcium in degenerative tissue, and it is not dependent upon an increase in the calcium content of the blood but appears to be influenced by a local relative alkalinity of the damaged tissue (Anderson, 1964). This is the most frequent type of pathological calcification and occurs in areas of tuberculous necrosis and in degenerative tumours, and gives rise to tumoral calcinosis in areas of subcutaneous fat necrosis as described in this paper.

Metastatic calcification is a precipitation of calcium salts owing to a disturbance of the calcium and phosphorus metabolism and is often associated with an excess of calcium in the circulating blood. This may be a sequela of hyperparathyroidism, hypervitaminosis D, and destructive bone tumours.

The ischaemic necrosis that results in tumour calcinosis is caused by intermittent pressure over a period of years, and it occurs in reasonably healthy adults. The skin is not initially involved. In all these respects this condition differs from the ischaemic necrosis commonly found in the bedridden, elderly, sick, or paraplegic patient.

It is interesting to speculate why in some cases of tumoral calcinosis the lesion grows rapidly even after the removal of the precipitating cause and why recurrence is apt to occur after incomplete removal. In these respects tumoral calcinosis behaves like a locally invasive neoplasm.

A detailed follow-up study of a series of these cases would be a difficult task but is long overdue and may well throw some light on this interesting condition.

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RUPTURED MYCOTIC ANEURYSM OF THE SPLEEN

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SUMMARY

The fourth recorded survivor of a ruptured splenic aneurysm is presented. He is also remarkable for his multiple pathology including bacterial endocarditis, aortic incompetence with multiple peripheral embolism, and neurofibromatosis.

It is emphasized that mycotic aneurysms of the spleen are an unusual complication of bacterial endocarditis, and a high index of suspicion is essential for their diagnosis. Treatment must be prompt and effective.

SINCE 1770 when Beaussier described the first case of splenic aneurysm there have been over 300 reported cases, but few cases survive rupture and fewer still are diagnosed prior to surgery or death. The incidence of splenic aneurysms in the general population is 0·05 per cent (Lindboe, 1932). Most authors agree that atherosclerosis is the most important aetiological factor, being responsible for 66–77 per cent of cases, but there is controversy as to whether congenital defects or mycotic emboli occupy second place (Cosgrove, Watts, and Kaump, 1947; Bergner and Bentivegna, 1967; Baron, Weinshelbaum, and Block, 1968).

The incidence of rupture of all splenic aneurysms is reported to be 34–46 per cent, but this may be an over-estimate because many patients have been treated conservatively with success for up to 18 years (Jones and Finney, 1968).

The case of ruptured splenic aneurysm reported by Baron and others in 1968 was the second to have been diagnosed preoperatively and only the third to survive. We now present the fourth survivor whose condition was also diagnosed correctly preoperatively.

CASE REPORT

A 23-year-old African man was admitted on 29 Jan., 1969, having awakened 4 hours earlier with mid-abdominal pain and dizziness followed by vomiting. In November, 1968, he had had an episode of pain in the right arm just above the elbow, of sudden onset, which had been succeeded by swelling. Both the pain and the swelling had persisted unaltered for 2 weeks and had then gradually subsided. Early in January, 1969, the patient had begun to have attacks of abdominal pain; initially the pain had been supra-umbilical but later it had become generalized. Two weeks before admission he had developed pain of sudden onset successively in his left ankle, 2–3 days later in the medial side of the left thigh just above the knee, and 3–4 days after that in the left groin which had soon been followed by a swelling. On admission he still had pain in all three positions in the left leg, but neither pain nor swelling was present in the arm.

The patient was grossly anaemic with slight ankle oedema, a collapsing pulse accompanied by a diastolic murmur of aortic incompetence, a blood-pressure of 200/90 (in the left arm), and a weak right radial and left posterior tibial pulse. In the upper part of the left thigh there was a mass with a thrill, a murmur, and expansile pulsation over its lower and medial part. The abdomen was tender and the spleen was palpable, but there were no splinter haemorrhages nor petechiae and the skin was disfigured by neurofibromata and café-au-lait patches. Diagnoses of aortic incompetence with subacute bacterial endocarditis and of multiple peripheral embolism with neurofibromatosis were made. At this stage the abdominal signs were considered to be due to mesenteric vascular occlusion but at no time was blood passed per rectum.

The patient's haemoglobin was 34 per cent with 12 per cent reticulocytes; packed cell volume, 16; mean corpuscular haemoglobin concentration, 31; white cell count, 7100; platelets, 125,000; erythrocyte-sedimentation rate, 35 mm. per hour. Electrolytes were normal and the urine showed no abnormality. The liver-function tests were normal, but the Venereal Diseases Research Laboratories' test was strongly positive. The blood cultures were always sterile.

During the next few days the patient improved after treatment with blood transfusion, digoxin, and frusemide, but on 9 Feb. he had an exacerbation of abdominal pain, collapsed, and became very anaemic. There was generalized abdominal tenderness, which was maximal in the left hypochondrium, with shifting dullness. Blood was obtained on abdominal paracentesis. A tentative diagnosis of a ruptured splenic artery aneurysm was made.

At laparotomy the peritoneal cavity contained dark blood with clots in the splenic region and pelvis and a ruptured spleen showing evidence of a recent infarction centrally and an old subcapsular haemorrhage. There was a small splenic artery aneurysm situated approximately 5 cm. from the splenic hilum but it was intact. The spleen was removed and the splenic artery was ligated proximal to the aneurysm.

The patient's postoperative progress was interrupted by sudden collapse and pyrexia 9 days after operation followed 4 days later by a severe herpetic eruption around the mouth and face. His collapse was attributed to septicaemia, but no organisms grew on blood culture. After a further 4 days the aneurysmal haematoma in the left thigh became painful and began to expand and pyrexia returned. It became clear that the aneurysm was now infected, and it was excised on 28 March, the haematoma being evacuated at the same time and the first perforating branch of the profunda femoris (the artery of origin) ligated. Sections of a portion of the resected artery showed some replacement of the smooth muscle of the media by collagen together with disruption of the internal elastic lamina, but there were no signs of inflammation.

The infected haematoma yielded a profuse growth of *Klebsiella* sp. which was sensitive to ampicillin, chloramphenicol, colistin, framycetin, garamycin, and tetracycline.

The patient has remained well since, and when last seen (on 21 Jan., 1970) the blood-pressure differed in the two brachial arteries, being 130/40 on the left and 130/60 on the right, but there were no other changes in his state.

DISCUSSION

Cosgrove and others (1947) reported 12 cases of mycotic aneurysms out of 60 splenic aneurysms

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(20 per cent). Their average age was 24 years and there was an equal distribution between the sexes. The aneurysms were 2–3 cm. in size and occurred on the finer branches of the splenic artery. In 7 of the 12 patients there were also multiple splenic infarcts. Microscopy showed intimal thickening with hyaline degeneration of the media and fibrosis.

Stengel and Wolferth (1923) discovered 15 mycotic aneurysms in 264 cases of splenic artery disease (6 per cent). They considered that the septic emboli were most frequently arrested at the primary bifurcation of the splenic artery and it was here that the aneurysms were mainly found.

Pregnancy seems to precipitate rupture of splenic aneurysms. Owens and Coffey (1953) found that 23 per cent of the cases in their series were pregnant while in the series of Cosgrove and others (1947) 25 per cent of the cases were pregnant, only 1 of whom survived.

The mortality-rate after rupture approaches 100 per cent, probably owing mainly to failure to recognize the condition even at laparotomy (Heggtveit, 1963). Rupture appears to occur in two stages in many patients, the first stage being rupture either slowly or quickly into the retroperitoneal tissues or the lesser sac. This stage is followed at a varying interval of time (up to 48 hours—Machemer and Fuge, 1939) by rupture into the general peritoneal cavity or into a viscus, often the stomach. The differential diagnosis is that of an acute abdomen with signs of sudden and profuse haemorrhage into the peritoneum or as a haematemesis and/or melaena.

Treatment of a ruptured aneurysm must be surgical with excision of the involved artery with or without splenectomy and partial gastrectomy if the stomach is involved.

CONCLUSION

The case reported here is remarkable for surviving a ruptured mycotic splenic aneurysm and for his multiple pathology. The diagnosis was suggested preoperatively by association of the facts that the patient was under treatment for bacterial endocarditis and had a history suggestive of multiple mycotic aneurysms and that there were overt signs of an aneurysm in the profunda femoris artery. The splenic artery is the second commonest intra-abdominal artery to form aneurysms, the aorta being the first (Bottiglieri, Palmer, and Litalo, 1964). Although nothing was grown from the blood and the histology of the aneurysm was non-specific, the peripheral aneurysm was infected macroscopically prior to surgical intervention and yielded a profuse growth of *Klebsiella* sp. at operation. Immediate operative intervention was essential for the survival of the patient.

It is stressed that mycotic aneurysms of the splenic artery are an uncommon complication of bacterial endocarditis, but can be rapidly fatal unless clinicians are aware of the condition and treatment is prompt and effective.

Acknowledgements.—We would like to thank Professor M. Gelfand for the medical management of this case, and Dr. M. H. Webster, O.B.E., Secretary for Health, Rhodesia, who gave permission for publication.

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A CASE OF GALL-STONE ILEUS IN THE ABSENCE OF A BILIARY-ENTERIC FISTULA

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Summary

A case of gall-stone ileus is reported in which at operation no fistula between the biliary tree and the gut was found. The obstruction was removed and cholecystectomy and exploration of the common bile-duct were performed with a successful outcome. The pathogenesis of intestinal obstruction due to gall-stones in the absence of a fistula is briefly discussed.

Gall-stone ileus is now well recognized and some series describe preoperative diagnostic rates of 80 per cent or more (Figiel, Figiel, Wietersen, and Dranginis, 1955; Haffner, Semb, and Askhus, 1969), but it is rare for intestinal obstruction to be caused by a stone which has entered the bowel through the ampulla of Vater and not via a fistula. Andersson and Zederfelt (1969) have recently stated: 'Since stones which pass the ampulla of Vater are small they do not cause obstruction unless anatomical strictures from cancer or inflammatory disease are present.' Not all share this view, but all agree that such occurrences are rare indeed.

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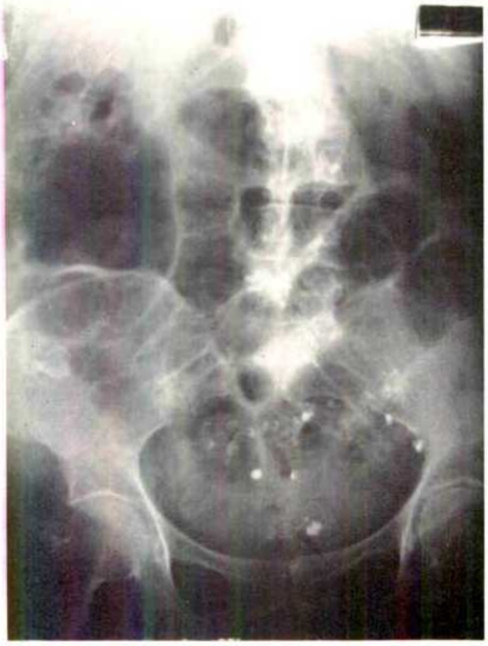

FIG. 1.—Supine radiograph of the abdomen, showing dilated loops of small bowel and an aberrantly located gall-stone in the right iliac fossa.

The purpose of this paper is to present a case of gall-stone ileus in which the causative enterolith undoubtedly entered the bowel from the common bile-duct via the ampulla of Vater.

CASE REPORT

Mrs. C. P., an 81-year-old woman, was admitted on 4 Dec., 1970, complaining of a constant ache in the right iliac fossa which had been present for 6 days. During this time she had been vomiting copiously, but this had not relieved her pain. There had been no alteration in bowel habit and she had passed faeces 24 hours before admission.

Previous history included an episode of rectal bleeding in 1970 which had required hospital admission and which had been diagnosed after barium-enema examination as being due to diverticular disease. There was no past history of jaundice or indigestion.

Examination revealed a well-orientated but dehydrated old lady who was neither anaemic nor jaundiced. Her temperature was 36·2° C., pulse-rate was 80, and blood-pressure was 150/90 mm. Hg. The abdomen was not distended but exhibited generalized tenderness which was most marked in the right iliac fossa. Bowel-sounds were normal, no masses were palpable, and rectal examination was normal.

The following investigations were performed: haemoglobin, 18·7 g. per 100 ml.; packed-cell volume 56 per cent; white blood-count, 18,000 per mm.^{3}; blood-urea, 140 mg. per 100 ml.; serum potassium, 3·2 mEq./l.; midstream urine, sterile. An abdominal radiograph showed a dilated loop of colon in the region of the hepatic flexure; there were no signs of obstruction.

A provisional diagnosis of diverticulitis was made and the patient was treated with intravenous fluids and antibiotics. Her condition remained satisfactory and her bowels were opened three times in the next 5 days. However, on 12 Dec. she developed abdominal pain and started to vomit again and increasing abdominal distension was noted. An abdominal radiograph (*Fig.* 1) confirmed intestinal obstruction and surgery was advised.

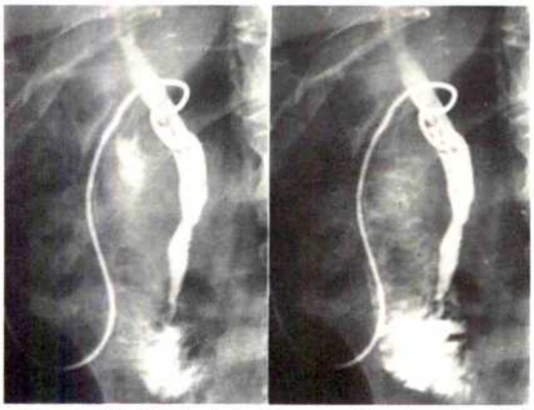

FIG. 2.—The T-tube cholangiogram performed on the eighth postoperative day, showing no remaining stones and no fistula between the common bile-duct and the gut. The lower end of the common bile-duct tapers normally.

At operation there was gross diverticular disease of the sigmoid colon and marked distension of the small bowel owing to an obstruction 60 cm. from the ileocaecal valve. The small bowel appeared otherwise normal. Gall-stones were palpable in the gall-bladder and common bile-duct. There were no adhesions between the gall-bladder and the bowel. The obstruction was found to be due to an impacted stone which broke on manipulation. An enterotomy was made and pieces of an obvious gall-stone were removed. Cholecystectomy and choledocholithotomy were performed, five stones being removed from the common bile-duct. Operative cholangiography was undertaken and showed that the common bile-duct was free of stones and no fistulous connexion with the bowel was shown, though both the cystic duct and the common bile-duct were noted to be dilated.

Postoperative progress was uneventful. A T-tube cholangiogram (*Fig.* 2) on the eighth postoperative day showed neither stones nor fistula.

The stones from the ileum, the common bile-duct, and the gall-bladder (*Fig.* 3) were analysed chemically and found to be identical, all containing cholesterol and bile-salts. The gall-bladder showed the histological changes of chronic cholecystitis.

DISCUSSION

In 1900 Courvoisier performed autopsies on 36 cases of gall-stone ileus, and in 7 he was unable to demonstrate a fistula. A similar finding was reported by Collins and Claxton (1966), who were unable to demonstrate a fistula at an autopsy performed 2 months after an operation for the relief of intestinal obstruction due to a gall-stone. However, it is known that fistulae can close spontaneously (Raiford,

1962) and it is impossible to be certain that this had not occurred in these cases. Three cases of gall-stone ileus in the absence of a fistula at operation have been reported; in 2 of these (Mulder and Flynn, 1958; Warner and Swann, 1951) the patient had previously undergone a gastrectomy of the Polya type, and the stones were thought to have enlarged whilst stationary in the afferent loop. In the third case (Dulin and Petersen, 1939) the stone had probably enlarged in a duodenal diverticulum. No such blind pockets were found at laparotomy in the present case.

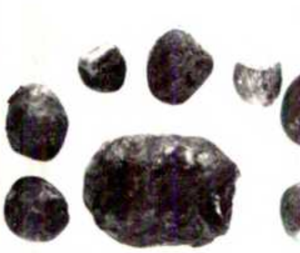

FIG. 3.—The gall-stones removed from the ileum, gall-bladder, and common bile-duct.

The various forms of enterolith have been reviewed by Singleton (1970), who classifies gall-stones as secondary true enteroliths because they are formed outside the intestine. Primary bile-acid enteroliths are much less common, but can enlarge in diverticula to a sufficient size to cause intestinal obstruction. It has been suggested that since these enteroliths resemble gall-stones they may be responsible for several cases of obstruction apparently due to a gall-stone (Armitage, Fowweather, and Johnstone, 1950). However, in the present case laboratory analysis of the stones from the ileum, the common bile-duct, and the gall-bladder showed them to be identical and there can be little doubt that the obstruction was caused by a stone or possibly an aggregation of small stones which had formed in the biliary tree.

Wakeley and Willway (1935) have discussed the ways by which stones enter the bowel and illustrate a case where a stone was about to ulcerate through the lower end of the common bile-duct into the duodenum. That such a fistula can form seems plausible, but none was present in the case presented here as two cholangiograms showed a relatively normal lower end to the common duct (*Fig.* 2). Choledochoduodenal fistulae are said not to heal spontaneously (Maingot, 1968) and would be unlikely to do so while several stones remain in the common bile-duct. The obstruction in this case must therefore have been formed by a stone or stones which had entered the bowel from the biliary tree. No fistula could be demonstrated either at laparotomy or by two cholangiograms and it would seem highly likely that the stone had passed through a dilated ampulla of Vater.

Acknowledgement.—I would like to thank Mr. H. J. Espiner for his permission to publish this case and for his help in preparing this report.

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HAEMOPERITONEUM COMPLICATING SECONDARY CARCINOMA IN THE LIVER

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SUMMARY

Haemoperitoneum complicating primary hepatic carcinoma is well documented but secondary hepatic carcinoma rarely causes intra-abdominal haemorrhage. A case of haemoperitoneum from secondary pancreatic carcinoma of the liver is reported.

A CASE of haemoperitoneum due to haemorrhage from a secondary hepatic carcinoma of pancreatic origin is described. This is the first report of such a case due to pancreatic carcinoma.

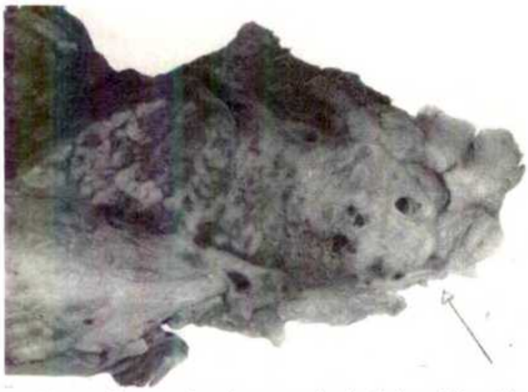

FIG. 1.—Pancreas showing tumour in the body and the tail.

CASE REPORT

W. H., a previously healthy 72-year-old man, was admitted to another hospital with a 3-week history of decreasing appetite, lethargy, and shortness of breath on exertion. On the day of admission he had felt unwell and had had a fainting episode.

On admission the patient was shocked, and he had a blood-pressure of 90/50 and was grossly anaemic (Hb, 55 per cent). The abdomen was distended and a vague epigastric swelling was palpable. Despite resuscitation the patient's condition deteriorated and the following day a peritoneal tap revealed fresh blood. A tentative diagnosis of a slowly leaking abdominal aortic aneurysm was made and the patient was transferred to the Manchester Royal Infirmary.

At laparotomy 2 litres of fresh blood were drained from the peritoneal cavity. The aorta and major vessels were intact. The pancreas felt hard and irregular and the upper para-aortic and coeliac lymph-nodes were enlarged and firm. The liver was enlarged and showed diffuse nodularity. The source of haemorrhage was a small ulcer on the inferior aspect of the right lobe of the liver. A biopsy was taken from this site and the area was sutured. The patient's condition deteriorated and he died a few hours later.

At autopsy the abdomen was distended and contained about 1·5 litres of deeply blood-stained fluid. A large clot was present in the right subphrenic area. Several grey-white nodules measuring up to 1 cm. in diameter were seen in the pelvic peritoneum and the posterior parietal peritoneum.

The head of the pancreas appeared normal. A hard, ill-defined, grey-white mass showing areas of haemorrhage and necrosis was present in the body and the tail of the pancreas (*Fig.* 1). Histologically the tumour was a poorly differentiated adenocarcinoma (*Fig.* 2).

The liver was enlarged and the external surface showed numerous, small, raised, reddish-brown nodules. On section the general pattern of the nodules was suggestive

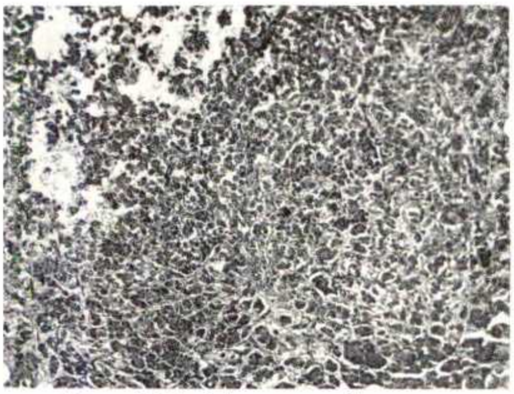

FIG. 2.—Histological appearance of the tumour.

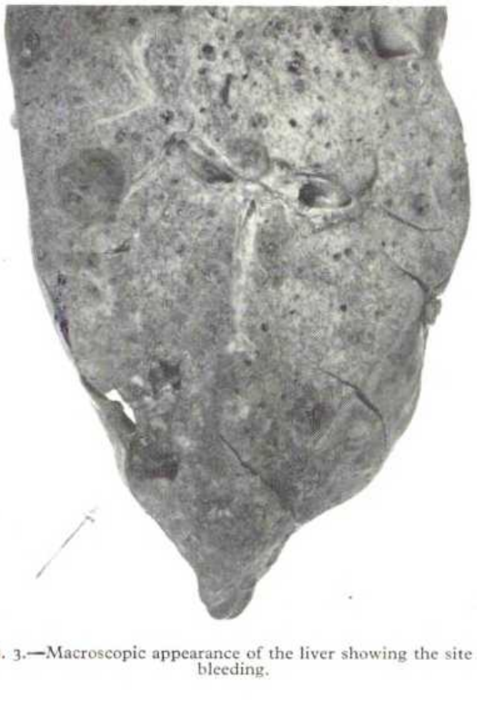

FIG. 3.—Macroscopic appearance of the liver showing the site of bleeding.

of a vascular distribution. A number of more typical grey-white secondaries measuring up to 1·5 cm. in diameter was seen. At one site in the right lobe there was a necrotic ulcerated area, 3 cm. in diameter, containing blood-clot (*Fig.* 3).

Histologically the appearance of the tumour deposits and the biopsy from the bleeding site resembled the primary lesion in the pancreas. The tumour was infiltrating the portal venous system and several deposits were seen in the hepatic parenchyma. Many of these deposits showed haemorrhage and necrosis.

The splenic vein was partially occluded by tumour but the main portal vein did not appear to be involved. The spleen (130 g.) was of normal size but the cardio-oesophageal veins were rather prominent, suggesting some degree of portal hypertension.

The lymph-nodes of the peripancreatic region and the porta hepatis were enlarged and contained tumour.

DISCUSSION

Haemorrhage from secondary hepatic carcinoma is a rare condition (Gribble and Blair, 1962). Specter and Chodoff (1950) reported a case of haemoperitoneum from a cavitated metastatic adenocarcinoma of the liver. The origin of the tumour was uncertain but histological appearances were suggestive of a primary in the kidney or the adrenal gland. Although these authors believed that their case of haemoperitoneum due to metastatic tumour of the liver was the first recorded case, Bettini (1956) was able to find 10 reported cases of haemorrhage from metastatic tumours and he added a further case of his own. None of these cases was of pancreatic origin.

Involvement of the portal vein by tumour is usually seen in pancreatic carcinomas arising in the head or the body of the pancreas, whereas invasion of the splenic vein and its possible extension into the portal vein are more apt to occur when the tumour is situated in the body or tail of the pancreas (Winston Evans, 1966).

In contrast to the rather slow, prolonged bleeding seen in the present case haemorrhage associated with primary hepatic carcinoma tends to be massive owing to the greatly increased hepatic blood-flow in the latter condition (Wartnaby, Bouchier, Pope, and Sherlock, 1963).

In the differential diagnosis of intra-abdominal haemorrhage this rather rare cause from secondary hepatic carcinoma should be borne in mind.

Acknowledgement.—We wish to express our thanks to Mr. W. McN. Orr, under whose care this patient was admitted, for his permission to publish the case and for his helpful advice and criticism.

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LUMBOSACRAL AGENESIS IN A 60-YEAR-OLD MAN

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SUMMARY

A case of lumbosacral agenesis below the third lumbar vertebra in a 60-year-old man is described. The patient is thought to be the oldest survivor with such an extensive defect.

CASE REPORT

C. McN., a 60-year-old man, one of a large family with both older and younger healthy brothers and sisters whose mother had died in her seventies, had first been admitted to hospital for the investigation of a urinary-tract infection and left-sided colic at the age of 59 years.

He had regarded himself as a freak of nature from an early age because he had never been able to walk. His legs had been diminutive and wasted at birth though movements at the hips and knees had been present and sensation intact. He had not gone to school because of difficulty in controlling micturition. He had taught himself to read and write and had grown to develop a healthy attitude to his deformity. He had dreaded the idea of being investigated in hospital as he felt nothing could be done for him. He found he could control micturition by regularly compressing his abdomen manually. Regular purgation kept his bowel movements under control. He had lived a wheel-chair life indoors till the age of 40 years, when he had procured an invalid car.

On examination the patient was found to have strong, well-developed upper limbs and shoulders but his trunk tapered to a small mobile pelvis and diminutive lower limbs. Movements of the hips and knees were reduced by wasting of all the muscles and gross contractures. Examination of the chest revealed a ventricular septal defect and an electrocardiograph showed a grossly abnormal record suggesting anterior myocardial infarction and left ventricular hypertrophy. Biochemical and haematological investigations revealed no gross pathology. A radiograph of the lumbar spine and pelvis (*Fig.* 1) showed the spine to terminate blindly at the third lumbar vertebra, the sacrum to be absent, the ilii joined at a synarthrosis, the pelvis and hips to be grossly distorted, and the left hip to be dislocated. Intravenous pyelography revealed no significant pathology. His urinary infection responded to a course of ampicillin and his renal colic subsided.

The patient is now at home where he dresses himself and attends to his own toilet. No further investigations are contemplated. Permission to take a photograph was not granted.

DISCUSSION

Since Hohl (1850) first reported a case of sacral agenesis increasing numbers of cases have been documented. Most describe various degrees of sacral and lumbosacral agenesis in infants and children. Freedman reviewed the literature in 1950 and classified previously recorded cases of spinal agenesis according to the level of the lowest vertebra present. *Table I* summarizes all recorded live cases of lumbosacral agenesis with their known period of survival. Those rare cases involving the lower thoracic vertebrae are included, while those with absence of the sacrum or coccyx as the only spinal defect are excluded.

Table I.—CASES OF LUMBOSACRAL AGENESIS AND THEIR KNOWN PERIOD OF SURVIVAL, REPORTED IN THE LITERATURE

LOWEST VERTEBRA PRESENT (either Rudimentary or Intact)	AUTHOR	SEX	DURATION OF SURVIVAL*
Thoracic 10	Friedel (1910)	F.	3 d.
	Rosenthal (1968)	M.	3 mth.
Thoracic 11	Sinclair, Duren, and Rade (1941)	M.	9 yr.
	Chilman and Tuszewski (1965)	M.	11 wk.
	Rusnak and Driscoll (1965)	M.	40 hr.
	Trapnell, Gibberd, Starer, Fletcher, Redhead, and Vitali (1970)	M.	12 yr.
Thoracic 12	Pirkey and Purcell (1957)	M.	9 mth.
	Pirkey and Purcell (1957)	M.	5 d.
	Velegeas (1959)	M.	1½ yr.
	Blumel, Evans, and Eggers (1959)	M.	10 yr.
	Blumel and others (1959)	F.	13 yr.
	Russell and Aitken (1963)	M.	13 yr.
	Russell and Aitken (1963)	M.	18 yr.
	Russell and Aitken (1963)	M.	9 yr.
	Frantz and Aitken (1967)	—	1 yr.
	Frantz and Aitken (1967)	—	3 yr.
	Rosenfelder (1968)	M.	12 hr.
	Rosenfelder (1968)	M.	20 yr.
	Pearlman and Bors (1969)	M.	18 yr.
	Trapnell and others (1970)	M.	25 yr.
	Perry, Bonnet, and Hoffer (1970)	M.	16 yr.
Lumbar 1	Blumel and others (1959)	M.	28 yr.
	Blumel and others (1959)	M.	8 yr.
	Blumel and others (1959)	M.	6 yr.
	Russell and Aitken (1963)	M.	16 yr.
	Rusnak and Driscoll (1965)	M.	3 d.
	Dimicoccoli (1966)	F.	2 yr.
	Frantz and Aitken (1967)	—	17 yr.
	Banta and Nichols (1969)	F.	25 yr.
Lumbar 2	Blumel and others (1959)	M.	7 yr.
	Blumel and others (1959)	M.	17 yr.
	Blumel and others (1959)	M.	4 yr.
	Blumel and others (1959)	F.	3 yr.
	Blumel and others (1959)	F.	2 yr.
	Blumel and others (1959)	F.	7 yr.
	Blumel and others (1959)	F.	6 yr.
	Herlinger (1964)	F.	4 yr.
	Rusnak and Driscoll (1965)	M.	6 d.
	Banta and Nichols (1969)	F.	7 yr.
	Banta and Nichols (1969)	M.	4 yr.
	Banta and Nichols (1969)	M.	9 yr.
Lumbar 3	Desfosses and Mouchet (1924)	F.	7 yr.
	Drehmann (1927)	M.	1 yr.
	Hamsa (1935)	F.	9 yr.
	Pouzet (1938)	M.	5 yr.
	Blumel and others (1959)	F.	6 yr.
	Blumel and others (1959)	F.	12 yr.
	Blumel and others (1959)	M.	8 yr.
	Blumel and others (1959)	F.	18 yr.
	Trapnell and others (1970)	M.	30 yr.
	Perry and others (1970)	M.	11 yr.
	Perry and others (1970)	F.	9 yr.
	Nicol (1972)	M.	60 yr.
Lumbar 4	Elmslie (1921)	M.	14 yr.
	Espasa (1928)	M.	7 yr.
	Brailsford (1929)	M.	5 yr.
	Hamsa (1935)	M.	9 yr.
	Zeligs (1940)	F.	7 mth.
	Del Duca, Davis, and Barroway (1951)	F.	4 yr.
	Katz (1953)	M.	7 yr.
	Blumel and others (1959)	M.	5 yr.
	Blumel and others (1959)	M.	5 yr.
	Blumel and others (1959)	M.	15 yr.
	Chaptal, Jean, and Bonnet (1965)	F.	2 yr.

* Duration of survival is estimated by the age at death or the age at the time of reporting.

The oldest case described by Banta and Nichols (1969) is a 25-year-old female with a rudimentary first lumbar vertebral body who was first seen at the age of 7 months. Freedman (1950) reported the case of a 61-year-old man with absence of the sacrum below the second sacral segment who was able to get about quite well though his legs had been wasted since infancy. His last 7 years had been spent in an institution. The case reported here is thought to be the longest survivor with the most extensive spinal defect.

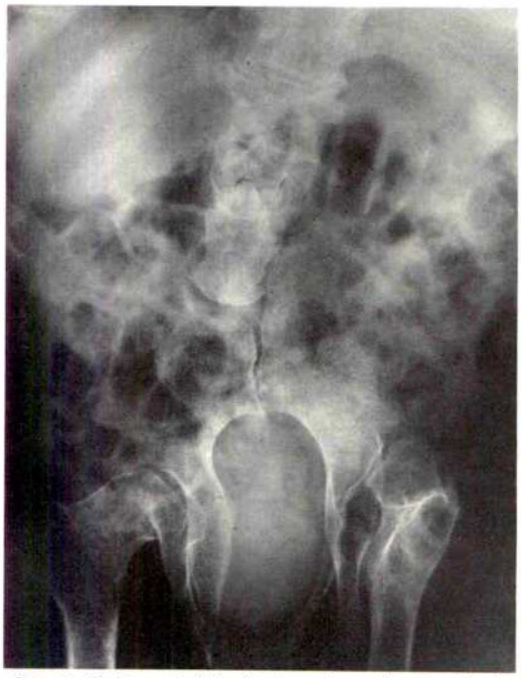

FIG. 1.—Radiograph of the lumbar spine and pelvis, showing the spine terminating blindly at the third lumbar vertebra, the sacrum absent, the ilii joined at a synarthrosis, and the pelvis and hips grossly distorted. The left hip shows dislocation which is probably neurogenic.

Acknowledgements.—I am indebted to Mr. J. P. A. Weaver, Senior Lecturer in Surgery, University of Dundee, for permission to examine his patient and for giving me access to his records; to Mr. K. L. G. Mills, Senior Lecturer in Orthopaedic Surgery, University of Dundee, for his constant encouragement; and to Mr. R. G. Donovan, Chief Photographic Technician, Department of Orthopaedic Surgery, University of Dundee, for considerably improving on a poor radiograph.

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LEIOMYOMA OF THE APPENDIX

BY T. H. CULLEN AND H. J. VOSS
KETTERING GENERAL HOSPITAL

SUMMARY

A case of a very large leiomyoma of the appendix is reported. References to this condition are rare and the presentation of this case is unusual.

ALL surgeons with some experience of abdominal surgery will have met with leiomyomas of the wall of the intestine. These benign tumours are often an incidental finding on abdominal exploration in the course of treating some other condition, although they may cause symptoms of their own accord, usually presenting as gastro-intestinal haemorrhage or intestinal obstruction.

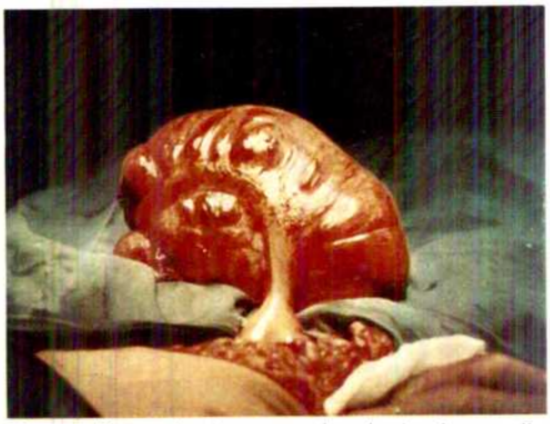

FIG. 1.—Photograph taken at operation, showing the appendix stretched out over the large leiomyoma.

Some are discovered only at routine post-mortem examination, having been symptomless during life.

The unusual features of the tumour reported here are the site of origin, the size, and the mode of presentation.

CASE REPORT

R. W., aged 50 years, was referred to the medical out-patients' clinic of Kettering General Hospital in June, 1970, for investigation of chest pain on exertion. Ten years previously this patient had had melaena from a duodenal ulcer, and in January, 1970, he had had deep-vein thrombosis in his right leg and had been treated with anticoagulants. Examination by a medical colleague revealed little of significance except for a mass in the lower abdomen which felt like an enlarged bladder. This mass did not appear to alter after the patient had passed a moderate amount of urine, but bimanually it seemed to be related to the prostate and bladder. On further questioning he complained of increased frequency and some dribbling at the end of micturition. He was then

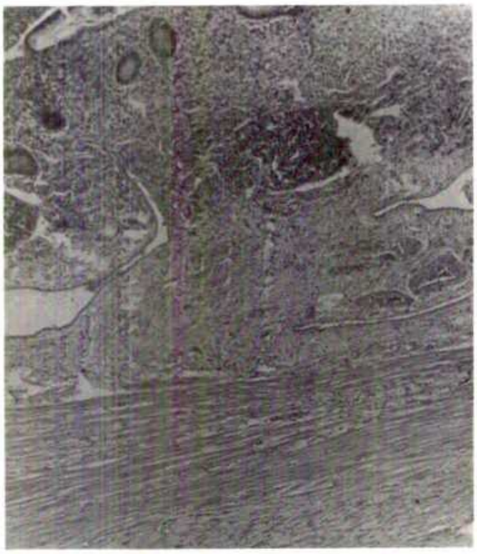

FIG. 2.—Leiomyoma arising from the outer muscular layer. H. and E. (× 42.)

seen by one of the authors (T. H. C.) and he certainly appeared to have chronic retention associated with a minimal degree of benign prostatic enlargement. His haemoglobin was 15·2 g. per cent, E.S.R. 4 mm. fall in 1 hour, blood-urea 31, and the midstream urine contained no white cells and was sterile on culture. An intravenous pyelogram revealed a soft-tissue tumour lying in the pelvis above the bladder; apart from a trace of residual urine in the bladder after micturition the urinary tract was normal. Lateral tomography did not help to elucidate the nature of the tumour and laparotomy was advised.

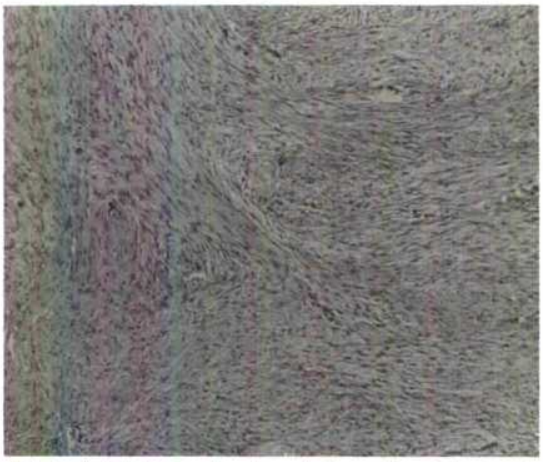

FIG. 3.—Interlacing bundles of muscle-fibres. H. and E. (× 42.)

OPERATION (T. H. C.).—On 9 Oct. the abdomen was explored through a right lower paramedian incision. A large, hard, encapsulated mass was found in the pelvis. A piece of gut was stretched over its surface and once this was identified as the appendix the mass and the appendix were easily removed (*Fig.* 1). No other abnormality was found in the abdomen.

The patient's postoperative progress was uneventful. He was discharged from hospital on the fourth day after operation.

PATHOLOGICAL REPORT (H. J. V.).—Naked-eye examination of the specimen revealed a circumscribed pale tumour with a glistening surface measuring 15 × 10 × 8 cm. Along one border the appendix (10 cm. in length) was partly embedded, one surface lying free, the other being half embedded in the tumour. On section the appendix was somewhat flattened by the tumour but not apparently inflamed. The tumour arose from or was continuous with the embedded muscular layer of the appendix. The tumour itself was pale buff coloured, firm, and of a whorled pattern—a typical appearance of a leiomyoma.

Microscopic examination showed a flattened but otherwise normal appendix. The mucosa and submucosa were surrounded by the normal longitudinal and concentric muscular layers. From the longitudinal layer there arose a leiomyoma (*Fig.* 2), consisting of interlacing bundles of smooth muscle-fibres (*Fig.* 3). Although there was some variation in the size of the cells there was little nuclear pleomorphism and no mitotic activity to suggest malignancy (*Fig.* 4). The appearance did not differ from that of a benign leiomyoma which is not infrequently found in the stomach or small intestine. In spite of its size the tumour had clearly grown outwards and had not projected into the mucosa.

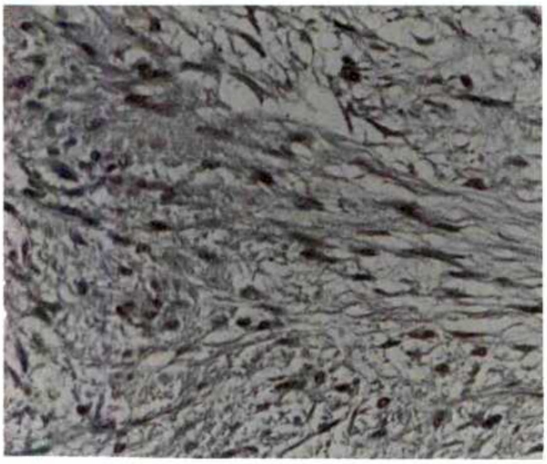

FIG. 4.—High-power view of the well-differentiated smooth muscle-fibres. H. and E. (× 86.)

DISCUSSION

We have been able to find two references to leiomyoma of the appendix in the literature.

Dobrov (1968) found one leiomyoma of the appendix in a series of 6662 appendicectomies carried out in the clinic of the Faculty of Surgery of the Medical Institute of Astrakhan; he was unable to find any reference to leiomyoma of the appendix in the literature. The leiomyoma reported in his paper was described as a thickening at the tip of the appendix the size of a hazel nut; this was discovered incidentally during a laparotomy for acute cholecystitis. Naka, Shinno, Aikawa, and Kuranishi (1969) also report a leiomyoma of the appendix, which was found in an appendix removed for acute appendicitis. It is described as a small, white, hard swelling the size of the tip of the little finger.

Doubtless other small tumours of this nature have been discovered in appendices removed at operation or found at routine post-mortem examination but have not been reported in the literature.

Acknowledgements.—We are indebted to Mr. R. R. Popham and to the technical staff of the Department of Pathology for the photographs.

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REVIEWS AND NOTICES OF BOOKS

Orthopaedics for the Undergraduate. Fractures. By W. A. CRABBE, M.D., F.R.C.S., Orthopaedic Surgeon, Guy's Hospital, London. 8½ × 5½ in. Pp. 256 + vii. Illustrated. 1971. London: William Heinemann Medical Books Ltd. £3·30.

THIS is a useful book for students, for it sets out in a lucid and dogmatic way the causes, treatment, and after-treatment of fractures. Quite a feature of the book is the large number of illustrations—all line drawings and very informative.

A good knowledge of this book would get any student a pass mark in orthopaedics at a final examination.

In this age of trauma a sound knowledge of the treatment of fractures is essential to all practitioners.

Tracheostomy and Artificial Ventilation. Second edition. Edited by STANLEY A. FELDMAN, Consultant Anaesthetist, Westminster Hospital, London, and BRIAN W. CRAMLEY, Consultant Anaesthetist, Canterbury Group of Hospitals. 9 × 6 in. Pp. 151 + viii. Illustrated. 1971. London: Edward Arnold (Publishers) Ltd. £3.

THE second edition of this most useful book has been brought up to date and new chapters have been added. Today with intensive-care units in an ever-increasing number of hospitals the usefulness of this book is very apparent. The illustrations are clear, and they do enhance the text.

All hospital residents, students, and nurses will find in this book a clear, factual account of the several problems involved in the care of tracheostomy cases.

Ano-rectal Malformations in Children. By F. DOUGLAS STEPHENS, D.S.O., M.S. (Melb.), F.R.A.C.S., Melbourne, and E. DURHAM SMITH, M.D. (Melb.), F.R.A.C.S., F.A.C.S., Melbourne. 9 × 6 in. Pp. 411 + xvi. Illustrated. 1971. London: Lloyd-Luke (Medical Books) Ltd. £11·70.

ANORECTAL malformations are common in children and the majority of cases are seen in paediatric hospitals. When it is considered that there are some 37 regularly occurring types of these deformities it will be seen how important is such a book as this. The authors have made a comprehensive survey of these deformities and have added their own personal survey of their cases.

The book commences with a historical review of anorectal deformities from the year 650 B.C. to the present day.

Deformities in the male are considered at some length and are contrasted with those occurring in the female. It is interesting to read of the proposed international classification of anorectal anomalies which should be accepted by surgeons throughout the world. The various deformities are described in detail and are illustrated by line drawings and clinical photographs. The pre- and postoperative clinical photographs are particularly good.

The various operative techniques are described in detail. The results of operative treatment, the complications which may arise, and the assessment of continence make interesting reading.

There is a comprehensive list of references at the end of the book as well as three appendixes which are of real value.

This is a most useful reference volume on an important subject.

Patients, Hospitals and Operational Research. By G. M. LUCK, B.A., M.Sc., J. LUCKMAN, M.Sc., B. W. SMITH, B.Sc., M.B.C.S., and J. STRINGER, M.A., Institute for Operational Research, London. 8½ × 5½ in. Pp. 210 + xv. Illustrated. 1971. London: Tavistock Publications Ltd. £3·75.

ANY advice which will improve the working of the National Health system in this country will be welcome, for it must be said that there is room for improvement at the present time.

The Institute for Operational Research, which has fostered this book, has done a good job. It seeks to improve the process of decision-making at all levels of management. Such problems as case study, uneven workloads in special departments, planning surgery, and nursing techniques are all considered and debated. Most of the projects described in this book concern the systems relating to the care of patients, including their admission, diagnosis, treatment, and discharge. There can be no doubt that doctors, administrators, and nurses will find this book useful. Anything which improves the efficiency of our hospital system is of value at the present day.

Progress in Pediatric Surgery. Vol. 3. Edited by P. P. RICKHAM, W. CH. HECKER, and J. PRÉVOT. 9 × 5½ in. Pp. 167. Illustrated. 1971. Munich: Urban and Schwarzenberg. DM.45.

THIS is the third volume in the present series and it contains some interesting articles. Quite a feature of this series is the summary at the end of each article in English, French, and German.

This paper-back is apt to stress the rare cases in paediatric surgery but perhaps this is a good feature. An interesting article on the forms of congenital deformities of the chest reveals the fact that depression deformities of the sternum are extremely common, while protrusion deformities of the sternum are less common. The aetiology and pathogenesis of funnel chest are considered in great detail.

Subvesical urinary obstruction is an important congenital defect and various experiments on rabbits and pigs reveal some interesting results.

Such problems as the administration and design for intensive therapy in surgery of the newborn, the results of long-term positive-pressure ventilation, and the function of the cardia in childhood are discussed at length.

This is an interesting and stimulating book and it should be read by all surgeons who have infants and children under their care.

It is not often that a book is edited by an Englishman, a German, and a Frenchman, but the result is a great success. Is this a forerunner of the Common Market and its surgical literature?

Facial Prostheses. By ALAN CLIVE ROBERTS, T.D., C.G.I.A., F.R.S.H., F.B.I.S.T., A.I.S.T., A.I.Mech.E., St. Luke's Hospital, Bradford. 9½ × 7 in. Pp. 128 + x, with 138 illustrations. 1971. London: Henry Kimpton. £3·50.

THIS book contains a wealth of material dealing with facial reconstruction by means of various prostheses. The use of prostheses goes back a long way in time. Artificial eyes were used in Egyptian mummies and the ancient Chinese made use of facial prostheses from clay, wax, and wood. Two world wars and the increase in road accidents have provided a spate of cases which called for facial prostheses often after surgery had done its best.

The modern use of plastics has played a part in the making of prostheses. In dental surgery also the use of a prosthesis is frequently called for.

The author of this useful book has had an enormous experience both in this country and America of cases which required special prostheses. He discusses preconstructive planning and techniques to obtain the exact topography of the defect. He also deals with the use of synthetic materials and the effects of colour and light so that there is a minimum of contrast.

At the end of the book there are a number of clinical case histories and photographs showing the condition before and after the fitting of a prosthesis.

This book will interest a wide range of clinicians and plastic and dental surgeons as well as ophthalmic surgeons.

Handbuch der Medizinischen Radiologie; Encyclopedia of Medical Radiology. Part 3. Spezielle Strahlentherapie Maligner Tumoren. Edited by A. ZUPPINGER, Bern. 10½ × 7½ in. Pp. 642 + xv. Illustrated. 1971. Berlin: Springer Verlag. DM.296.

THIS volume which is part of the extensive encyclopaedia of medical radiology is devoted to the radiation treatment of tumours of the female genital organs, the male genitalia, and the urinary tract. All the chapters are authoritatively written by experts whose vast personal experience in their respective fields comes through very well. The chapters dealing with the female genitalia and uterus are in German, while the large section on the urinary tract is in English and the extensive contribution by Bloom and Wallace is particularly good. There are extensive references for all the chapters and, as usual, a detailed index. The illustrative radiographs are clear but unfortunately the publishers have stuck to the positive reproduction method.

This volume will be welcomed by radiotherapists and indeed by anybody treating malignant tumours and will obviously become a standard reference work. It is likely, however, that at £36 this book will be for libraries only. It is also somewhat debatable whether an authoritative volume like this should be produced in two languages, two-thirds of the book being in German and one-third in English. If the book were all in English its appeal would almost certainly be greater.

Congenital Deformities of the Testis and Epididymis. By C. GORDON SCORER, M.A., M.D., F.R.C.S., F.R.C.S. (Edin.), and GRAHAM H. FARRINGTON, M.Ch., F.R.C.S. 9½ × 5½ in. Pp. 203 + ix. Illustrated. 1971. London: The Butterworth Group. £4·20.

THIS book would have been enjoyed by John Hunter. Undescended testis affects about seven out of every thousand males born alive in this country, or about five thousand new babies every year, but its diagnosis and treatment are still uncertain and clouded with doubts about the time when operative treatment should be undertaken and what should be done. For every boy with a really undescended testis who is referred to a surgeon eight or nine boys with retractile testes are also referred by general practitioners and school medical officers who have examined their patients with cold hands or in a chilly room. There is not much doubt that the very good results of surgical treatment which have sometimes been claimed in the past depended very largely on the inclusion in the series of a very large proportion of boys with retractile rather than undescended testes.

This is an excellent book which gives a clear account of the whole subject of congenital abnormalities of the testes. It is well illustrated with good, simple diagrams and photomicrographs. There is a proper emphasis on early operative treatment to allow of what normal development may be possible after placing the testis in the scrotum. There is a reasonable discussion of the risks of malignant change in the undescended testis and of the results of treatment and the chances of fertility. This book should be read by all surgeons who have to deal with undescended testes and by all paediatricians who will find much to stimulate thought about this very difficult surgical and social problem as well as the means to modify some of the extravagant and erroneous opinions which are still too widely accepted about the results and value of even modern methods of treatment of the undescended testis.

Schweitzer. A Biography. By GEORGE MARSHALL and DAVID POLING. 9 × 6 in. Pp. 342 + xviii. Illustrated. 1971. London: Geoffrey Bles. £3·50.

THIS is by far the best book that has so far been published about that controversial figure, Albert Schweitzer. The authors of this book have carried out their task in an excellent fashion and have written a true biography of a great man. The photographs in this book are excellent and the reader is given a very good idea of the mentality and characteristics of Schweitzer.

The footnotes and chapter references are very helpful, as is the chronological biography at the end of the book.

It is given to few men to study theology, philosophy, music, and medicine and to become an expert in all. In this book we get an image of the real man, namely a respected philosopher, a renowned Biblical scholar, and a liberal rebel in a conservative European Protestant church. He was an accomplished organist and interpreter of Bach, a crusader for world peace, and a winner of the Nobel Peace Prize in November, 1953. He made his philosophy of 'reverence for life' an ethic for the world. His hospital in Lambaréné, which is still in operation, is a model of what the European might have given to the African native throughout colonial history.

Schweitzer was a prolific writer, not only on medical and social subjects, but also on musical ones.

This biography, which is praised by his only daughter, Rhena, is a wonderful book of memories of a really great man.

Physiology of the Eye. Third edition. By HUGH DAVSON, D.S.C. (Lond.), London. 9 × 6 in. Pp. 643 + vii. Illustrated. 1972. Edinburgh: Churchill Livingstone. £6.

WE welcome the new third edition of this important work because it is an excellent exposition of ophthalmic physiology in one volume.

All branches of surgery today demand a very thorough knowledge of physiology, and in ophthalmology this is even more important.

This book, which is well illustrated, is divided into five sections: the vegetative physiology and biochemistry of the eye, the mechanism of vision, the muscular mechanisms, visual perception, and visual optics.

The problem of intra-ocular pressure is discussed in detail. Visual acuity and colour vision are explained in a very practical way.

Many of the illustrations in this book are original. They are also very striking and do help to explain the written word. There are some 80 new illustrations in this edition.

This book should prove invaluable to physiologists and ophthalmologists and also for students taking the B.Sc. in physiology.

Shands' Handbook of Orthopaedic Surgery. Eighth edition. Edited by R. BEVERLY RANCY, sen., M.D., North Carolina, and H. ROBERT BRASHEAR, jun., M.D., North Carolina. 9½ × 6½ in. Pp. 543 + xiv. Illustrated. 1971. London: Henry Kimpton. £7.

THIS is the eighth edition of *Shands' Handbook of Orthopaedic Surgery* and Dr. A. R. Shands, jun., has now joined the editorial board. A book that has held its own for 35 years with eight editions over this period must be good. In the sixteen chapters which comprise this volume every facet of orthopaedic surgery is considered.

The volume is written in clear, decisive prose and the illustrations have been well chosen and are well produced.

The chapters on bone tumours and amputations are outstanding.

This new eighth edition will prove even more popular with students and practitioners than earlier ones.

The Lacrimal System. Edited by EVERETT R. VEIRS, M.D., Texas. 9½ × 6½ in. Illustrated. 1971. London: Henry Kimpton. £10·10.

THE various articles in this volume were presented at a symposium held in Mexico City in March, 1970. Every aspect of the lacrimal system has been well covered.

The book is divided into six parts. Part 1 deals with the congenital anomalies of the lacrimal system, such as absence of the gland, absence of tear secretion, and aberrant gland tissue. Part 2 is concerned with disorders of the lacrimal gland including tumour formation.

In part 3 disorders of the lacrimal canaliculi come under review. The use of silicone lacrimal tubes is advocated in some cases of injury.

Part 4 deals with disorders of the lacrimal sac, part 5 is concerned with external dacryocystorhinostomy, and part 6 is a summary of the various papers.

Mr. A. Werb, a surgeon at the Corneo-plastic Unit, Queen Victorial Hospital, East Grinstead, Sussex, contributes a very practical article on the surgical technique of dacrocystorhinostomy, and illustrates his article with some excellent pictures.

It is only by reading such a book as this that one realizes how many surgical conditions may affect the lacrimal apparatus.

This book should be in every medical library as an important book of reference.

Current Concepts of the Histology of Oral Mucosa. Edited by C. A. SQUIER, The London Hospital Medical College, and JULIA MEYER, Chicago. 10 × 7 in. Pp. 305 + xvi. Illustrated. 1971. Springfield, Ill.: Charles C. Thomas. $18.75.

THIS book contains the proceedings of a symposium held at the University of Illinois College of Dentistry in June, 1970. It is an important book because it represents the first comprehensive account of the histology of the mucous membrane of the mouth.

The numerous illustrations are excellent and are quite a feature of the book. They include some good electron micrographs.

The book should prove an excellent reference volume to dental students and pathologists. It should also interest all research workers in oral histology and dermatologists who may be interested in this special field.

Although, as one would expect, the majority of the contributors come from America there are some from Canada, England, and Scotland.

This is a useful reference volume on an important subject.

Notes on Dental Materials. By E. C. COMBE, M.Sc., Ph.D., A.R.I.C., Illinois. 9 × 5¼ in. Pp. 265 + xi. Illustrated. 1972. Edinburgh: Churchill Livingstone. £2·90.

THIS book is a *must* for all dental students, for it is the only book which gives a synopsis of the subject of dental materials. No student today can carry all these facts and figures in his head and this small book will be a valuable reference book. The book is small enough to go into the pocket and, what is more, the price is very reasonable.

The book is divided into two sections: dental materials science and applied dental materials. The whole field is covered in a very comprehensive way.

Newer dental materials are also discussed, including polycarboxylate cements, composites, spherical amalgam alloys, polyester impression materials, and epimines.

At the end of the book there are a dozen blank pages for notes—an excellent idea, for the student can make notes of the ever-appealing new materials used in dentistry.

Fundamental Skills in Surgery. Second edition. By THOMAS F. NEALON, jun., M.D., New York. 9¾ × 6½ in. Illustrated. 1971. London: W. B. Saunders Co. Ltd. £5.

THE second edition of this book for students and hospital residents has been carefully revised, and it will continue to take its place as one of the really useful books for students. The illustrations which are mostly line drawings are quite a feature of the book.

Die Fettembolie. By Dr. GYORGY SZABO, D.S.M., Budapest. 9¼ × 6½ in. Pp. 284. Illustrated. 1971. Budapest: Akadémiai Kiadó. £4·20.

THE problems of fat embolism are discussed in this book. Having studied many publications from all over the world the Hungarian author of this book, which is edited in German, gives the results of his own investigations in which he and his colleagues checked the tests made by others or invented original tests.

Some facts seem to be proved according to this book; for instance, the fat of fat emboli in the lungs originates from the bone-marrow, which seems logical as the majority of the cases occur after bone fractures.

Transport of the fat is by the venous pathways and the circulating fat obstructs the lung capillaries, but breakdown of the fatty acids may cause toxic damage to the capillary walls.

Having passed the barrier of the lung capillaries the fat enters the main circulation, often resulting in fat embolism of the brain and the kidneys.

The obstruction of the lungs may cause dilatation of the right heart, while arterial hypoxaemia is the most dangerous consequence.

Diagnosis of fat embolism must be made in the first place by clinical observation; dyspnoea, rising body temperature a few hours or days after serious fractures, unrest, impaired consciousness, some neurological symptoms, and petechiae of the skin should arouse suspicion of the presence of fat embolism.

The radiographic picture of the lungs is rather typical (snow-storm), and arterial hypoxaemia is one of the most important laboratory findings.

Attempts at systemic treatment, which means elimination of the fatty substances from the circulation, did not meet with convincing results; the hopeful publications about therapy with decholin, heparin, and humalbin that should combine and neutralize the fatty acids did not convince the author, although the author still uses humalbin.

Symptomatic treatment may be life-saving; treatment of shock helps the patient to survive the effects of fat embolism; oxygen therapy certainly is indispensable and probably the most important measure. The author does not mention the use of protease inhibitors, such as trasylol which is employed by some German authors.

The final chapter mentions the juridical implications; the problems for the pathologist are the conclusion of death by violence after having noticed a fat embolus and the question whether the fat embolism was the main cause of death.

An excellent book that should be studied with great interest.

Ileostomy Care. By MARSHALL SPARBERG, M.D., Chicago. 9 × 6 in. Pp. 161 + xi. Illustrated. 1971. Springfield, Illinois: Charles C. Thomas. $9.75.

THIS is a useful little book, for it gives a detailed account of the after-treatment of an ileostomy. It is a very practical account and the illustrations depicting the changing of the various ileostomy appliances and dressings are excellent.

The book is divided into three sections. Section 1 deals with the immediate preoperative and postoperative care, the construction of the ileostomy, and the application of the appliance. Section 2 is devoted to ileostomy complications, while Section 3 contains some useful appendixes, including a glossary of ileostomy terms.

Surgery and the Allergic Patient. Edited by CLAUDE A. FRAZIER, M.D., Ashville, North Carolina. 9¾ × 6½ in. Pp. 191 + xviii. Illustrated. 1971. Springfield, Illinois: Charles C. Thomas. $12.50.

THIS book has been written by a group of well-known American medical specialists and edited by a distinguished allergist. Every facet of this curious condition has been discussed in detail, and preoperative care in an allergic patient is set out in full.

With the extensive use of penicillin all over the world the number of penicillin-sensitive patients has increased enormously. This is particularly stressed in this book.

It often happens that a known allergy of a patient, such as asthma or urticaria, may occur before an operation.

In this book there is a very thorough coverage of the management of anaphylaxis; a special kit has been designed for immediate treatment of this condition.

This book will appeal to all surgeons and physicians who have to deal with allergic patients.

BOOK NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.]

The Importance of Cineangiography in the Hemodynamic Study of Aortic Valvular Disease. By HAROLD EIE. 8¾ × 6 in. Pp. 97, with 28 illustrations. 1970. Oslo: Universitetsforlaget. N.Kr. 75.

Aide-Mémoire de Détermination Bactérienne. By R. G. CAPET, Montreal. 9¾ × 7 in. Pp. 135. 1970. Paris: Vigot Frères.

Scaphoide Genou—Jambe Spastique. By R. JUDET, Paris. 9½ × 6½ in. Pp. 188. Illustrated. 1971. Paris: Masson et Cie Editeurs. 74F.

The Metabolic Basis of Surgical Care. By WILLIAM F. WALKER, Ch.M., F.R.C.S. (Edin.), F.R.C.S. (Eng.), Dundee, and IVAN D. A. JOHNSTON, M.Ch., F.R.C.S. (Eng.), Newcastle upon Tyne. 8½ × 5½ in. Pp. 251 + x. Illustrated. 1971. London: William Heinemann Medical Books Ltd. £3.

Orthopaedics in Infancy and Childhood. By G. C. LLOYD ROBERTS, M.Chir. (Cantab.), F.R.C.S., London. 8¾ × 5½ in. Pp. 337 + x. Illustrated. 1971. London: The Butterworth Group. £6·75.

Proceedings of the Symposium on Epidural Analgesia in Obstetrics. Edited by ANDREW DOUGHTY, M.B., B.S., F.F.A. R.C.S., Kingston-upon-Thames. 8¾ × 5½ in. Pp. 119. Illustrated. 1972. London: H. K. Lewis. £1·50.

Surface and Radiological Anatomy. By W. J. HAMILTON, M.D., D.S.C., F.R.C.S., F.R.C.O.G., F.R.S.E., London, G. SIMON, M.D., F.R.C.P., D.M.R.E. (Cantab.), F.F.R., London, and S. G. IAN HAMILTON, M.A., M.Chir. (Cantab.), F.R.C.S. Pp. 397 + x. 1971. Cambridge: W. Heffer and Sons Ltd. £6.

Die Inaktivitäts-Osteoporose. By J. MACH, Rostock. 8½ × 5¾ in. Pp. 207. Illustrated. 1971. Berlin: Verlag Volk und Gesundheit. 44.80 M.

Dextran: Current Concepts of Basic Actions and Clinical Applications. Compiled and edited by JOHN R. DERRICK, M.D., Texas, and M. MASON GUEST, Ph.D., Texas. 9 × 6 in. Pp. 222 + xiv. Illustrated. 1971. Springfield, Illinois: Charles C. Thomas. $14.75.

Urologische Operationslehre. Vol. 8. By G. W. MÜLLER, Magdeburg, W. WELRHEIM, Magdeburg, and G. W. HEISE, Magdeburg. 10½ × 7¼ in. Pp. 172. Illustrated. 1971. Leipzig: Georg Thieme. 53 M.

Cancer do Pulmão. By JESSE P. TEISCEIRA, Rio de Janeiro. 8½ × 6 in. Pp. 197 + xiv. Illustrated. 1971. Rio de Janeiro: Editora Guanabara Koogan S.A. No price given.

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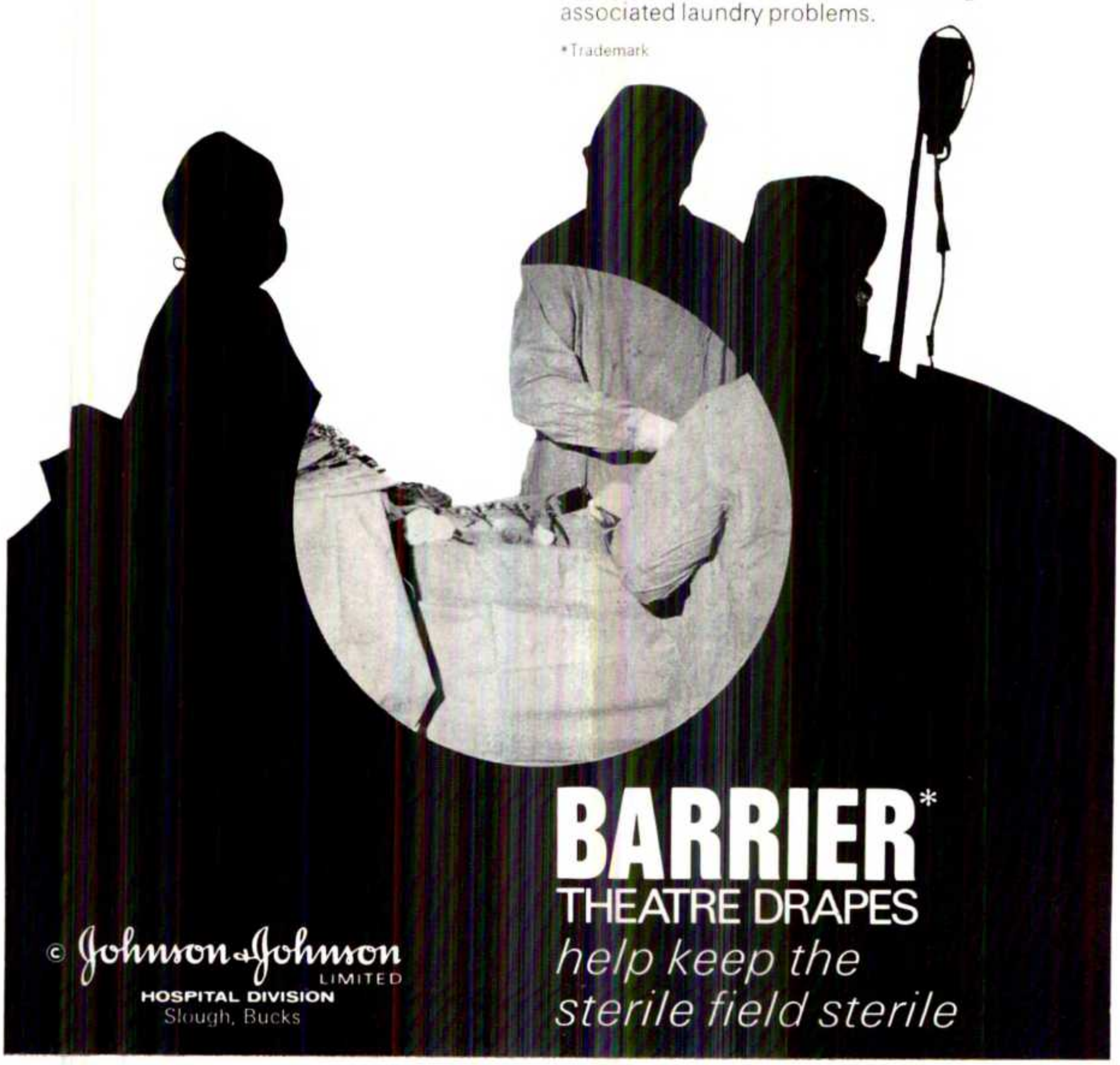

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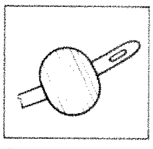

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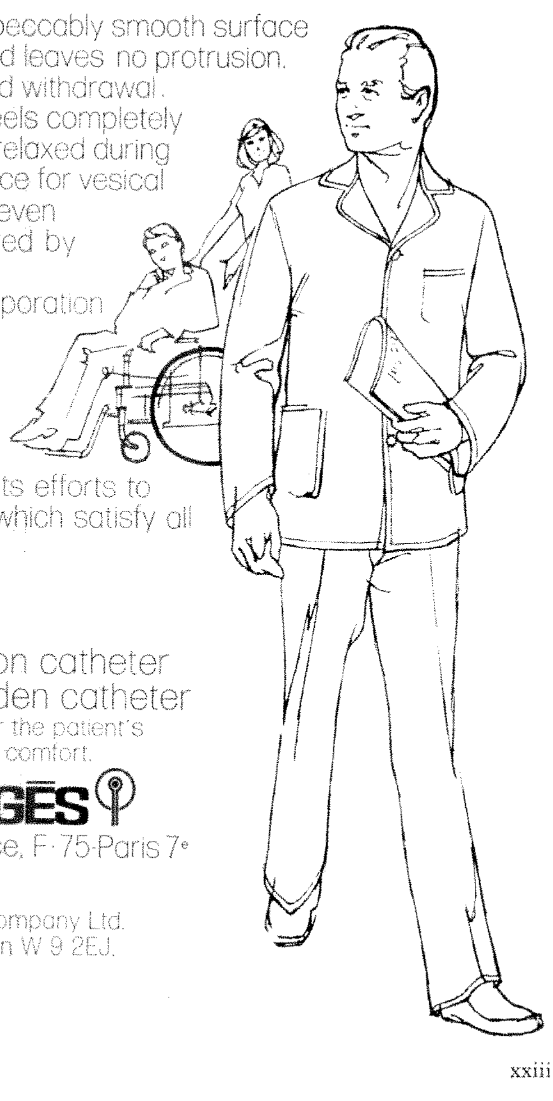

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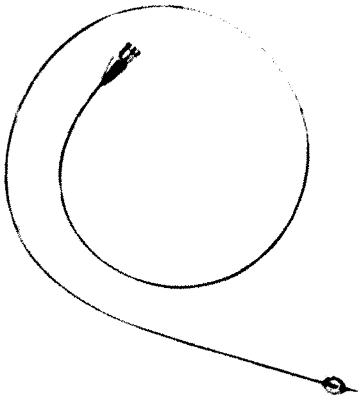

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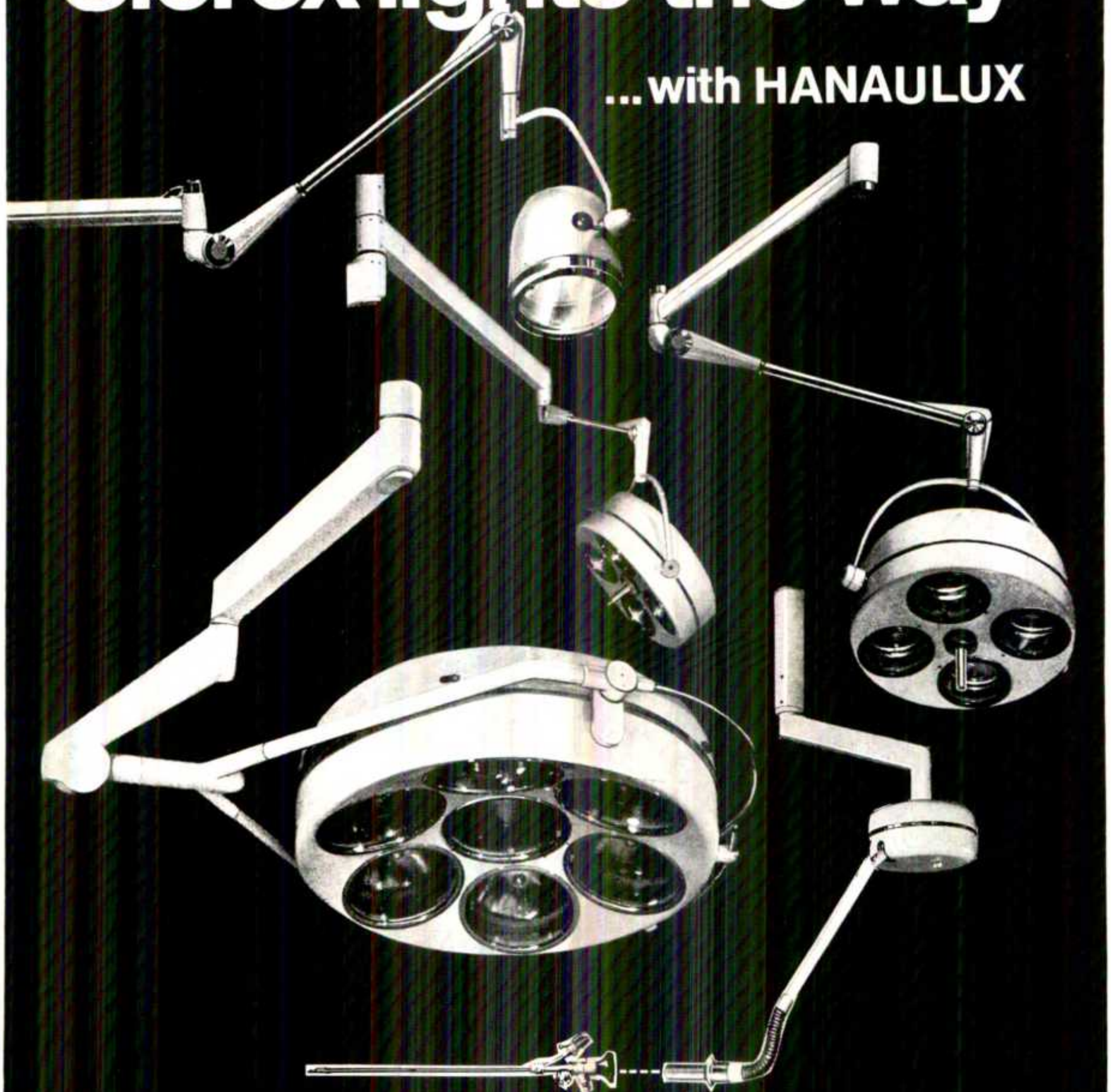

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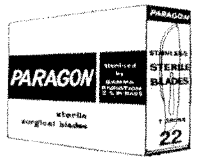

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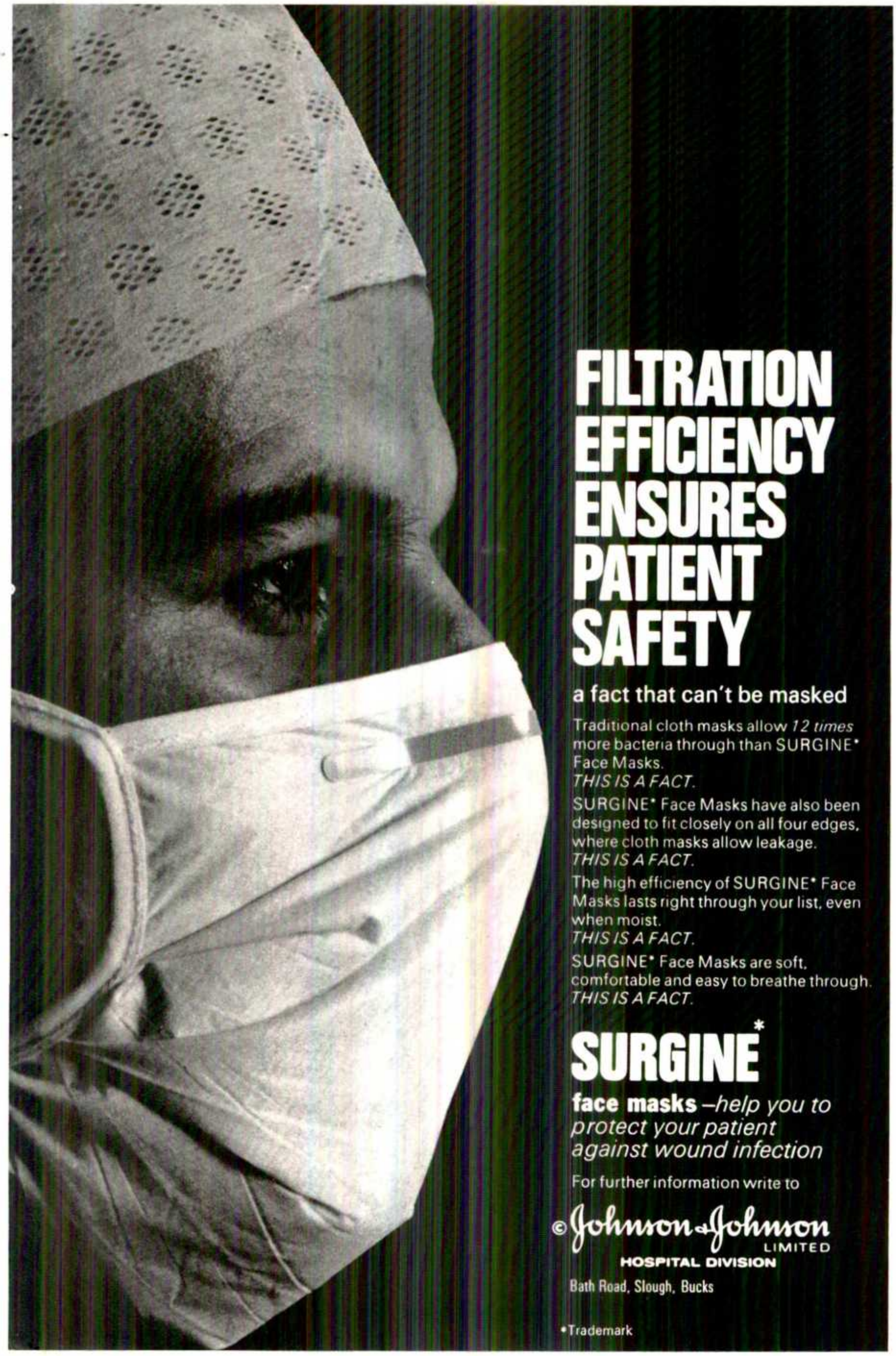

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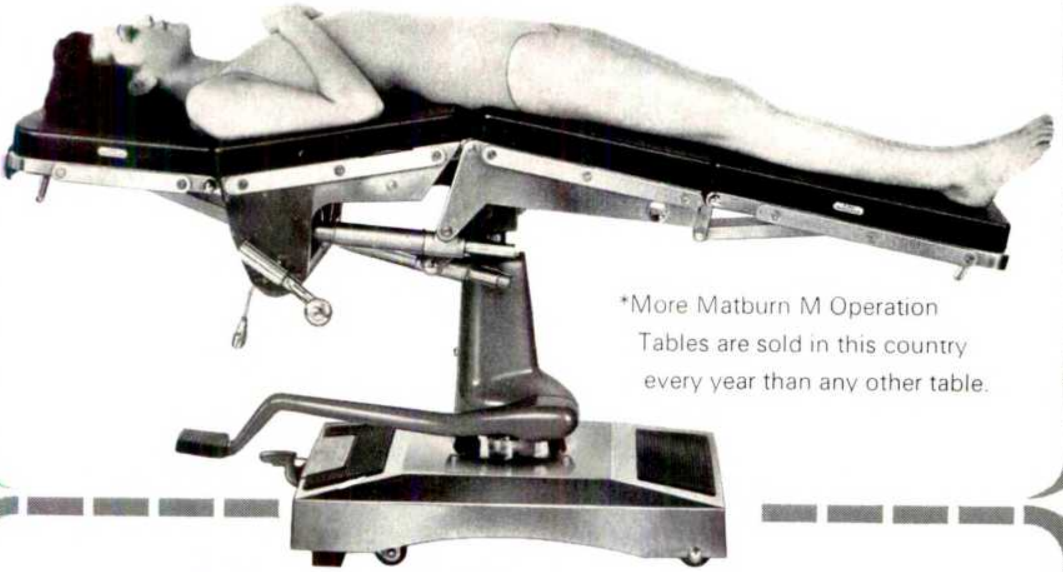

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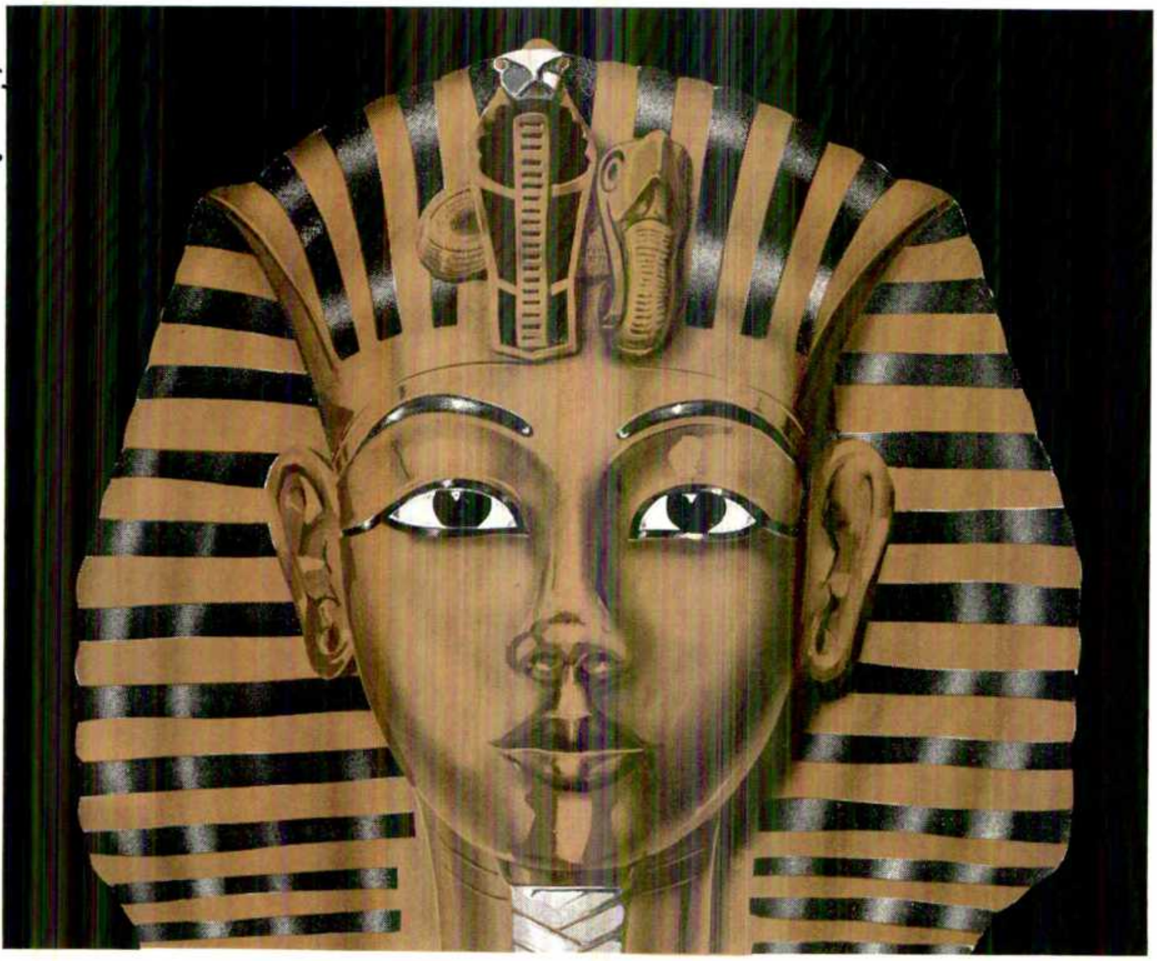

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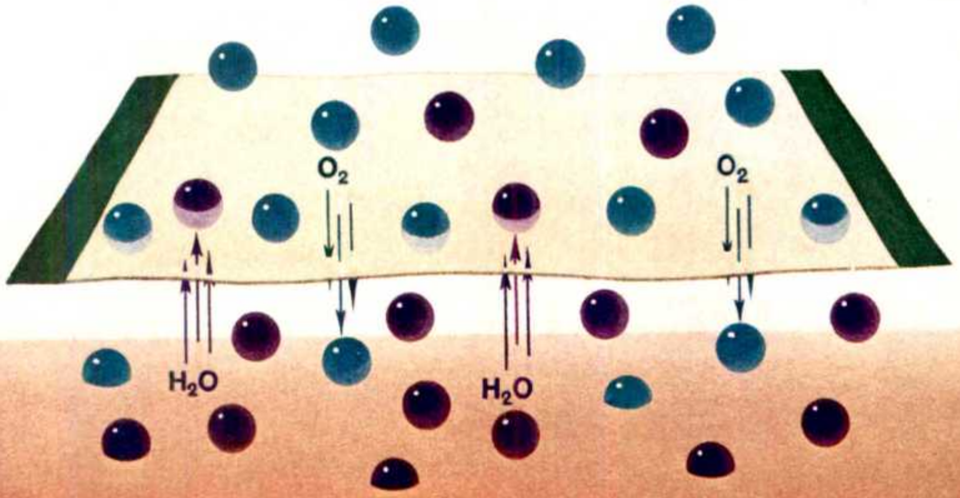

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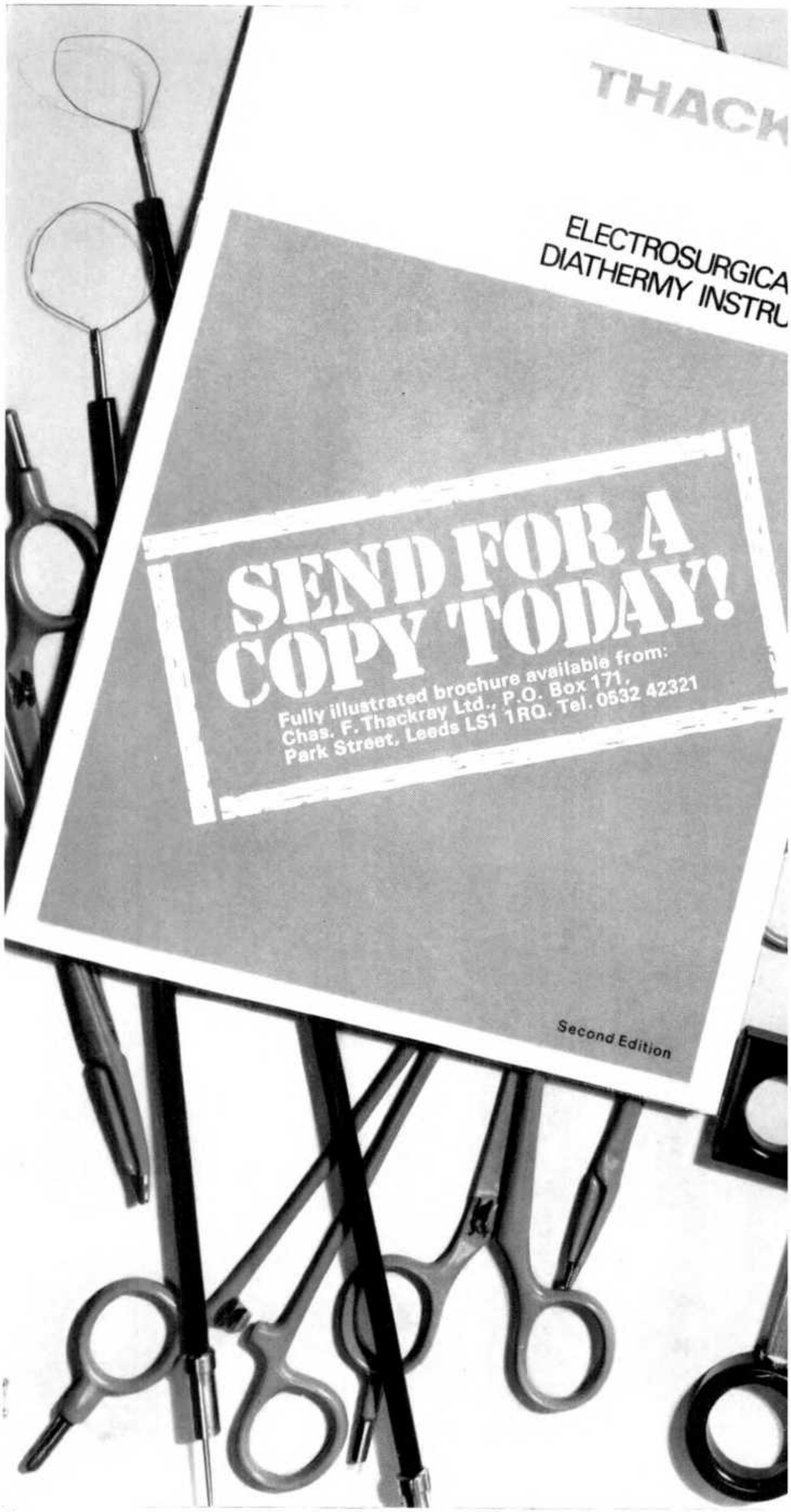

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CONTENTS

PAGE

ORIGINAL PAPERS

FRACTURES OF THE FLOOR OF THE ANTERIOR CRANIAL FOSSA - - *Antony Jefferson and Gerald Reilly* 585

VESICO-INTESTINAL FISTULAE - - - - - - - *Norman Slade and Christopher Gaches* 593

ABDOMINAL TUBERCULOSIS - - - - - - - - *A. Gunn and N. C. Keddie* 597

ACID-FUNDIC SELECTIVE VAGOTOMY OF THE STOMACH WITHOUT DRAINAGE IN THE TREATMENT OF DUODENAL ULCER: TECHNIQUE AND RESULTS - - *Luigi Imperati, Costanzo Natale, and Francesco Marinaccio* 602

A RANDOMIZED PROSPECTIVE TRIAL COMPARING THREE ESTABLISHED METHODS OF GASTRIC DECOMPRESSION AFTER VAGOTOMY - - - - *D. F. Miller, J. R. Mason, J. McArthur, and I. Gordon* 605

INFLAMMATORY ANEURYSMS OF THE ABDOMINAL AORTA *D. I. Walker, K. Bloor, G. Williams, and I. Gillie* 609

FEMORAL ANEURYSMS - - - - - - - - *D. G. Hardy and D. G. A. Eadie* 614

THE HISTOPATHOLOGY OF SMALL VESSELS FOLLOWING MICROVASCULAR REPAIR *Thelma J. Baxter, B. McC. O'Brien, P. N. Henderson, and R. C. Bennett* 617

THE INCIDENCE OF RIGHT INGUINAL HERNIA FOLLOWING APPENDICECTOMY *Peter Leech, Gordon Waddell, and Robert G. Main* 623

VENTILATION IN AN ARTIFICIALLY PRODUCED GAS CAVITY UNDER BASAL CONDITIONS - *Lade Wosornu* 624

POST-ANGIOGRAPHIC VERTEBRAL ARTERIOVENOUS FISTULAE *Vira Sangruchi, Edward Hitchcock, and A. A. Donaldson* 627

POSTOPERATIVE CHANGES IN BLOOD VISCOSITY AND THE INFLUENCE OF HAEMATOCRIT AND PLASMA-FIBRINOGEN *J. V. Harvey Kemble and J. A. Hickman* 629

MALIGNANT MELANOMATA: AN AID TO PREOPERATIVE DIAGNOSIS - - - *Rona M. Mackie* 632

HAEMANGIOMATA OF SKELETAL MUSCLE - - - - - - - *I. L. C. Fergusson* 634

NASOGASTRIC TUBE MANAGEMENT - - - - - - - - *Laurence Tinckler* 637

TREATMENT OF PERITONITIS WITH PER- AND POSTOPERATIVE IRRIGATION OF THE PERITONEAL CAVITY WITH NOXYTHIOLIN SOLUTION - - - - - - - - - *R. G. Pickard* 642

SPONTANEOUS RUPTURE OF THE OESOPHAGUS *M. R. B. Keighley, R. W. Girdwood, M. I. Ionescu, and G. H. Wooler* 649

SHORT NOTES OF RARE OR OBSCURE CASES

A CASE OF PRIMARY LIVER TUMOUR ASSOCIATED WITH PORPHYRIA - - - *R. T. Waddington* 653

PEDUNCULATED TERATOMA OF RECTUM INFESTED WITH BILHARZIASIS - - - - *Y. El-Katib* 655

JOINT RUPTURE IN REITER'S DISEASE - - - - - *Richard W. Garner and Alastair G. Mowat* 657

CENTRAL RUPTURE OF THE LIVER WITH MASSIVE LIVER-CELL NECROSIS - *S. R. Soni and V. Persaud* 660

MALAKOPLAKIA OF THE COLON - - - - - *W. Birkenstock and J. H. Louw* 662

REVIEWS AND NOTICES OF BOOKS

The Detective-Physician: The Life and Work of Sir William Willcox, K.C.I.E., C.B., C.M.G., M.D., F.R.C.P.—*Phillip H. A. Willcox.* Blood Volume and Extracellular Fluid Volume—*Solomon N. Albert.* Regionale Anästhesie mit dem Langzeitanästhetikum Bupivacain—*Hans Nolte and Justus Meyer.* Head Injuries: Proceedings of an International Symposium held in Edinburgh and Madrid 2nd to 10th April, 1970. Recent Advances in Cancer and Radiotherapeutics—ed. *Keith E. Halnan.* Diagnostische und therapeutische Fortschritte in der Krebschirurgie—*F. Linder, G. Ott, and H. Rudolph.* Surgery of Rheumatoid Arthritis—ed. *Richard L. Cruess and Nelson S. Mitchell.* Manual of Preoperative and Postoperative Care—ed. *John M. Kinney, Richard H. Egdahl, and George D. Zuidema.* Contemporary Burn Management—ed. *Hiram C. Polk and H. Harlan Stone.* Chest Injuries—*Roshan Lall Gupta.* Stapedectomy—*Harold F. Schuknecht.* Septic Shock in Man—ed. *S. G. Hersky, Louis R. M. Del Guercio, and Rita McConn.* The Thyroid: A Fundamental and Clinical Text—ed. *Sidney C. Werner and Sidney H. Ingbar.* A Practice of Anaesthesia—ed. *W. D. Wylie and H. C. Churchill-Davidson.* Chirurgische Differential-Diagnostik—ed. *Karl Vosschulte and Ludwig Zukschwerdt.* The Anatomical Basis of Medical Practice—*R. Frederick Becker, James W. Wilson, and John A. Gehweiler.* Anatomy, Regional and Applied—*R. J. Last.* Praxis der Schockbehandlung—ed. *Theodor Ott Lindenschmidt, Erich Rugheimer, and Hans Willenegger.* An Atlas of Diseases of the Eye—*E. S. Perkins and Peter Hansell.* Surgical Departments in Hospitals. The Surgeon's View—ed. *D. M. Douglas.* Symposium on the Hand, Vol. 3—ed. *Lester M. Cramer and Robert A. Chase.* 665

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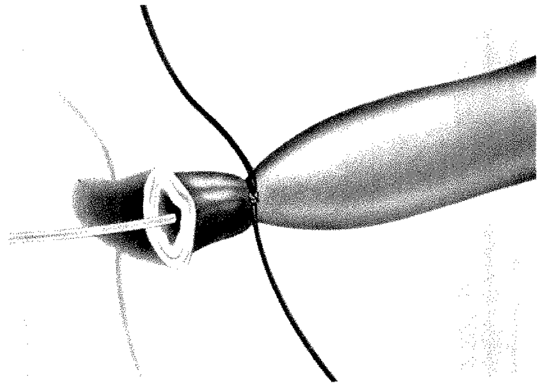

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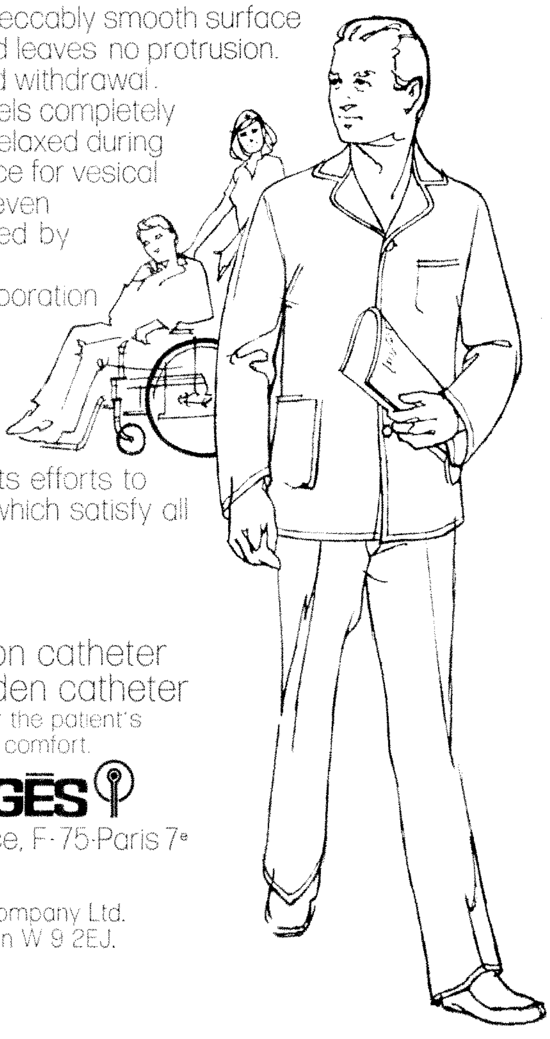

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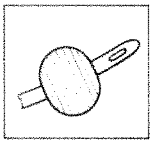

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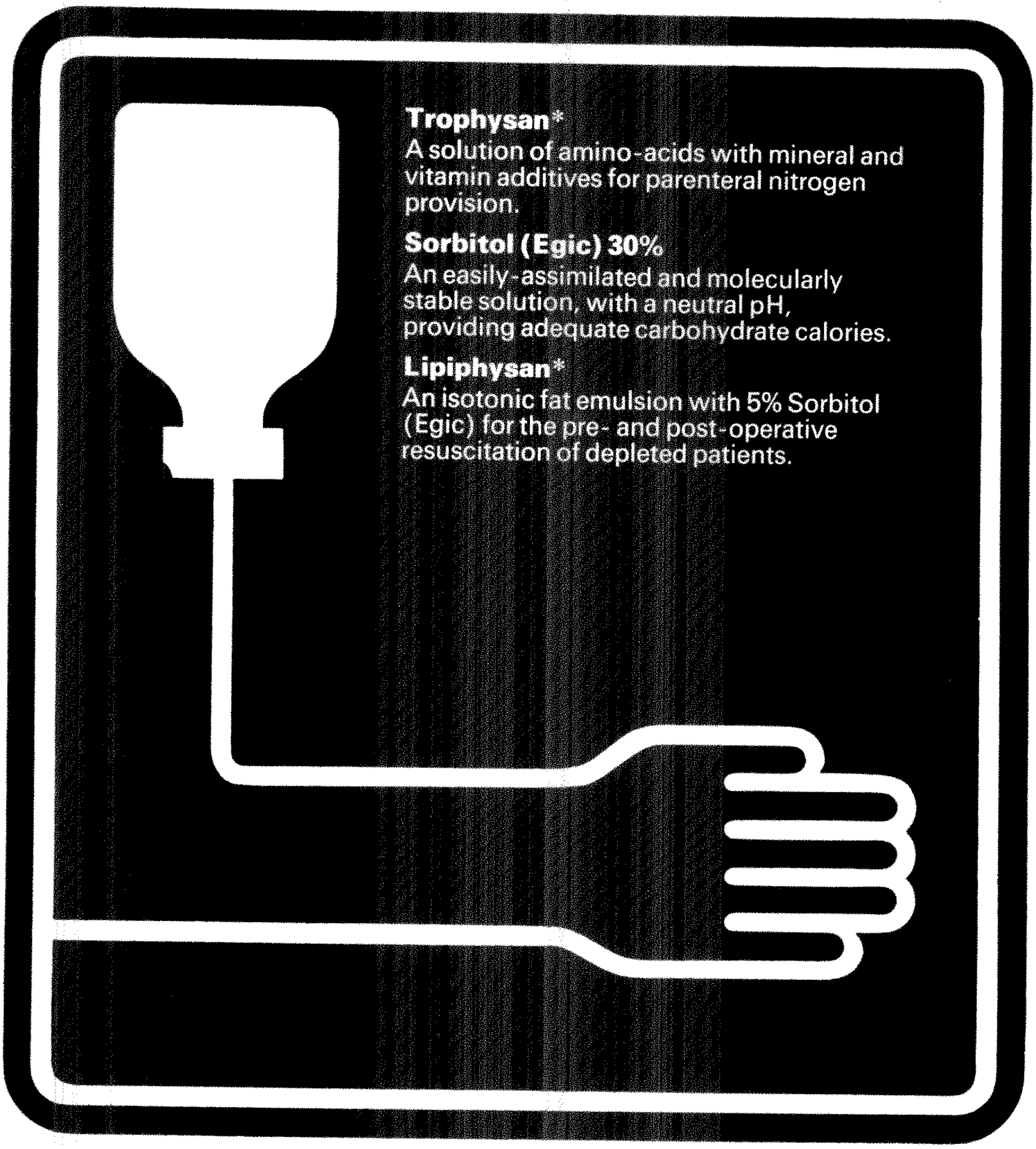

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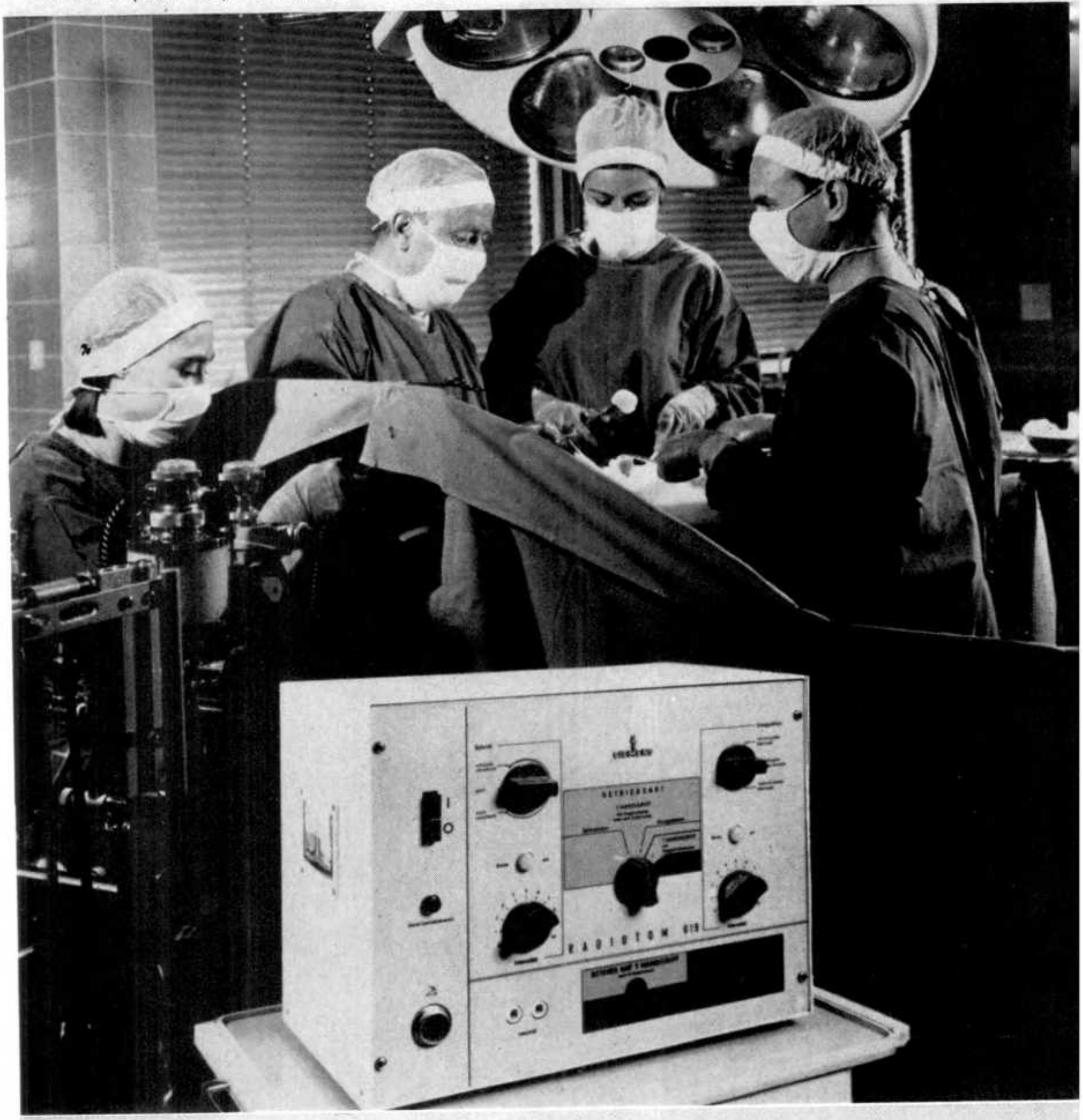

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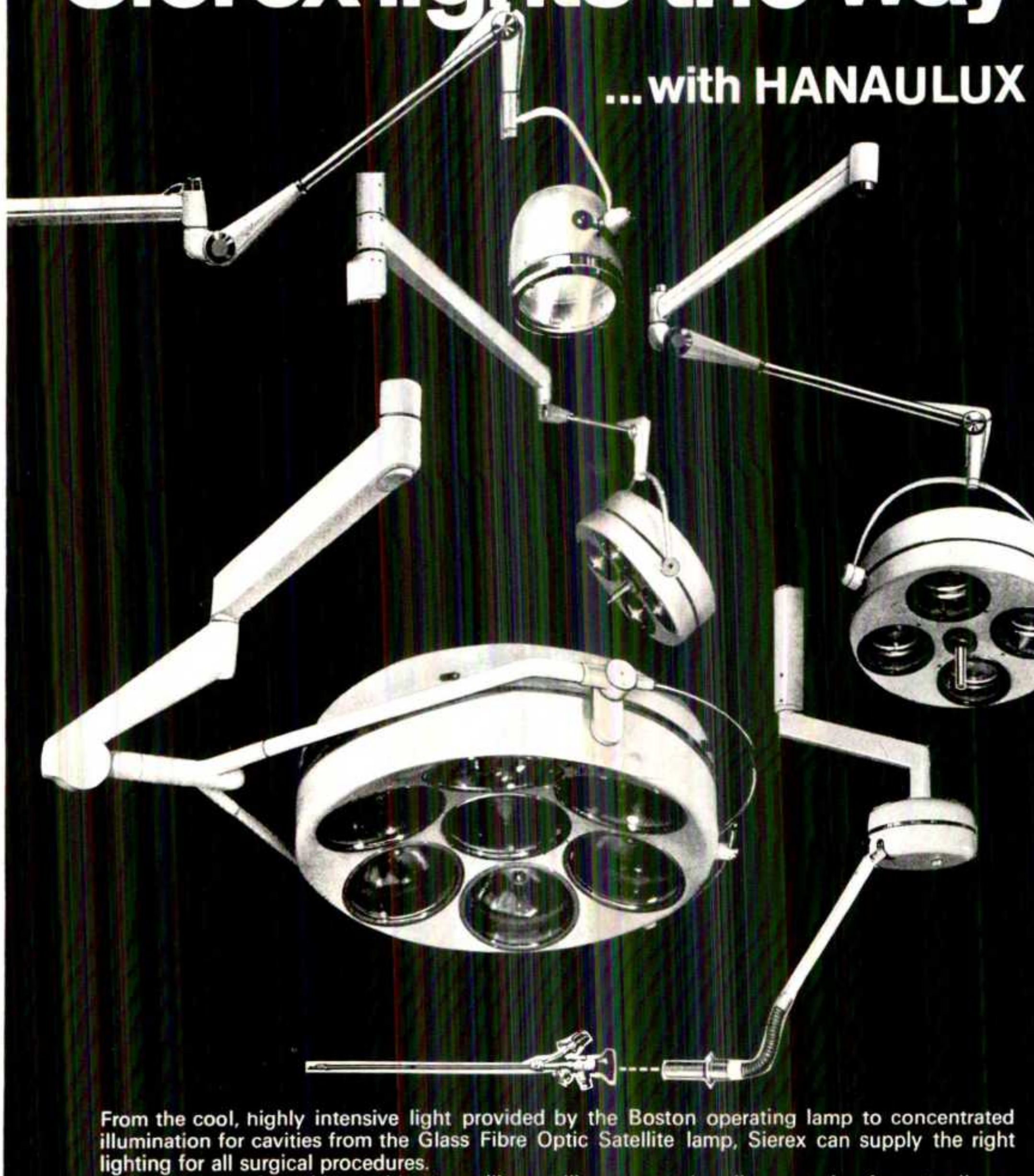

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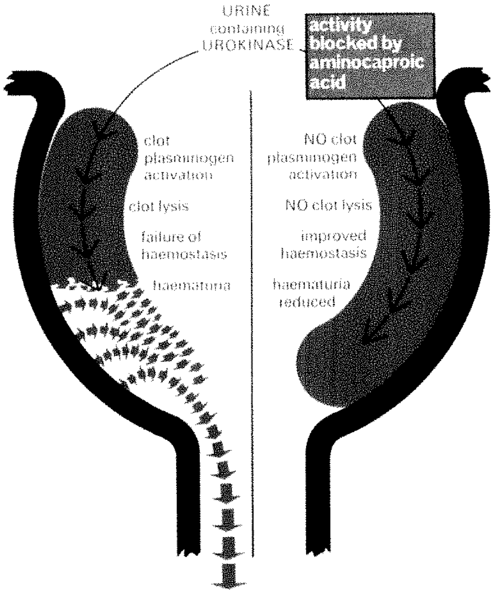

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BRITISH JOURNAL OF SURGERY

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ORIGINAL PAPERS

FRACTURES OF THE FLOOR OF THE ANTERIOR CRANIAL FOSSA

THE SELECTION OF PATIENTS FOR DURAL REPAIR

By ANTONY JEFFERSON and GERALD REILLY

DEPARTMENT OF NEUROLOGICAL SURGERY, THE ROYAL INFIRMARY, SHEFFIELD

SUMMARY

1. A series of 87 patients operated on because of subfrontal fractures is reported. In 73 of these a fistulous lesion (connecting the brain with the nose or the accessory air sinuses) was displayed and was repaired. Almost always a bifrontal exploration has been made, because the lesions were bifrontal in 43 per cent of cases. The mean follow-up period was 4 years; to date no instances of postoperative meningitis or rhinorrhoea have occurred.

2. Our experience suggests that cerebrospinal rhinorrhoea accompanying fractures of the facial bones (without fractures of the skull vault) can safely be treated conservatively.

3. Damaged brain adheres to the lips of the torn dura and *permanently* prevents natural healing, thereby creating a continuing threat to life. Consequently it is recommended that all frontal fractures lying below the hairline and all comminuted anterior temporal fractures should be referred for expert neurosurgical/neuroradiological assessment. This is because 42 per cent of the patients requiring operative repair were selected after tomographic studies of the anterior fossa; they had not presented with the classic criteria of cerebrospinal rhinorrhoea, intracranial air, or meningitis.

FRACTURES of the floor of the anterior cranial fossa which allow the intracranial contents to communicate with the nasal cavity or with the accessory air sinuses are widely recognized to be potentially dangerous. This fact is known to every general surgeon, who will most probably expect a history of meningitis, cerebrospinal rhinorrhoea, or air within the skull to substantiate the diagnosis.

In an earlier communication (Jefferson and Lewtas, 1963) an instance was cited of an 18-year-old male who died of his first attack of pneumococcal meningitis without any preceding cerebrospinal rhinorrhoea. It was this event which first focused our attention on the potential dangers of these lesions. The intervening years have been marked by no exactly similar instances, although we have seen cases from time to time which prove that pneumococcal meningitis (even when promptly treated) can still prove fatal. This subsequent period has also allowed us to accumulate more data and to crystallize our ideas. To our certain knowledge dangerous fractures exist in the absence of cerebrospinal rhinorrhoea, intracranial air, or meningitis. We believe that it is possible to identify the majority of these lesions before serious complications develop. It is our purpose in this contribution to define how this may be done, for the need to detect and to repair the fistulous fracture remains as urgent as ever.

Table I.—AGE AND SEX OF THE PATIENTS IN THE PRESENT SERIES

Age-group (years)	*Male*	*Female*
0–10	2	1
11–20	18	4
21–30	16	2
31–40	21	
41–50	12	
51–60	8	
61–70	3	
Total	80	7

Table II.—REASONS FOR OPERATION IN THE PRESENT SERIES

Reason for Operation	*No. of Patients*
Radiographic	35
Initial trauma (e.g., compound fracture)	13
Meningitis	11
Watery nasal discharge	19
Intracranial air	7
Exploration to confirm anticipated intact dura	2
Total	87

CASE MATERIAL

The cases considered here are an unselected series of 87 patients operated upon in the Department of Neurological Surgery, the Royal Infirmary, Sheffield, under the care of one of us (A. J.) over a 15-year period. The distribution according to age and sex is shown in *Table I*, and the reasons for operation are listed in *Table II*.

All except 8 patients underwent exploration using a bifrontal osteoplastic bone-flap (brief details of the operation are included below). The balance of the operated patients had a unilateral bone-flap or a frontal trephine. (Exploration through a frontal trephine was used in 2 of the earliest cases as a means of confirming that *no* potentially dangerous lesion was present.)

A further 32 patients were considered as possible candidates for surgical repair but were rejected after appropriate study.

It should be noted that 30 per cent of the patients needing repair were referred without the possibility that a fistulous fracture might exist having been suspected.

OPERATIVE TECHNIQUE

Because a bifrontal exploration has been proved to be necessary in 43 per cent of the patients who required a dural repair, and because we have found no absolute method of identifying preoperatively those lesions which are bilateral, we recommend that a bifrontal exploration should be used routinely.

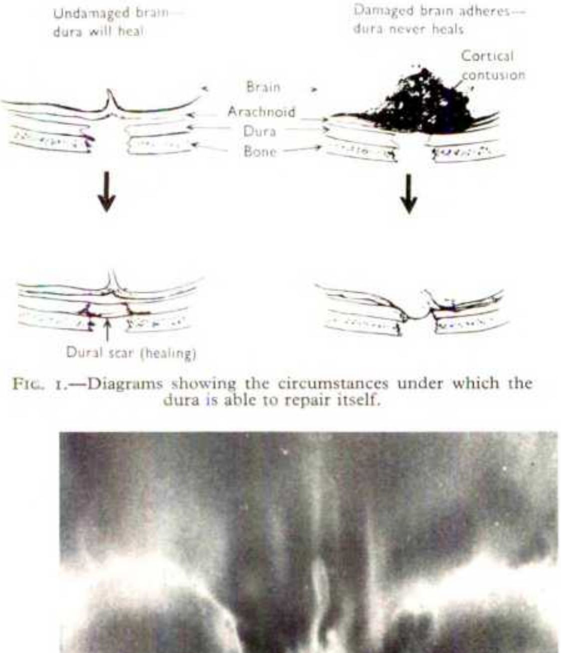

FIG. 1.—Diagrams showing the circumstances under which the dura is able to repair itself.

A coronal skin incision is made and a six-point bone-flap outlined. It is important to place the central bur holes exactly in the midline. While the bone-flap is being elevated the dura must be stripped carefully from the inside of the skull. In contrast to the views of some neurosurgeons, we have ample proof that the resultant exposure of the sagittal sinus creates no special hazards.

The dura is opened bilaterally and both subfrontal regions are thoroughly inspected from within the dura. All adhesions between pia-arachnoid and dura are systematically divided using sharp dissection. Extensive probing of the dural defects can only serve to increase them and consequently we do not recommend it. A dural graft is necessary whenever a fracture (usually a comminuted fracture) is located lying within an area of defective dura and overlying either an accessory air sinus or the roof of the nose. The injured area on the cortex is covered with gelatin foam and a tissue graft is placed on the floor of the

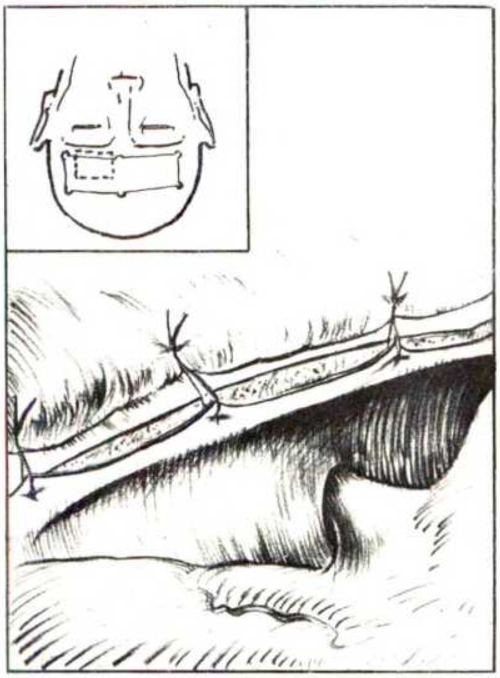

FIG. 2.—Left subfrontal region approached intradurally. The left frontal pole is held retracted. A funnel of brain is herniated into the dural defect; sharp dissection will be necessary to free this.

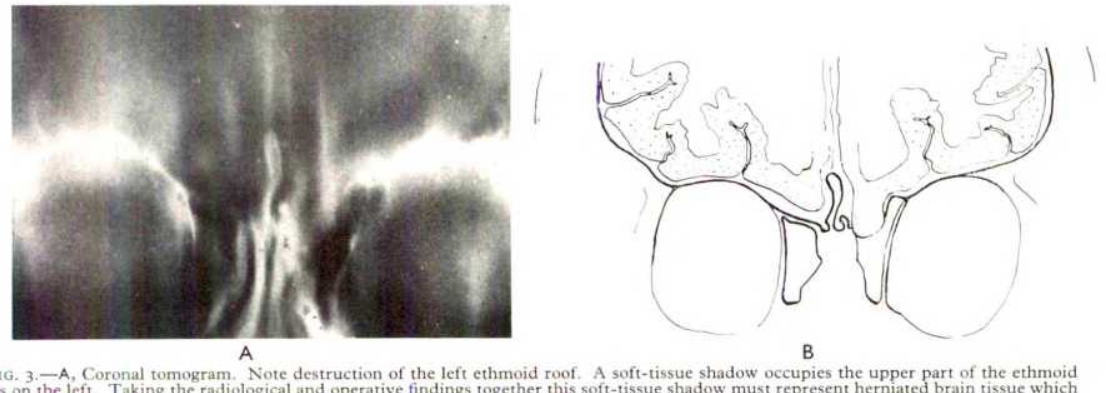

FIG. 3.—A, Coronal tomogram. Note destruction of the left ethmoid roof. A soft-tissue shadow occupies the upper part of the ethmoid sinus on the left. Taking the radiological and operative findings together this soft-tissue shadow must represent herniated brain tissue which is shown diagrammatically in B.

anterior fossa to cover the dural defect by a comfortably wide margin. In 85 per cent of the cases the tissue used has been pericranium stripped from the bone-flap itself. Only when the amount of pericranial tissue available is insufficient for the needs of the situation is a graft of fascia lata employed. It is in the minority of cases (approximately 15 per cent) that sutures are necessary to hold the graft in position; as a rule one may rely on surface tension with confidence.

If the olfactory tracts have not been ruptured at the time of the accident it is usually necessary deliberately to divide one or both of them in order to ensure satisfactory positioning of the graft(s). (Every effort is made to spare one olfactory tract, but if this is not possible there should be no hesitation about sacrificing it.) The blandness of the operation is shown by the results. The only postoperative death in this series was caused by bronchopneumonia in a man of 67 on whom we were forced to operate, in the face of a known chest infection, because of progressive drowsiness associated with an increasing collection of intracranial air. Moreover, there have been only 3 instances of postoperative complications (1 haematoma, 1 cerebral oedema, and 1 postoperative bone-flap infection in a case where the frontal sinus had been shattered by the accident). These complications all received appropriate treatment with a satisfactory outcome.

Apart from loss of olfactory function, there have been no instances of any neurological deficits following these operations.

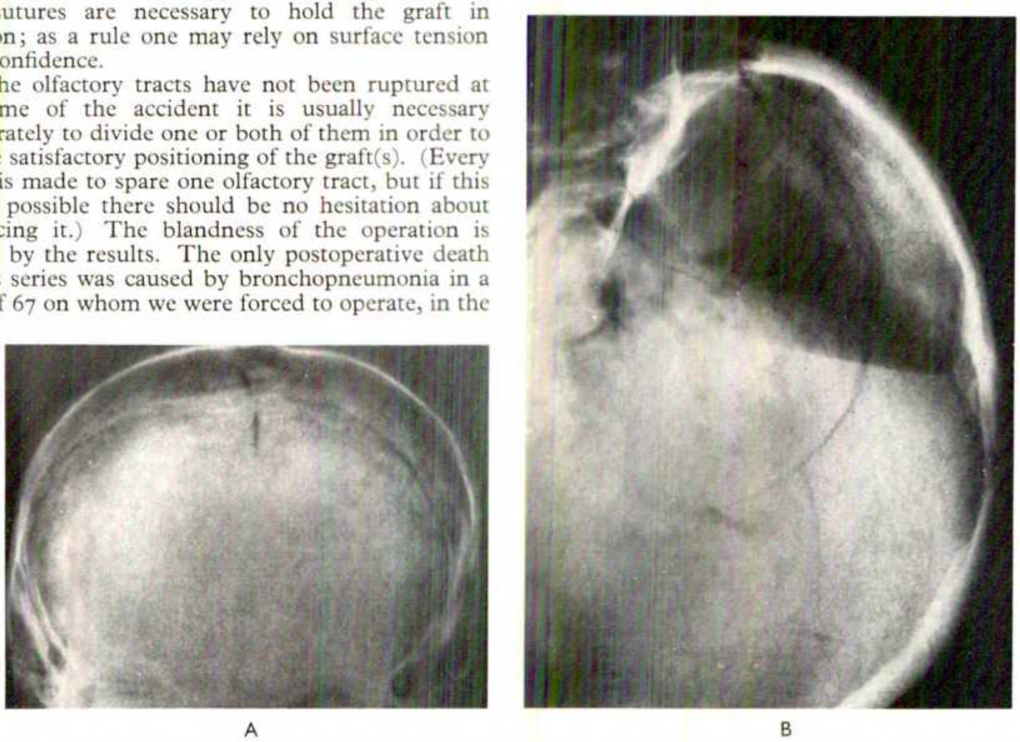
A B

FIG. 4.—A, Anteroposterior radiograph of the skull. Note the small collection of air subdurally adjacent to the falx. B, Brow-up lateral radiograph of the skull. The sharp horizontal posterior outline of the main collection of air reveals this to be in the subdural plane.

PATHOLOGY

Although the dura is able to repair itself, it is not sufficiently recognized that when dura has been lacerated, and the overlying brain and arachnoid have also been injured, healing is *permanently* prevented by the damaged tissue which has adhered to the lips of the torn dura. When these circumstances accompany a fracture in the roof of an air sinus a permanent potential path between the intracranial cavity and the external world will result. This concept is shown diagrammatically in *Fig.* 1. The typical appearance of a herniated sleeve of brain and arachnoid as seen at operation is shown in *Fig.* 2.

Fig. 3 illustrates the radiological correlate of this appearance. This radiograph was obtained in a patient who had been injured 7 years previously and who was referred on account of headaches and mild diplopia. He had never suffered cerebrospinal rhinorrhoea, meningitis, or been known to have had any intracranial air. At operation a large wedge-shaped defect in the roof of the anterior part of the ethmoids was disclosed; it measured at least 0·5 cm. at its widest point and 2·5 cm. from front to back. The defect was closed using a pericranial graft.

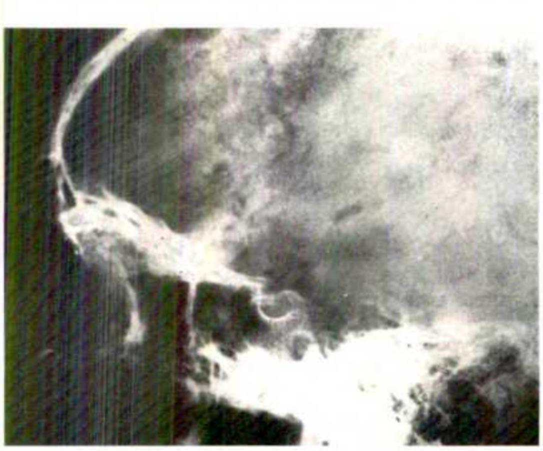

FIG. 5.—Brow-up lateral radiograph of the skull. Note that air, although diffusely scattered in the subarachnoid plane, is concentrated in the suprasellar region. This patient had a fracture involving the sphenoid sinus (*see Fig.* 11 A).

CLINICAL PRESENTATION

From the clinical point of view the fractures with which we are concerned are usually considered under the following headings:—

1. The Presence of Intracranial Air.—Apart from any sagittal projections which may seem appropriate, the radiographs which are essential in the study of post-traumatic intracranial air are those obtained using the brow-up lateral projection and a horizontal beam. Any air which is detected may be in one of four planes.

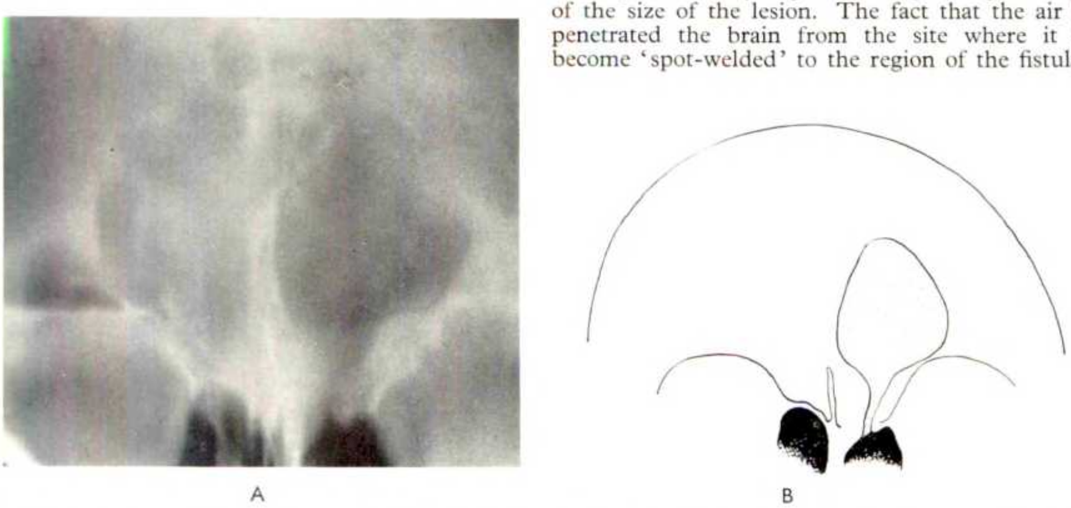

FIG. 6.—A, Tomogram of the skull with coronal cut through the ethmoid roof. Note (*a*) the disruption of the ethmoid roof on the left, and (*b*) the air-filled stalk running from the ethmoid sinus into the left frontal intracerebral aerocele. B, Explanatory line drawing traced from the original film and omitting the frontal sinus shadow.

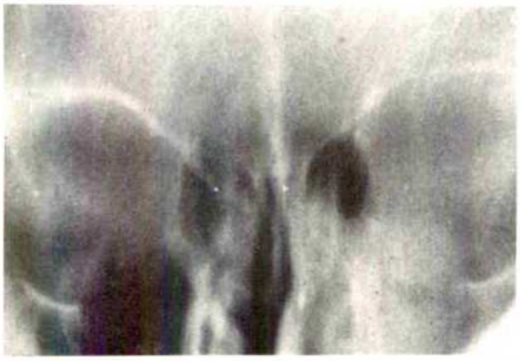

FIG. 7.—Coronal tomogram of the skull, showing an extensive defect in the right ethmoid roof.

a. Subdural.—When air from an anteriorly placed subfrontal fistula gains access to the inside of the skull it can collect in the subdural plane if the damaged arachnoid has not adhered to the margins of the fistula. The amount of air in the subdural space may be minute, as in *Fig.* 4 A, or massive, as in *Fig.* 4 B.

b. Subarachnoid.—Subarachnoid air is relatively uncommon and is most likely to be found in quantity when the fracture involved the sphenoid sinus (*Fig.* 5). This is because cerebrospinal fluid drains very freely via this particular fracture and large amounts of air reach the subarachnoid space (chiasmatic and carotid cisterns) in exchange.

c. Intracerebral.—After the brain has become adherent to the fistulous lesion a sudden increase in air pressure within the sinus or nose may result in the explosive entry of air into the substance of the frontal lobe. Such air splits the white matter, usually causing remarkably slight neurological signs in spite of the size of the lesion. The fact that the air has penetrated the brain from the site where it has become 'spot-welded' to the region of the fistula is sometimes dramatically shown by the shape of the pattern of air, i.e., a clear-cut stalk may be seen running from the floor of the skull (*Fig.* 6).

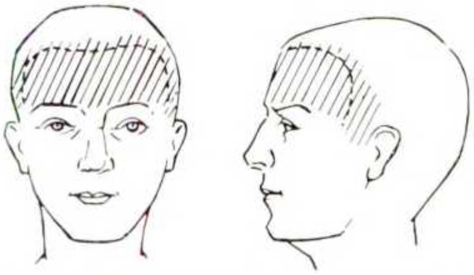

FIG. 8.—Diagram in which the shaded area outlines the region in which skull fractures may prove to be compound; such fractures may cause the intracranial cavity to communicate with the nose or an accessory nasal air sinus.

d. Intraventricular.—Early after an injury air may reach the ventricles either when there is a very large amount of subarachnoid air or when a frontal intracerebral aerocele has ruptured into the anterior horn. As a delayed or late phenomenon following an extensive frontal lobe and subfrontal injury, air can enter the frontal horn directly from the fistula via a fairly short 'corridor' which is traversing an area of softened atrophic brain.

2. Cerebrospinal Rhinorrhoea.—Among our patients there were no more than 19 (22 per cent) in whom cerebrospinal rhinorrhoea was the factor initiating a dural repair. Copious rhinorrhoea is associated with fractures which involve the sphenoid sinus, fractures which have damaged the cribriform plate (where there is no brain to plug the opening), or when post-traumatic atrophy has allowed the lateral ventricle to empty directly into the fistula (*see* Intraventricular Air above). In most other circumstances rhinorrhoea is sporadic.

It must be remembered that when there have been fractures which involve the accessory air sinuses (including the maxillary sinus) there may be a post-traumatic nasal discharge not easily distinguished from cerebrospinal fluid. Vasomotor rhinitis may cause diagnostic difficulties which can sometimes be resolved simply by the administration of antihistaminic drugs. (Indeed, there were 2 patients in this series whom we diagnosed retrospectively as suffering from rhinitis. Both of them had had frontal injuries but exploration showed no lesion and their nasal discharge persisted harmlessly at intervals for some years postoperatively.)

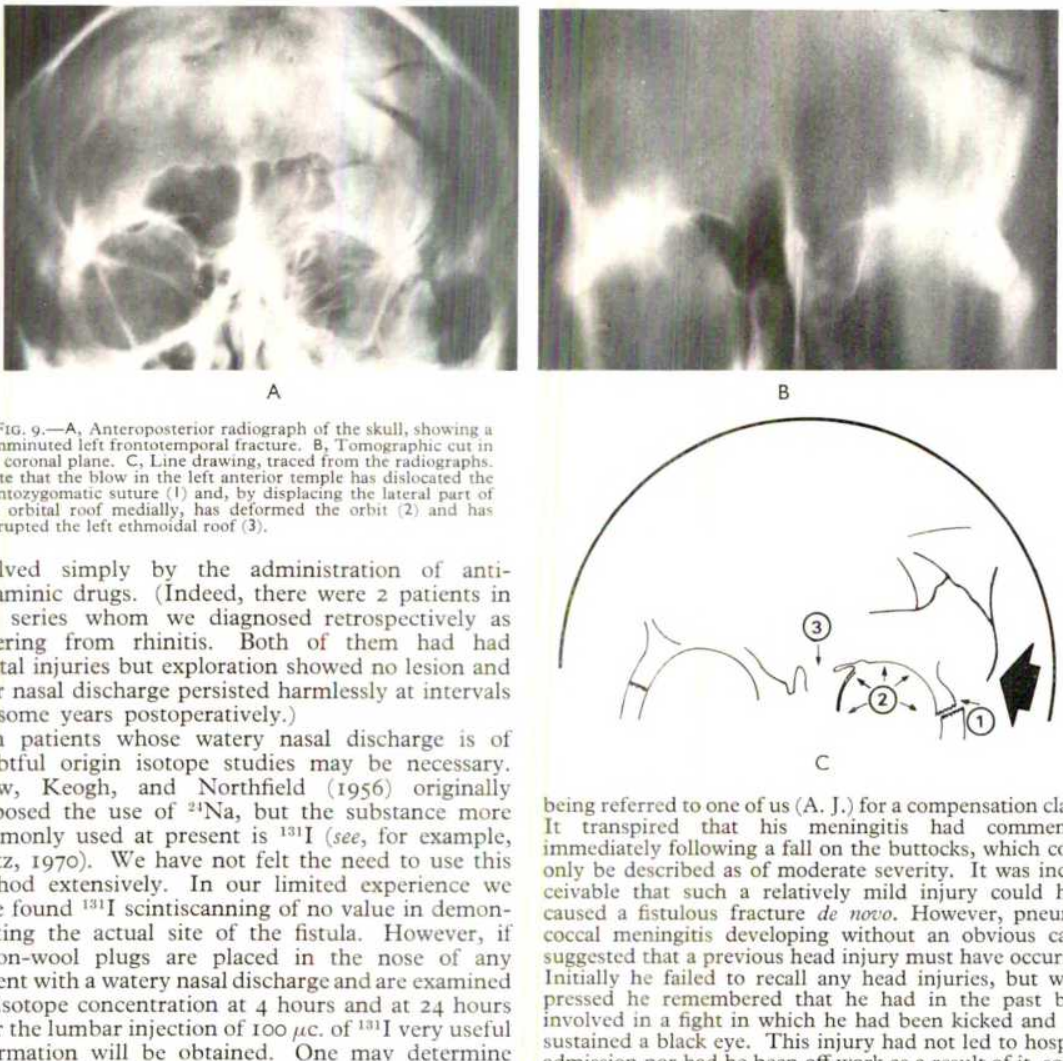

FIG. 9.—A, Anteroposterior radiograph of the skull, showing a comminuted left frontotemporal fracture. B, Tomographic cut in the coronal plane. C, Line drawing, traced from the radiographs. Note that the blow in the left anterior temple has dislocated the frontozygomatic suture (1) and, by displacing the lateral part of the orbital roof medially, has deformed the orbit (2) and has disrupted the left ethmoidal roof (3).

In patients whose watery nasal discharge is of doubtful origin isotope studies may be necessary. Crow, Keogh, and Northfield (1956) originally proposed the use of ^{24}Na, but the substance more commonly used at present is ^{131}I (*see*, for example, Dietz, 1970). We have not felt the need to use this method extensively. In our limited experience we have found ^{131}I scintiscanning of no value in demonstrating the actual site of the fistula. However, if cotton-wool plugs are placed in the nose of any patient with a watery nasal discharge and are examined for isotope concentration at 4 hours and at 24 hours after the lumbar injection of 100 μc. of ^{131}I very useful information will be obtained. One may determine thereby whether or not the fluid is indeed cerebrospinal fluid and one may gain an estimate of the rate at which it is being poured out. Some further remarks on cerebrospinal rhinorrhoea are found below in connexion with fractures of the middle third of the face.

3. Meningitis.—Eleven patients in this series underwent operation because of a preceding attack of meningitis. The responsible organism was the pneumococcus in 4 of them, while no organism could be isolated in the remainder. A dural graft was found to be necessary in every patient in whom preceding meningitis provided the reason to explore the subfrontal fracture.

One case illustrates the dangers of accepting the diagnosis of pneumococcal meningitis (in the absence of a known pneumococcal septicaemia) without inquiring very closely into the patient's past history.

Case 1.—A male, aged 30 years, had been admitted under a general physician and received effective treatment for a proved pneumococcal meningitis 11 months prior to being referred to one of us (A. J.) for a compensation claim. It transpired that his meningitis had commenced immediately following a fall on the buttocks, which could only be described as of moderate severity. It was inconceivable that such a relatively mild injury could have caused a fistulous fracture *de novo*. However, pneumococcal meningitis developing without an obvious cause suggested that a previous head injury must have occurred. Initially he failed to recall any head injuries, but when pressed he remembered that he had in the past been involved in a fight in which he had been kicked and had sustained a black eye. This injury had not led to hospital admission nor had he been off work as a result of it, so the event had not impressed itself on his memory. Armed with this past history, tomograms of his skull were obtained (*Fig.* 7) and a defect was seen in the roof of the right anterior ethmoid with clear evidence of an associated right frontal skull fracture. At operation a large defect (8 × 4 mm.) was found in the roof of the right ethmoid; it lay within an even bigger area of defective dura (4 × 3 cm.). The brain was prolapsed into the defect. The prolapsed brain was cut free and the defect was closed with a pericranial graft. He has remained well thereafter.

One must assume that the fall on to the buttocks caused a tear of the scar tissue at the fistula sufficient to allow pneumococci to penetrate from the ethmoid sinus into the subarachnoid space.

4. Radiological Studies including Tomography.—It has been our practice to regard with suspicion every patient with a fracture inferior to the hairline or with a comminuted fracture of the anterior temporal region (*Fig.* 8). This is because either group may harbour a fistulous fracture involving the floor of the anterior cranial fossa. In the case of the anterior temporal fracture the danger is associated with the medial limits of the fractured area, which may extend up to (*Fig.* 9) or even across the midline in the floor of the anterior fossa.

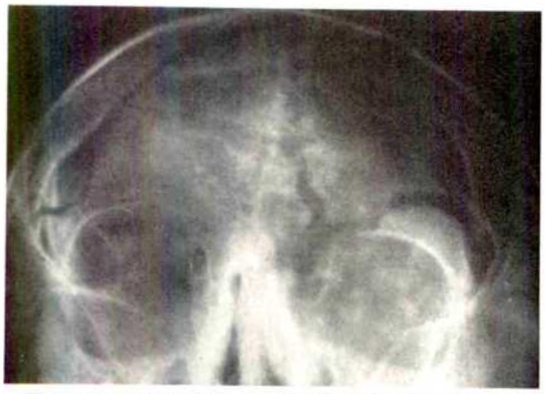

FIG. 10.—Anteroposterior radiograph of the skull of a male, aged 17 years, without previous rhinorrhoea, meningitis, or intracranial air. The severity of this fracture of itself indicates that a compound fracture must be present.

There are occasions when the extent and position of the fractures shown on the plain radiographs make it indisputably clear that the floor of the anterior cranial fossa must have been disrupted (*Fig.* 10). However, only about half of the plain radiographs have spelt out a clear danger signal. For this reason we refer all patients suspected of a fistulous fracture for tomography. It is essential that the tomograms are obtained using individual cuts at 0·5-cm. intervals. Tomographic cuts in the coronal plane (*see Figs.* 3, 6, 7, 9 B) are easier to interpret and more often useful than those in the sagittal plane, but sagittal tomograms are sometimes diagnostic (*Fig.* 11).

5. Anosmia.—Preoperative examination showed that 19 of our patients had bilateral and 12 had unilateral anosmia. Although traditional clinical medicine attaches considerable importance to the presence of anosmia in the assessment of patients with fistulous subfrontal fractures, our experience has forced us to place little or no reliance on the presence of anosmia in the selection of patients for surgery. As an example one may cite a patient in whom bifrontal exploration showed the dura to be intact on the side on which olfaction was absent, and it was necessary to divide the functioning olfactory tract in order to effect a satisfactory repair on the other side.

6. Optic Nerve Injuries.—Unilateral damage to the optic nerve was noted in 25 per cent of the patients, and in a further 2 per cent there was bilateral damage. In our series optic nerve injury has had no relevance to the selection of cases for surgical repair of the torn dura, so that although these injuries are of great interest and importance it is inappropriate to discuss them further here.

7. Frontal Lobe Syndromes.—Florid frontal lobe syndromes (e.g., apathy, personality disturbance, incontinence) occasioned by severe trauma to both frontal lobes have occurred in 16 per cent of the patients. With 1 exception such patients have required a dural graft.

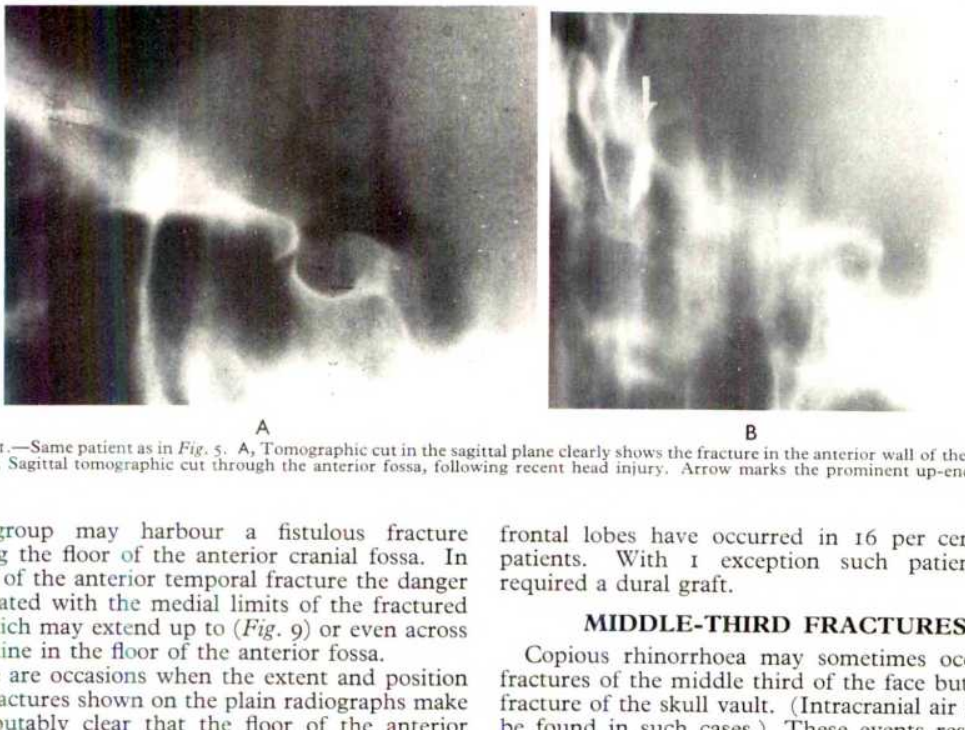
A B

FIG. 11.—Same patient as in *Fig.* 5. A, Tomographic cut in the sagittal plane clearly shows the fracture in the anterior wall of the pituitary fossa. B, Sagittal tomographic cut through the anterior fossa, following recent head injury. Arrow marks the prominent up-ended sliver of bone.

MIDDLE-THIRD FRACTURES

Copious rhinorrhoea may sometimes occur with fractures of the middle third of the face but with *no* fracture of the skull vault. (Intracranial air may also be found in such cases.) These events result from a split in the dura above the roof of the nose which differs from the other instances to which we have referred in one vital essential, which is that with every facial fracture the impact (and consequent acceleration/deceleration injury) has been partially absorbed by the crumbling of the facial skeleton. In consequence there is little likelihood of injury to the brain (cf. *Fig.* 1). In these circumstances one may confidently predict that when reduction of the facial fracture leads to prompt cessation of the rhinorrhoea (or to rapid resolution of the intracranial air), then no further surgery will be required, for the dura will heal unimpeded by the interposition of pia-arachnoid and brain.

The truth of these contentions was impressed upon us after 5 patients with rhinorrhoea following fractures of the middle third of the face had been subjected to negative exploration of the floor of the anterior fossa. Following this experience we refer such patients for tomographs of the floor of the anterior fossa when the treatment of the facial fracture has been completed and the splints have been removed. If the tomographs confirm that the floor of the anterior fossa now appears to be intact the patients are discharged from further neurosurgical supervision. Follow-up of these patients has shown that they have all remained free from further rhinorrhoea and from meningitis.

EFFICACY OF THE TREATMENT AND THE CASE SELECTION

The effectiveness of these intradural grafts is proved by the fact that so far we have not encountered any instances of postoperative meningitis or postoperative recurrence of cerebrospinal rhinorrhoea. The mean period of follow-up of the operated patients in this series is 4 years.

We have had the opportunity to study the late histological appearance of an intradural pericranial graft in a patient with spontaneous cerebrospinal rhinorrhoea which arose from the chronic raised pressure of an intracranial tumour. Macroscopically the graft was seen to have adhered where it had been placed, and *Fig.* 12 shows it to have merged with the normal dura, re-creating a complete protective barrier against infection.

Table III.—PATIENTS SUBJECTED TO NEGATIVE SURGICAL EXPLORATION IN THE PRESENT SERIES

Reasons for Operation	*No. of Patients*
Rhinorrhoea with middle-third fractures	5
Rhinitis	1
Subdural air	2
Exploration to confirm anticipated intact dura	2
Misinterpretation of the radiographs (i.e., fistulous fracture falsely identified)	4
Total	14

We have to admit that in evolving what we now regard as sound principles for the management of these patients we were initially guilty of excess enthusiasm. This caused 14 patients to be subjected to a negative surgical exploration. The reasons for these operations are shown in *Table III.*

We are naturally embarrassed to report an incidence of 16 per cent with negative findings at operation but we feel sure that the figure now would not exceed 5 per cent, for we have learned to reject the misleading middle-third fractures, and we know that small amounts of subdural air which resolve within 2 days may be ignored when the radiographs are normal. Two cases were explored 10 years ago, in the very early stages, when we wished to verify our predictions at a time when we were breaking new ground. Finally, not only have we learned to read the radiographs more precisely, but also we have learned that only really first-class films may be relied upon. In the past 5 years a total of 37 patients underwent exploration and only 2 have provided negative findings.

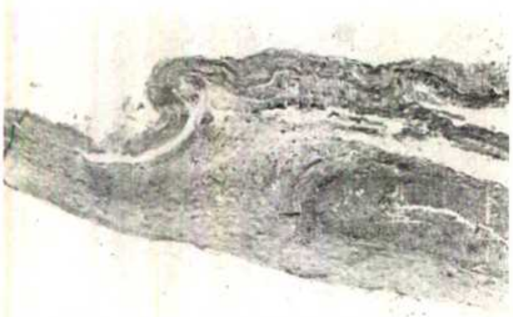

FIG. 12.—Histological appearance of an intradural pericranial graft (× 18) obtained 7 months after an operation made necessary by an intracranial tumour. Note that the grafted area has fused densely with the normal dura which is seen on the left.

With regard to the diagnostic weight which may be attached to a history of meningitis, intracranial air, or rhinorrhoea in the head-injured patient we have found as follows. Preceding meningitis is always (100 per cent) diagnostic of a fistulous fracture. Intracranial air has been misleading on 2 occasions out of the 7 in which it has been observed, whilst watery nasal discharge was misleading 6 times and diagnostic on 13 occasions (*Table III* explains how these 'false positives' arose).

The justification of our criteria of case selection may be found in the fact that among the 73 patients who needed a dural repair no less than 31 were selected entirely because of the radiographic features of the skull fracture. In other words, 42 per cent of necessary operations were *not* based on the classic criteria of preceding meningitis, intracranial air, or cerebrospinal rhinorrhoea.

DISCUSSION

The management of the particular variety of compound skull fracture which is created by fistulous fractures in the floor of the anterior fossa has been gradually evolving over the years. Before the advent of antibiotics and before improvement in anaesthetic techniques neurosurgical procedures had a potential danger that probably equalled that of the fistulous fracture. It was thus originally reasonable for didactic authorities to recommend conservative treatment; that is to say, if cerebrospinal rhinorrhoea ceased, then operation could be avoided. However, it is generally agreed that such 'healing' of these fractures can be proved histologically at autopsy to be most unsafe (Linell and Robinson, 1941). Dietz (1970) in his recent thorough review of the problem castigates such 'healing' as 'sham-healing'.

Our point of view is based firmly on that of Jefferson and Lewtas (1963), who said that one of the chief enemies of logical thought concerning fractures involving the frontal and ethmoid sinuses was that most published articles were concerned largely, if not wholly, with cases which at some time had been known to have cerebrospinal rhinorrhoea, air within the skull, intracerebral abscess, or meningitis. If they lived long enough all cases with fistulous subfrontal fractures would eventually fit into at least one of these categories. However, because the infective complications would not invariably respond to treatment they were convinced that the fistulous dural lacerations must be recognized before infection developed.

It is perhaps not generally recognized just how long the interval between injury and meningitis may be. In 1 of our own patients it was 24 years, and in a case recorded by Strenger (1958/9) it was 31 years. Thus, given a fistulous fracture the affected person simply has to go on living and sooner or later invasive bacteria (usually pneumococci) will penetrate the flimsy tissues at the border of the air sinus and the brain. Because the Department of Neurological Surgery at the Royal Infirmary, Sheffield, does not admit unselected patients with head injuries we can provide no meaningful figures concerning the number of affected patients. However, the observed frequency of cerebrospinal rhinorrhoea among large series of skull fractures is approximately 2·5 per cent (Lewin, 1954; Mincy, 1966; Raaf, 1967). Our own findings suggest that for every patient with a skull fracture and cerebrospinal rhinorrhoea there are two additional patients who harbour fistulous lesions which require repair. Utilizing the above figures one may compute that at least 7 per cent of patients with skull fractures require a dural repair. Whilst this figure may be excessive one must conclude at least that the fistulous fractures are sufficiently numerous to demand that those in charge of the head-injured patient are aware of the extent and nature of this particular problem.

If it be agreed that all these injuries should be carefully studied the means of detecting the fistulous lesions require a brief discussion. It must be made clear at the outset that the final case selection which involves specialized techniques and critical interpretation of the radiological data is a matter for the specialist. Thus, the general or accident surgeon who can refer his patients to the neurological surgeon needs only to be aware of the problem, and we advise him to be guided mainly by the simple rule illustrated in *Fig.* 8 and to remember that the trauma may seem trivial to the injured individual (*see* the present *Case* 1). Reverting to techniques of case selection, radiological methods provide the key to most of these; apart from the plain radiographs, tomographs (Dietz, 1970), or stereoscopic radiographs (Johnson and Dutt, 1947; Grote, 1966), subdural air injections have been proposed (Jefferson and Lewtas, 1963). However, we may report that over the years subdural pneumography, although still of occasional use, has been largely supplanted by ever more technically skilful tomography.

It was Eden (1942) who introduced the intradural approach which was taken up and whose merits were made so clear by Lewin (1954). We have always used the intradural approach because, in view of the anatomy of the lesions as depicted in *Fig.* 1, it is a logical necessity to do so. Our results (i.e., no recurrences to date) are not unique and they compare favourably with the 12 per cent recurrence rate (Adson and Uihlein, 1949) of the extradural approach.

Our management of this problem has been in most respects similar to that of Lewin (1966) although it is probably the nearest of all to that of Dietz (1970). Lewin (1966) appears not to have looked for these lesions quite so aggressively as Dietz (1970), who believed that *all* fistulous fractures must be picked out from among the general run of head injuries before the dangerous complications develop. It is interesting that among the dangerous complications we have encountered only 1 abscess. This was a small 'silent' lesion which was displayed during the course of a routine operation. (Its presence merely caused us to perform the operation in two stages.) Perhaps the rarity of abscesses in this series reflects one of the benefits of treating all patients at risk *before* the complications develop.

Unlike other series (cf. Dietz, 1970) we have encountered no patients with fistulous fractures associated with injuries of the intracranial portion of the internal carotid artery.

The views which we have adopted regarding rhinorrhoea or intracranial air associated with fractures of the middle third of the face without an associated fracture of the skull vault may not be universally held, but we believe that time will show them to be valid. That such fractures seldom require a dural repair was also the view of Boering and Beks (1963).

The seeking out of the potentially dangerous fracture by the neurosurgeon backed by a skilled radiological department seems, as a policy, to have justified itself. As long as antibiotics cannot be relied upon to control every attack of meningitis aggressive surgery recommends itself when the surgical risks are negligible. We may conclude by recalling that the régime propounded here has made 31 vulnerable patients (who would otherwise have remained undetected and at risk) safe from the hazards of intracranial infection.

Acknowledgements.—It is a pleasure to record our very real gratitude to Dr. N. A. Lewtas for his radiological advice and opinion. We are also indebted to Miss J. M. Osborne and Mrs. K. Byron-Thomson for their skilled radiographic technique.

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VESICO-INTESTINAL FISTULAE

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SUMMARY

Vesico-intestinal fistulae carry a serious prognosis by the nature of the underlying pathology. The inflammatory lesions offer the best hope for surgery and the necessity for early radical surgery in this group is stressed. The clinical details of 74 cases of vesico-intestinal fistulae are given together with their investigations, treatment, and results. The improved results over the past 10 years appear to bear out the necessity for early treatment.

THE first description of a vesico-intestinal fistula was probably made in A.D. 200 (Pascal, 1899), but the first full case reports were not recorded until much later by Cripps (1888). Further reports then followed of increasing numbers of cases (Sutton, 1921; Kellogg, 1938; Mayo and Blunt, 1950; Pugh, 1964).

It should be noted that a fistula between the urinary and alimentary systems can occur at any level—from the duodenum to the rectum and the renal pelvis to the urethra (Critchley, 1967)—but that the vast majority involve the terminal ileum or the sigmoid colon with the bladder or prostatic urethra.

Table I.—THE AETIOLOGY OF ACQUIRED VESICO-INTESTINAL FISTULA IN THE PRESENT SERIES

Aetiology	*No. of Cases*
Diverticulitis	35
Tuberculosis of the prostate	1
Crohn's disease	7
Post-prostatectomy	2
Post-abdominoperineal resection	6
Direct rectal trauma	1
Carcinoma of the caecum	1
Carcinoma of the colon	19
Carcinoma of the rectum	2
Total	74

Table II.—THE AETIOLOGY OF VESICO-INTESTINAL FISTULAE REPORTED IN THE LITERATURE

AUTHORS	NO. OF CASES	AETIOLOGY	
		Inflammation (per cent)	Cancer (per cent)
Cripps (1888)	63	71	14
Abeshouse, Robbins, Gann, and Salik (1957)	526	47	14
Present series (1972)	74	58	38

Table III.—THE SYMPTOMS AND SIGNS RELATED TO THE AETIOLOGY OF THE VESICO-INTESTINAL FISTULAE

	DIVERTICULITIS	CARCINOMA OF COLON	CROHN'S DISEASE
Number of cases	35	19	7
Mean age	64·5 yr.	61 yr.	46 yr.
Male : female ratio	2·75 : 1	3·5 : 1	6 : 1
Mean length of bowel history	1 yr. 7 mth.	7·8 mth.	3·0 yr.
Mean length of urinary history	9·5 mth.	6·2 wk.	6 mth.
No. of cases with pneumaturia	24	16	3
No. of cases with a mass in L.I.F./R.I.F. on examination	11	14	4
No. of cases with tenderness in L.I.F./R.I.F. only	7	—	1
No. of cases with no abnormality on examination	9	4	1

L.I.F./R.I.F. = Left iliac fossa/right iliac fossa.

The aetiology of vesico-intestinal fistula has varied considerably over the past century as the once common diseases, such as typhoid, tuberculosis, amoebiosis, and actinomycosis, have become rare and most cases now have either diverticulitis or malignancy as their underlying aetiological cause (Ewell, 1954, Lockhart-Mummery, 1958; Pugh, 1964). Such fistulae are complications of pre-existing disease and their prognosis is determined by the primary pathology. In general the permanent spontaneous closure rate is probably very low, being most likely in the prostato-rectal or vesico-rectal examples of traumatic origin. The average life expectancy after the development of a fistula was 3 years (Kellogg, 1938). Pugh in his 1964 series gives a gross mortality of 18 per cent. The present series of 74 cases of acquired vesico-intestinal fistulae (*Table I*) represents the experience in the Bristol Urology Department during the years 1950–70. These cases have been treated at the Southmead General Hospital or at the Bristol Royal Hospital, either by urologists or in conjunction with their general surgical colleagues. The vesico-rectal fistulae form a small group on their own and have been included for the sake of completeness. These 12 cases consist of 8 postoperative fistulae (prostatectomy and abdominoperineal excision of the rectum), 2 cases arising directly from a rectal carcinoma, and 1 involving trauma to the rectum. An additional case arose as a result of extension of a tuberculous prostatic abscess. It is interesting to recall that there have been very few post-prostatectomy fistulae and none in the last 10-year period. Both examples of this fistula type followed the attempted enucleation of a small firm prostate and not a carcinoma as might have been expected. This finding would tend to underline the importance of transurethral prostatic resection in the treatment of such cases. Those cases arising after abdominoperineal excision of the rectum may often be in advanced carcinoma where the general condition of the patient and local recurrence preclude any surgical repair. There are certainly many more terminal cases of rectal carcinoma with fistula formation that are not repaired as such, or indeed, may never been seen in hospital. The traumatic case followed an accident in which the patient, a male aged 26 years, alleged he sat down suddenly on a lavatory brush handle, the latter entering the rectum and penetrating the anterior rectal wall and the bladder just above the inter-ureteric bar. The fistula healed spontaneously after a period with an indwelling urethral catheter and defunctioning colostomy.

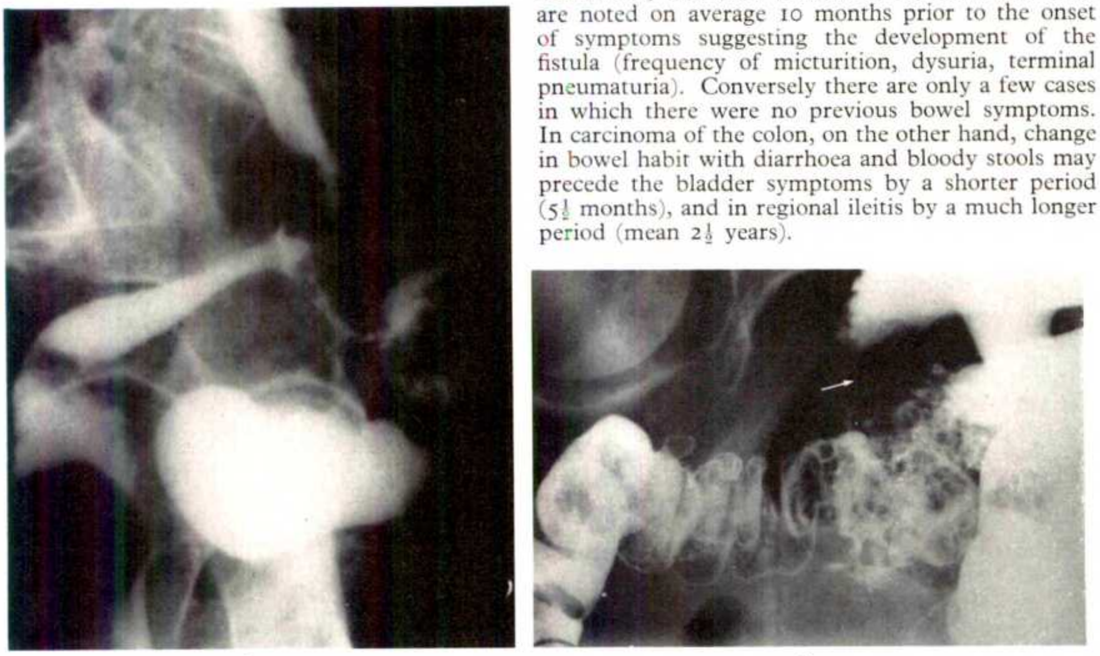

FIG. 1.—Barium-enema radiographs demonstrating fistulous tracks. A, Communications via a pericolic abscess cavity. B, Direct communication from an area of diverticular disease.

The two remaining groups of vesico-colic and vesico-ileal fistula form the great majority of the total cases, and are the most interesting from a diagnostic and therapeutic viewpoint. They are by no means rare, but are less frequently seen today owing to earlier diagnosis and treatment of the causal disease. This trend has become increasingly apparent over the past 20 years.

Whereas the number of fistulae caused by neoplasms of the bowel and bladder have remained roughly constant, those caused by chronic inflammatory disease have been reduced in number and show a marked change in sex incidence and aetiology. Robinson (1953) compared the 1921 and 1940 Mayo reports. In the 1921 series the majority of cases was in females and was caused by salpingitis, whereas in the 1940 series no case of salpingitis was quoted and the majority was in males and was the result of diverticulitis. This pattern is shown in comparison with other authors (*Table II*).

The age and sex distribution of the present series are given in *Table III*.

SYMPTOMS

Symptoms may be due either to the abnormal communication between the bowel and the bladder or to the primary pathological process (*Table III*). The latter usually precedes the former by a period of months or years depending on the nature of the disease. In diverticulitis, for example, colicky pain, tenderness, and even a mass in the left iliac fossa are noted on average 10 months prior to the onset of symptoms suggesting the development of the fistula (frequency of micturition, dysuria, terminal pneumaturia). Conversely there are only a few cases in which there were no previous bowel symptoms. In carcinoma of the colon, on the other hand, change in bowel habit with diarrhoea and bloody stools may precede the bladder symptoms by a shorter period (5½ months), and in regional ileitis by a much longer period (mean 2½ years).

It is inevitable that such a bizarre symptom as terminal pneumaturia is so often the precipitating cause for a patient seeking medical advice, and indeed this is pathognomonic of vesico-intestinal fistula if recent endoscopy and diabetes mellitus can be excluded. The passage of faecal matter in the urine and urine per rectum also suggest a fistula and call for urgent investigation. The differential diagnosis of diverticultis from carcinoma of the colon is naturally of great importance. A previous history of diverticulitis alone where this is the cause of the fistula is given in 50 per cent of cases (Lockhart-Mummery, 1958). Only in approximately 12 per cent of patients with colonic carcinoma is there a history suggesting diverticultis, with coexisting carcinoma and diverticulitis in 3 per cent of cases.

INVESTIGATIONS

A summary of those investigations concluded in this current series is given in *Table IV*. Routine excretion pyelography is unlikely to further the diagnosis but is of importance in the assessment of renal function and to exclude abnormality in the upper urinary tract. Barium-enema examination may demonstrate the presence of diverticulosis or diverticulitis or may suggest the presence of a colonic neoplasm. Demonstration of the fistula by modern techniques and screening methods is becoming increasingly common (*Fig.* 1).

From *Tables III* and *IV* it can be seen that cystoscopy and bimanual pelvic examination under anaesthesia, together with the history, make a firm diagnosis possible in the majority of cases. The importance of careful bimanual palpation under anaesthesia cannot be overestimated. The cystoscopic appearances are characteristic: the fistula, usually small, lies on the posterior bladder wall—on the left side in vesico-colic and on the right side in vesico-ileal fistula. Pus, faecal matter, or gas bubbles may sometimes be seen issuing from it, or the bladder fluid may be seen to be passing into it. The surrounding area is oedematous and dusky red, often with heaped-up polypoidal mucosa which at first sight may be mistaken for tumour. The muscle bundles are prominent with an appearance of local trabeculation and the bladder usually shows a generalized gross cystitis. Occasionally it is remarkably normal apart from the fistulous area. A bladder-wall biopsy is often useful (*Fig.* 2), but it should be noted that a negative biopsy taken in cases of suspected carcinoma by no means excludes the diagnosis.

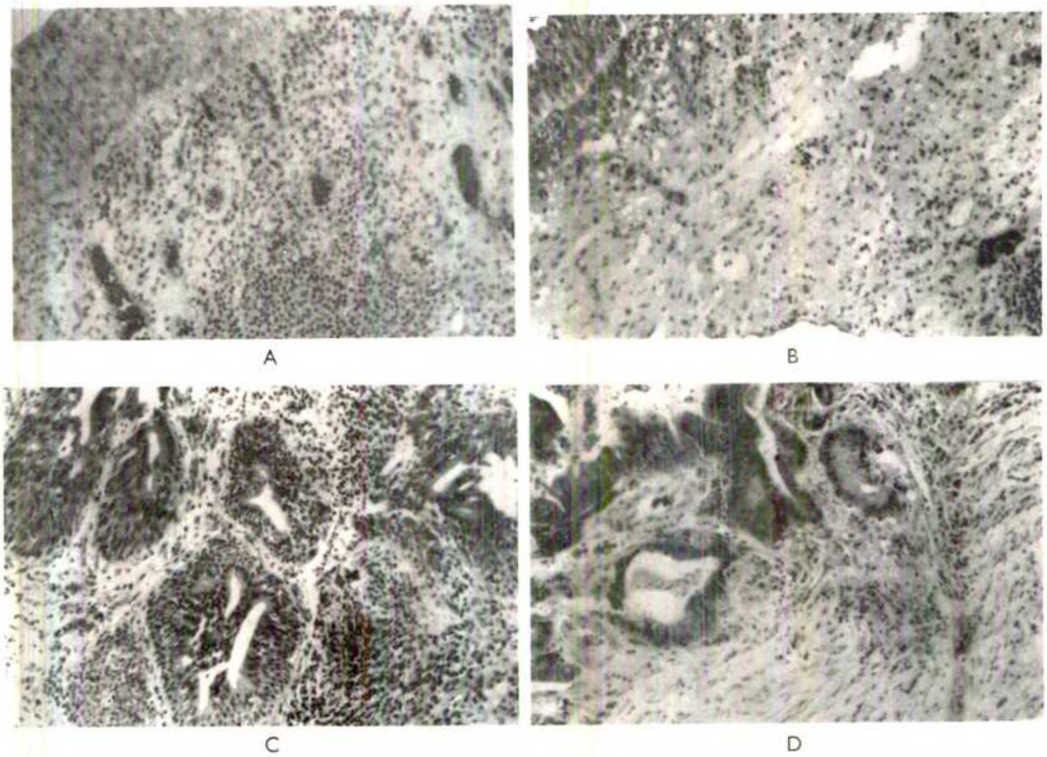

FIG. 2.—Bladder biopsies obtained by transurethral resection. H. and E. (× 150.) A, Chronic inflammatory change of diverticulitis. B, Mild inflammation but no neoplastic invasion seen (carcinoma of the colon). C, Intense round-cell infiltration suggestive of Crohn's disease. D, Identification of adenocarcinoma in addition to inflammation (carcinoma of the colon).

Table IV.—THE INVESTIGATIONS CARRIED OUT IN THE PRESENT SERIES

INVESTIGATION	DIVERTICULITIS		CARCINOMA OF COLON	
	No. of Cases (Total, 35)	Findings	No. of Cases (Total, 19)	Findings
Urography	22	21 normal; 1 irregular bladder base. No fistula seen	8	7 normal; 1 irregular bladder base. No fistula seen
Barium enema	21	21 with diverticular disease. 9 fistulae seen	6	6 showed evidence of carcinoma
Sigmoidoscopy	12	Of no value	8	6 showed tumour—no other help
Cystoscopy	34	31 with inflammation/oedema. 15 fistulae seen	16	16 with inflammation/oedema. 5 fistulae seen
Examination under anaesthetic	28	24 with a mass in the left iliac fossa or pelvis adherent to the bladder	19	19 with a mass in the left iliac fossa or pelvis adherent to the bladder
Bladder biopsy	11	11 with inflammation only	13	8 showed carcinoma. 5 with inflammation only

On bimanual examination a mass can nearly always be felt and its size, extent, and fixity to the bladder assessed. Finally, dye solution instilled into the bowel or bladder may help to demonstrate the fistula. Where colonic carcinoma is the cause of the fistula the case is usually advanced and a palpable mass is the rule, fixed to the bladder. Finally, laparotomy is indicated in all but a few cases and is another reason why further elaborate investigations can be avoided.

TREATMENT

By the very nature of the lesion causing vesico-intestinal fistula the prognosis is serious and one can assume that to cause fistula formation there must be moderate to gross extramural extension of the pathological process. There appears to be few recorded cases of spontaneous cure even in the inflammatory cases. From 1843, when Borrier de Melle suggested colostomy, until 1884 this simple method of drying up the fistula was used. From 1884 onward (Cripps, 1888) direct attack on the fistula, either transvesical or transperitoneal, was attempted with or without a preliminary colostomy.

Mayo and Miller (1940), who attributed the causes to diverticulitis in 60 per cent of cases, considered that a proximal colostomy should precede any surgical approach. This was supported by Dixon (1936), Jones (1936), and Pemberton (1945), who agree that fistulae rarely close spontaneously and colostomy alone is not a cure. In 5 of our cases a fistula developed in spite of a defunctioning colostomy.

Table V.—DETAILS OF THE TREATMENT CARRIED OUT IN THE PRESENT SERIES

TREATMENT	DIVERTICULITIS	CARCINOMA OF COLON	CROHN'S DISEASE
Total number of cases	35	19	7
No operation	4	4	0
Preliminary colostomy	11	4	0
Resection with previous colostomy	11	4	0
Resection with additional colostomy	13	9	1
Resection without colostomy	5	0	6
Closure of colostomy	10	2	1

Table VI.—THE MORTALITY IN PATIENTS WITH CARCINOMA OF THE COLON

Mortality	*No. of Cases*
Less than 1 week	6
2 months	3
3 months	3
6 months	3
8 months	1
12 months	1
18 months	1
4 years	1
Total	19

In deciding on the type of surgery indicated the extent and character of the primary lesion must be considered, together with the possible presence of sepsis and obstruction. The fistula in an otherwise uncomplicated carcinoma of the sigmoid with a direct communication into the bladder through the base of the ulcer must be quite different from that due to diverticulitis which is the result of rupture of a peri-diverticulitic abscess into the bladder—the 'foyer intermédiaire' of Chauvannez.

In this present series the stages of treatment to which the patients were subjected are indicated in *Table V*. Simple diversion of the faecal stream by colostomy is a reasonable palliative procedure in cases of advanced neoplasm with some expectation of life. In those cases of operable carcinoma the surgical procedure indicated is that for the uncomplicated carcinoma with the addition of partial cystectomy where the bladder-wall has been invaded. The very poor prognosis in those patients with carcinoma of the colon has again been borne out in this present series (*Table VI*) as in those of other authors (Mayo and Miller, 1940; Goodwin, Winter, and Turner, 1960). There were only 3 survivors over a 12-month period, the longest survival time following operation being 4 years.

It is the inflammatory cases which offer a real chance to the surgeon, and here the treatment consists of resection of the sigmoid colon with restoration and repair of the bladder with or without a preliminary colostomy. Colostomy alone is now rarely practised for cases of diverticultis as advised by Lockhart-Mummery (1929). Even if the fistula closes after an interval there is a high incidence of recurrence of the fistula or recrudescence of the diverticulitis if the colostomy is closed. Colostomy and simple repair of the fistula were practised by Grey Turner and Rutherford Morrison. This involved separation of the colon from the bladder and repair of the defects which were covered with omentum. This procedure is open to the same objection as colostomy alone, and anything short of resection frequently fails to cure the fistula as it does not remove the primary cause.

Table VII.—THE MORTALITY IN PATIENTS WITH DIVERTICULAR DISEASE

Time of Death after Operation (weeks)	*No. of Cases*	*Cause*	
1	7	Pulmonary embolus	2
		Coronary thrombosis	3
		Cerebrovascular accident	1
		Bronchopneumonia	1
2	2	Peritonitis	
4	1	Cardiac failure	
	10 (28 per cent)		

One patient died at 3 months from superadded carcinoma of the colon. Twenty-two cases were symptom-free for more than 5 years. There were no cases of recurrent fistula formation.

With regard to preliminary colostomy the interval previously accepted (many months in some cases) seems unreasonably long, and it could be argued that in this era of careful bowel preparation and chemotherapy it is unnecessary even in the presence of bowel obstruction. Moreover, the mimicry of neoplasm by diverticulitis, and vice versa, is well known, and the possibility of both conditions being present can rarely be ruled out at laparotomy. In favour of preliminary colostomy is the fact that fistula formation means peridiverticultis with abscess formation, and at laparotomy a formidable inflammatory mass involving the large bowel, small bowel, and bladder is sometimes found which precludes immediate resection.

It would seem reasonable that where the patient's general condition is good and there is no significant large-bowel obstruction, all cases should be prepared in the usual way for a single-stage procedure, and if at all possible the sigmoid colon should be excised with end-to-end anastomosis. This usually results in a small defect in the bladder which may be closed in layers. A relieving transverse colostomy may be performed at the conclusion, and this can be closed in a few weeks. Where the inflammatory mass makes resection too hazardous a procedure, a defunctioning transverse colostomy for 2 or 3 months prior to definitive surgery may be effective in reducing the size of the mass. However, in recent years we have not had to resort to this preliminary colostomy, and primary anterior resection *without* relieving colostomy is increasingly used.

In the very old and infirm these major procedures are sometimes not justified, in which case the symptoms may be considerably reduced by the use of chemotherapy. The risk of postoperative complications in this group of patients with diverticular disease is not inconsiderable (*Table VII*), and an overall mortality of 28 per cent occurred (cf. Kellogg, 1938, 25 per cent; Mayo and Blunt, 1950, 6·5 per cent).

VESICO-ILEAL FISTULA (REGIONAL ILEITIS)

Of the 7 cases of Crohn's disease (*Table V*), 5 were treated by a single-stage right partial or full hemicolectomy with excision of 50 cm. of terminal ileum and repair of the bladder defect. This procedure would agree with Williams (1954) and Lockhart-Mummery (1958), who stated that a cure of the fistula would follow excision of the fistulous track together with the diseased ileum. One of our cases was very similar to a case described by Robinson (1953). At laparotomy an inflammatory mass involving the bladder, terminal ileum, and caecum was found and ileotransverse colostomy was performed. After a stormy convalescence the sequel was one of steady improvement, and cystoscopy performed on two occasions subsequently showed healing of the fistula. The mass in the right iliac fossa has resolved slowly and at a 5-year follow-up the patient was symptom-free.

The remaining case was known to have Crohn's disease and he presented with urinary symptoms, having had an ileotransverse colostomy some years previously. At laparotomy a fistula between an enormous bowel mass and the bladder was treated by simple repair and omental interposition. He remains well after 6 months.

The possible high recurrence rate of Crohn's disease and recurrent fistula formation as suggested by Pollock (1958) has not been borne out in this series. There has been no recurrent fistula formation; 3 cases are alive and well after 10 years.

It is worthy of note that in vesico-intestinal fistulae, no matter what their aetiology, there was a high incidence of bladder calculi (approximately 14 per cent). This is probably related to the foreign material in the bladder and also to the presence of *B. proteus* urinary infection which was present in most of those patients with calculi.

Acknowledgements.—We would like to thank our urological colleagues and the general surgeons at the two hospitals for the inclusion of their cases in this survey.

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ABDOMINAL TUBERCULOSIS

BY A. GUNN AND N. C. KEDDIE

MANCHESTER ROYAL INFIRMARY

SUMMARY

Twelve cases of abdominal tuberculosis are presented. They illustrate the great variability in the clinical features of this condition, making diagnosis extremely difficult. In particular, we draw attention to the problem of tuberculosis of the reticulo-endothelial system in the abdomen. Biopsy and culture are essential at laparotomy if a correct diagnosis is to be made.

DESPITE a great reduction in the incidence of tuberculosis in Britain it remains a persistent problem due, in part, to the presence of an immigrant population. However, clinical awareness has probably declined with the disease so that although tuberculosis is not uncommon it causes certain diagnostic difficulties. In abdominal tuberculosis in particular we have found that the clinical features suggest advanced malignancy until histological evidence has shown otherwise. A review of all the forms of abdominal tuberculosis (excluding tuberculosis of the genito-urinary system) admitted to the Manchester Royal Infirmary during the 5-year period 1965–9 revealed 12 cases. These cases are most readily divided into tuberculosis of the intestinal tract, of the peritoneum, and of the reticulo-endothelial system.

The diagnosis of tuberculosis was based on the criteria of (1) typical tuberculous granulomata with caseation, (2) the demonstration of acid-fast bacilli within the diseased tissues, or (3) the isolation of *Mycobacterium tuberculosis* by culture or guinea-pig inoculation.

The present series is reported in the hope that the diagnosis of abdominal tuberculosis will be considered more frequently and, in particular, to stress the great importance of biopsy and culture of tissue in cases which macroscopically are typical of abdominal carcinomatosis.

Table I.—DETAILS OF THE CASES OF INTESTINAL TUBERCULOSIS IN THE PRESENT SERIES

CASE NO.	AGE AND SEX	NATIONALITY	SITE	PREVIOUS HISTORY	CHEST RADIOGRAPH	CLINICAL DIAGNOSIS	BASIS OF DIAGNOSIS OF TUBERCULOSIS	TREATMENT	RESULT
1	26 M.	Pakistani	Ascending colon	None	Normal	Carcinoma of colon	Tuberculous caseation	Right hemicolectomy. Anti-tuberculous drugs for 5 mth.	Well 5 yr. later
2	40 F.	English	Ileum, jejunum, and ascending colon	None	Bilateral cavitation	Carcinoma or Crohn's disease of colon	Tuberculous caseation. *Mycobacterium tuberculosis* cultured	Anti-tuberculous drugs still continuing	Well 1 yr later
3	65 M.	English	Sigmoid colonic carcinomatous ulcer	None	Inflammatory changes in right upper lobe	Carcinoma of colon	Tuberculous caseation. Acid-fast bacilli present	Resection of sigmoid colon. Antituberculous drugs	Died 10 d. after resection from tuberculous bronchopneumonia
4	23 F.	Nigerian	Ileum	None	Normal	Tuberculosis	*Mycobacterium tuberculosis* cultured from loin abscess	Resection of ileum. Antituberculous drugs	Well 3 yr. later

Table II.—DETAILS OF THE CASES OF TUBERCULOSIS OF THE PERITONEUM IN THE PRESENT SERIES

CASE NO.	AGE AND SEX	NATIONALITY	TYPE	PREVIOUS HISTORY	CHEST RADIOGRAPH	CLINICAL DIAGNOSIS	BASIS OF DIAGNOSIS OF TUBERCULOSIS	TREATMENT	RESULT
5	64 F.	English	Ascitic with a palpable mass	None	Calcified lesion of right upper lobe	Carcinoma of colon	Tuberculous caseation. Acid-fast bacilli	Anti-tuberculous drugs	Alive 2 yr. later with persistent diarrhoea
6	16 F.	English	Turbid ascites with fibrinous adhesions	None	Effusion of left base	Crohn's disease	Tuberculous caseation	Anti-tuberculous drugs	Well 2 yr. later
7	18 M.	English	Plastic peritonitis	Enlarged hilar gland 2 yr. previously	Normal	Intestinal obstruction. ? tuberculosis	Tuberculous caseation. *Mycobacterium tuberculosis* cultured	Anti-tuberculous drugs	Well 1 yr. later
8	29 M.	Pakistani	Plastic peritonitis	Tuberculous peritonitis 5 yr. previously. On drugs for 15 months	Normal	Tuberculous peritonitis	*Mycobacterium tuberculosis* cultured 5 yr. previously	Resection of 30 cm. of intestine; division of adhesions. Anti-tuberculous drugs	No trace
9	35 F.	English	Ascitic	Miliary tuberculosis when 10 yr. old	Scattered calcification	? Gall-stones. ? Carcinoma	Tuberculous caseation. Acid-fast bacilli	Anti-tuberculous drugs	Well 18 mth. later

GENERAL FEATURES

The main features of the cases reviewed are shown in *Tables I, II*, and *III*, but some case histories are given in detail later in the text.

Non-specific features such as rapid loss of weight (present in 4 out of the 12 patients), malaise, a raised erythrocyte sedimentation rate, and unexplained pyrexia are all factors which should raise a suspicion of tuberculosis. Usually, however, these features make the clinician suspect malignancy. Thus 7 of our 12 patients were thought clinically to have a malignant tumour and even at operation the macroscopic features of tuberculosis were mistaken for malignancy in 5 patients.

The age range of the patients was 6 to 64 years, but it should be noted that children are not usually admitted to the Manchester Royal Infirmary except as an emergency such as a road accident. Five patients

(42 per cent) were from overseas and there was an equal number of males and females.

A chest radiograph was normal in 5 of the 12 cases. Definite evidence of active pulmonary tuberculosis was only present in 3 cases. None of our cases of reticulo-endothelial tuberculosis (*Table III*) showed evidence of active lung disease.

INTESTINAL TUBERCULOSIS (*Table I*)

Two of these patients had well-recognized forms of tuberculosis, 1 suffering from primary hypertrophic ileocaecal tuberculosis (*Case* 1) and 1 from ulcerative intestinal tuberculosis with active pulmonary disease (*Case* 2). Even so, the diagnosis was only made in these patients after histological examination of the affected tissues. In *Case* 3 tuberculosis was found in association with a carcinoma of the sigmoid colon. It seems probable that tuberculous infection followed malignant ulceration of the colon. Although histology of the ileal strictures in *Case* 4 showed non-specific inflammatory changes, the presence of tuberculous pus tracking from the retroperitoneal area makes tuberculosis the likely diagnosis.

Case 1.—A 26-year-old male Pakistani was admitted to hospital complaining of a pain in the right hypochondrium with vomiting, shivering attacks, and sweating for 3 months; during this period he had lost 19 kg. in weight. Examination revealed an ill-looking man with no lymphadenopathy, but a fixed mass was present in the right hypochondrium; haemoglobin, white cell count, and liver-function tests were normal, but an occult blood test was positive. A barium-enema examination showed a filling defect in the ascending colon and laparotomy revealed a mass in the ascending colon involving the caecum and ileum with enlarged mesenteric nodes. A right hemicolectomy was performed with an end-to-side ileocolic anastomosis. Histology showed a deep 2-cm. ulcer with tuberculous granulomata involving the ascending colon and caecum; there was caseation of the mesenteric lymph-nodes and acid-fast bacilli were demonstrated. Culture was not performed as the mass was thought to be either a carcinoma or Crohn's disease.

The patient made an uneventful postoperative recovery and was placed on streptomycin, para-aminosalicylic acid, and iso-nicotinic acid hydrazide, which the patient probably discontinued 5 months after the operation. However, he was fit and well 5 years after the operation.

Case 2.—A 40-year-old English woman was seen in the out-patients' department with a 4-month history of passing four or five loose motions daily with associated lower abdominal discomfort, malaise, and the loss of 12·7 kg. in weight. She was emaciated with a temperature of 37·4 C. and a fixed mass in the right iliac fossa. She did not complain of a cough. Her serum albumin was 3 g. per cent; globulin, 4·3 g. per cent; alkaline phosphatase, 21 K.A. units; and haemoglobin, 58 per cent. A barium-enema examination showed a filling defect of the ascending colon which was thought to be due to a carcinoma or Crohn's disease although it did, in fact, show features indicative of tuberculosis (*Fig.* 1). The patient's condition was so poor that she was soon admitted to hospital and after a blood transfusion a laparotomy was performed. She was found to have twelve inflammatory segments, each 2 cm. in length, scattered through the small intestine with a large inflammatory mass in the ascending colon. One of the diseased ileal segments was excised for biopsy, continuity being restored by an end-to-end anastomosis; an enlarged lymph-node was removed for culture. Histology of the excised small intestine showed typical tuberculous granulomata without caseation but acid-fast bacilli were present.

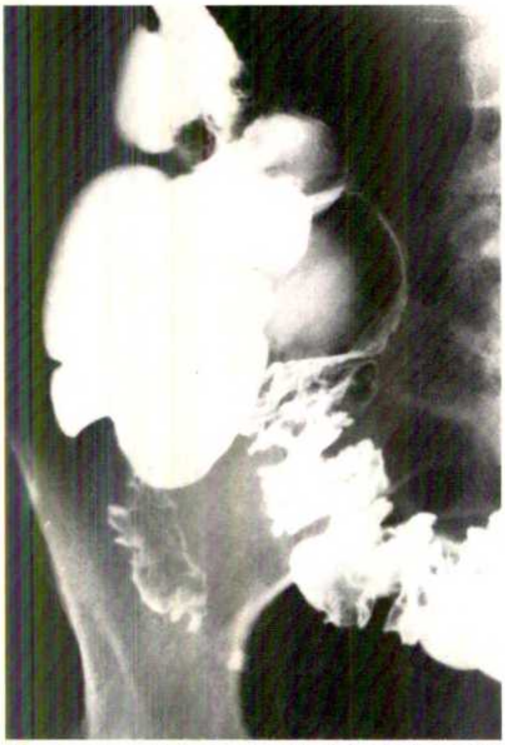

FIG. 1.—*Case* 2. Barium-enema radiograph, showing an obtuse ileocaecal angle and apparent disappearance of the caecum. A stricture is present in the ascending colon.

Table III.—DETAILS OF THE CASES OF TUBERCULOSIS OF THE RETICULO-ENDOTHELIAL SYSTEM IN THE PRESENT SERIES

CASE No.	AGE AND SEX	NATIONALITY	SITE	PREVIOUS HISTORY	CHEST RADIOGRAPH	CLINICAL DIAGNOSIS	BASIS OF DIAGNOSIS OF TUBERCULOSIS	TREATMENT	RESULT
10	52 F.	Indian	External iliac lymph-node	None	Fibrosis right upper lobe	Secondary carcinoma or reticulosis	Tuberculous caseation. Acid-fast bacilli	Excision of lymph-node	Well 2 yr. later
11	6 M.	English	Spleen	None	Normal	Ruptured spleen	Tuberculous caseation	Splenectomy	Well 5 yr. later
12	53 M.	West Indian	Mesenteric and coeliac lymph-nodes	Pulmonary tuberculosis 1 yr. previously	Fibrosis right upper lobe	Carcinomatosis	Tuberculous caseation	Anti-tuberculous drugs	Well 1 yr. later

Culture of the excised lymph-node later confirmed the presence of *Mycobacterium tuberculosis*. A postoperative chest radiograph showed advanced bilateral lung disease with cavitation.

The patient was treated with streptomycin, para-aminosalicylic acid, and iso-nicotinic acid hydrazide, but because of her diarrhoea rifampicin and ethambutol were substituted for the para-aminosalicylic acid. The streptomycin was discontinued after 5 months, but she was still taking oral anti-tuberculous drugs 1 year later when she was clinically well and had gained 5·4 kg. in weight.

Case 3.—A 65-year-old English man was admitted as an emergency with a 7-day history of constipation, vomiting, and generalized abdominal pain. He had apparently been well previously, although he had been investigated 2 years earlier for a suspected carcinoma of the colon with a negative barium-enema examination and sigmoidoscopy. On admission the patient was dehydrated, his temperature was 36·2° C., and his abdomen was distended. A plain radiograph of the abdomen confirmed the diagnosis of intestinal obstruction. Laparotomy revealed a stenosing carcinoma of the sigmoid colon and a loop transverse colostomy was performed. A chest radiograph showed diffuse inflammatory changes of the right upper and middle lobes of the lungs and culture of his sputum produced a growth of *Haemophilis influenza* and *Pneumococcus*; he was therefore treated with intramuscular ampicillin. His general condition improved and 10 days later a resection of his sigmoid colon was performed and continuity restored by means of an end-to-end anastomosis. Histology of the excised specimen showed a well-differentiated adenocarcinoma of the colon with a metastatic deposit in an adjacent lymph-node. There were also several tuberculous granulomata with central caseation immediately deep to the colonic tumour and within several of the paracolic lymph-nodes. Acid-fast bacilli were present in the granulomata.

Because of the histological findings and later the discovery of acid-fast bacilli in his sputum, the patient was treated with streptomycin, para-aminosalicylic acid, and iso-nicotinic acid hydrazide. His general condition deteriorated, however, paralytic ileus and atrial fibrillation supervened, and he died 1 week after his second operation. Post-mortem examination showed no evidence of residual carcinoma or tuberculosis in the abdomen, but there was a tuberculous bronchopneumonia affecting mainly the right upper and middle lobes.

Case 4.—A 23-year-old Nigerian woman presented with malaise and an abscess in her left renal area. There were no other abnormal physical findings; a chest radiograph, haemoglobin, and white cell count were normal. Her Heaf test was positive grade III, her E.S.R. was 16, and a radiograph of the lumbosacral spine showed no definite evidence of tuberculous involvement of the vertebra. The abscess was aspirated and 6 weeks later *Mycobacterium tuberculosis* was isolated on culture. Eight weeks after the aspiration of the abscess, the abscess was explored and traced to the retroperitoneal area but there was no communication with the vertebra. After drainage, the wound was closed and the patient was nursed on a plaster bed and treatment with streptomycin, para-aminosalicylic acid, and iso-nicotinic acid hydrazide was begun. Four weeks later she developed signs of intestinal obstruction and at laparotomy three discrete strictures were demonstrated in a 30-cm. length of ileum. This piece of ileum was resected and continuity restored by means of an end-to-end anastomosis. Histology of the strictures showed epithelial ulceration and non-specific inflammatory changes.

Following this, the patient made a good postoperative recovery and all anti-tuberculous treatment was stopped after a period of 18 months. She was well and symptom-free 3 years after the last operation.

TUBERCULOUS PERITONITIS

These 5 cases presented considerable diagnostic problems and preoperative investigations were of little value. None of these was easily classified into the usually described forms of tuberculous peritonitis. Malignancy was suspected in 2 patients preoperatively and at laparotomy; the correct diagnosis was made from a biopsy. The importance of biopsy of peritoneal deposits is illustrated in *Case* 9.

Case 9.—A 35-year-old English woman was admitted to hospital with a 1-year history of epigastric and lower sternal pain occurring once a week and lasting for periods of between 10 minutes and 4 hours. There was no vomiting and the pain was not related to meals. The pain had been very severe on two occasions and the patient had lost 11·7 kg. in weight. She had had miliary tuberculosis when she was 10 years old and had been in hospital for 18 months. There were no abnormal findings on physical examination, her white cell count was 11,800, but the haemoglobin, liver-function tests, urea and electrolytes, barium-meal examination, and a cholecystogram were all normal. A chest radiograph showed scattered areas of calcification in both lung fields.

A laparotomy was performed, when the patient was found to have fibrinous adhesions around the gall-bladder and in the pelvis. There were 2-mm. nodules scattered throughout the peritoneum and in the omentum which were thought to be due to carcinomatosis. An omental biopsy was taken and this was shown to contain tuberculous granulomata with central caseation and acid-fast bacilli were demonstrated.

The patient was treated with streptomycin, para-aminosalicylic acid, and iso-nicotinic acid hydrazide. She made a good recovery and was symptom-free 18 months later.

TUBERCULOSIS OF THE RETICULO-ENDOTHELIAL SYSTEM

These were patients in whom tuberculosis of part of the reticulo-endothelial system was demonstrated without evidence of tuberculosis elsewhere in the abdomen. In *Cases* 10 and 11 the tuberculosis was discrete, affecting an external iliac lymph-node and the spleen respectively. In *Case* 12 there was diffuse involvement of the mesenteric and retroperitoneal lymph-nodes, presenting a difficult diagnostic problem.

Case 12.—A 53-year-old Jamaican man was admitted to hospital with a 7-week history of ill-defined pain in the right side of the abdomen with anorexia. He had recently noted increasing dyspnoea with exercise. One year previously he had been treated with anti-tuberculous drugs as an in-patient for 4 months because of active pulmonary tuberculosis. He had discontinued the anti-tuberculous drugs after 9 months (i.e., 3 months prior to admission).

On examination the patient looked reasonably well, but there was some abdominal swelling and tenderness in the right side of the abdomen. His haemoglobin, electrolytes, Wassermann reaction, barium-enema examination, and cholecystogram were all normal. His serum albumin was 4·4 g. per 100 ml. and the globulin, 5·4 g. per 100 ml. A chest radiograph showed evidence of healed tuberculosis of the right upper lobe of the lungs and pleural calcification of the right lateral chest wall. His white cell count was 3600 with 47 per cent lymphocytes.

Laparotomy revealed a uniformly pale liver. There were grossly enlarged lymph-nodes, 4–5 cm. in diameter, in the mesentery, around the duodenum, and along the lesser curve of the stomach. There were no lesions of the stomach or the large or small intestines. Milky fluid was aspirated from one of the mesenteric lymph-nodes for culture and one was excised for biopsy. Histology of the lymph-nodes showed typical tuberculous granulomata with central caseation; there were no acid-fast bacilli and culture for *Mycobacterium tuberculosis* proved negative.

The patient was treated with streptomycin, para-aminosalicylic acid, and iso-nicotinic acid hydrazide. He made a good recovery and was fit and well 1 year later, when he was still taking the oral therapy.

DISCUSSION

A number of recent papers have focused attention on tuberculosis of the intestinal tract (Campbell, 1961; Howell and Knapton, 1964; Anscombe, Keddie, and Schofield, 1967) and of the peritoneum (Johnston and Sanford, 1961; Faulkner, 1964; Dowling, 1968). Little has been written about tuberculosis of the reticulo-endothelial system within the abdomen.

Tuberculosis of the intestine is usually divided into ulcerative, hypertrophic, and ulcerohypertrophic. It may occur anywhere from the stomach (Palmer, 1950) to the rectum (Hawley, Wolfe, and Fullerton, 1968), but the ileocaecal area is the most common site affected (Abrams and Holden, 1964).

In ulcerative tuberculosis the clinical picture is often dominated by the pulmonary tuberculosis, but the abdominal complaints of diarrhoea, abdominal pain, loss of weight, and sometimes an abdominal mass may predominate. In the present *Case* 2 there were no respiratory symptoms of note despite gross radiographic changes. Treatment of these patients is usually by chemotherapy, but it must be remembered that complications requiring surgical intervention, such as adhesions or perforation, can still occur after anti-tuberculous therapy has been started (Sweetman and Wise, 1959).

Patients with hypertrophic ileocaecal tuberculosis usually complain of abdominal pain, change in bowel habit, weight-loss, and general deterioration in health (Anscombe and others, 1967). The finding of an abdominal mass together with the radiological demonstration of a stricture in the caecum or ascending colon makes the diagnosis of Crohn's disease or carcinoma likely. The chest radiograph is often normal (Anand, 1956).

It should be noted that there are typical features of tuberculosis visible on the barium-enema examination. These are a shortened ascending colon with a stricture and an obtuse angle at the ileocaecal junction (Aird, 1957a). Treatment is usually by right hemicolectomy (Anand, 1956; Anscombe and others, 1967), but it would seem wise to give chemotherapy if there is widespread involvement of the peritoneum or of the mesenteric glands. There is little evidence on this point. Histology of the intestinal lesions is often equivocal, but the mesenteric lymph-glands nearly always show caseation (Anand, 1956). Routine culture of the mesenteric glands in equivocal intestinal lesions is a recommended practice.

The association of tuberculosis with carcinoma of the intestine is rare, but tuberculosis has been reported in association with carcinoma of the stomach (Tanner and Swynnerton, 1956). The present *Case* 3 demonstrated tuberculosis in association with carcinoma of the sigmoid colon. Barson and Kirk (1970) have reported this case previously and we agree with their conclusion that tuberculous infection was probably secondary to the carcinoma.

The histological diagnosis of an ileal stricture is often difficult and the picture may be one of non-specific inflammation. Crohn's disease may then be the favoured diagnosis, but evidence of tuberculosis in the mesenteric or retroperitoneal glands indicates tuberculous infection, as in the present *Case* 4.

Tuberculous peritonitis may be acute or chronic in onset, but is usually divided into ascitic or plastic forms. In addition, there is a purulent or caseating peritonitis. Like other authors (Faulkner, 1964) we did not find the differentiation of the varying forms of peritonitis easy. The patients usually present with abdominal swelling or discomfort and pyrexia (as in 3 out of 5 patients in our series). Johnston and Sanford (1961) drew attention to rigors in 4 out of 7 patients in their series. If ascites is present and paracentesis performed, examination of the fluid may be helpful. Thus 3 out of the 6 fluids examined in Johnston and Sanford's (1961) series showed acid-fast bacilli or yielded *Mycobacterium tuberculosis* on culture. A high protein content of the ascitic fluid (> 3 g. per 100 ml.) with a specific gravity of over 1016 is in favour of tuberculous infection (Dowling, 1968). However, the diagnosis is usually by means of laparotomy and biopsy. The appearance of the tubercles on the peritoneum and omentum can easily be mistaken for carcinomatous deposits, and thus biopsy is mandatory (*Case* 9).

Whatever the site of entry of the tuberculous organism, the disease may rarely be found apparently confined to one part of the reticulo-endothelial system of the abdomen.

Case 10 had a large tuberculous external iliac lymph-node presenting as a mass in the right iliac fossa. Barium-enema, gynaecological, and urinary-tract investigations and radiographs of the spine and pelvis were normal.

Tuberculous mesenteric adenitis in children has been recognized for many years (Aird, 1957b, Maingot, 1970) but it is less widely appreciated that this disease may occur in adults. Quattlebaum (1960) reported 5 cases of tuberculosis of the mesenteric and retroperitoneal lymph-glands. The nodes were very large, often palpable on abdominal examination, usually affecting the pancreaticoduodenal and coeliac areas, and sometimes causing duodenal obstruction. Retroperitoneal tuberculous lymph-nodes may also obstruct the ureter (Mitty and Faegenburg, 1964).

The clinical picture in these patients may be very confusing. Gerace, Weed, and Nichols (1959) found that laparotomy in patients with a fever of unknown origin revealed that 7 per cent had tuberculosis as the cause of their fever, and this is often the only way to make the diagnosis in these patients (e.g., *Case* 12).

Primary tuberculosis of the spleen (Aird, 1957c) has received little attention but it seems likely that this occurred in *Case* 11. The spleen was removed as an emergency following a road accident and at that time there was no evidence of abnormality amongst the other intra-abdominal organs. Usually, however, these patients present with malaise and a tender, palpable spleen. Recently, 2 cases of primary tuberculosis of the spleen have been reported by McGowan (1965).

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ACID-FUNDIC SELECTIVE VAGOTOMY OF THE STOMACH WITHOUT DRAINAGE IN THE TREATMENT OF DUODENAL ULCER: TECHNIQUE AND RESULTS*

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SUMMARY

Out of 415 patients with duodenal ulcer undergoing vagotomy in the past 6 years, 198 truncal vagotomies (T.V.) and 217 selective vagotomies (S.V.) were performed. Of the 217 S.V.s, 134 cases had a total selective vagotomy of the stomach (preserving the pyloroduodenal nervous peduncle), and in 83 cases a proximal selective vagotomy was performed (preserving also the antral branches of the two principal nerves of the gastric lesser curve or Latarjet nerves). The authors prefer the name 'acid-fundic selective vagotomy (A.F.S.V.) of the stomach' for the latter procedure.

In 89 of the patients having S.V. no gastric drainage procedure was performed; in 27 of these a total S.V. had been performed and in 62 cases an A.F.S.V.

In patients undergoing S.V. without gastric drainage the clinical results and gastric emptying were fairly good in the cases with a total S.V. (follow-up time, 12 months), and very good in the cases with an A.F.S.V. (follow-up time, 6 months). Basal acid output (B.A.O.) and maximal (pentagastrin-stimulated) acid output (M.A.O.) were evaluated in those patients undergoing A.F.S.V. before and 10 days after operation. B.A.O. was reduced by 80·5 per cent and M.A.O. by 68·5 per cent. An insulin test performed 3 months after operation was negative in 80 per cent of cases (complete vagotomy); in the other cases the vagotomy was adequate.

Clinical results, although after only a short follow-up, suggest that the procedure can be considered as the treatment of choice in most patients with an uncomplicated duodenal ulcer (76 per cent in our series). Gastric drainage is required only in cases of stenosing duodenal ulcer with delayed gastric emptying. Pyloroplasty is also mandatory in the treatment of bleeding ulcer and of perforated ulcer (if the suture is stenosing).

TOTAL selective vagotomy inhibits acid secretion and antral motility. To prevent gastric stasis it is necessary to perform a pyloroplasty. This method has complications (leakage) and side-effects (dumping syndrome, duodenal regurgitation, diarrhoea) which are mainly the result of a lack of duodenal regulation of gastric emptying, as McKelvey (1970) has recently demonstrated.

By preserving the pyloroduodenal peduncle (arising from the hepatic plexus of the anterior vagal trunk) Burge and Frohn (1969) have been able to perform a number of total selective vagotomies without drainage.

Our first results after total selective vagotomy without drainage were fairly satisfactory in some selected cases; in other cases delayed gastric emptying followed (Imperati, Natale, and Marinaccio, 1970).

More encouraging results have been obtained by confining the denervation to the acid- and pepsin-secreting area so that the distal 5–7 cm. of the stomach were left innervated. This procedure has been called 'vagal denervation of parietal cell mass' (Griffith and Harkins, 1957), 'proximal selective vagotomy' (Holle, 1967), or 'highly selective vagotomy' (Johnston and Wilkinson, 1970); we prefer the term 'acid-fundic selective vagotomy of the stomach' (*Fig.* 1). This operation, preserving the normal motility and emptying of the stomach, can be performed without gastric drainage in all uncomplicated duodenal ulcer patients.

MATERIALS AND METHODS

Four hundred and fifteen consecutive duodenal ulcer patients (January 1965–March, 1971) have had a vagotomy procedure; 198 had a truncal subdiaphragmatic vagotomy and 217 had selective vagotomy (*Table I*). In 83 cases the selective vagotomy was limited to the acid-fundic area.

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* Based on a paper presented to the Fourth World Congress of Gastro-enterology at Copenhagen on 17 July, 1970, and a paper presented to the First World Congress of Digestive Surgery at San Remo on 22 May, 1971.

In 89 patients selective vagotomy was performed without gastric drainage; 27 of these had been treated by total selective vagotomy and 62 by acid-fundic selective vagotomy (*Table II*). Gastric drainage was not performed in patients with a gastric emptying time of 4 hours or less with no evidence of pyloroduodenal stenosis at operation.

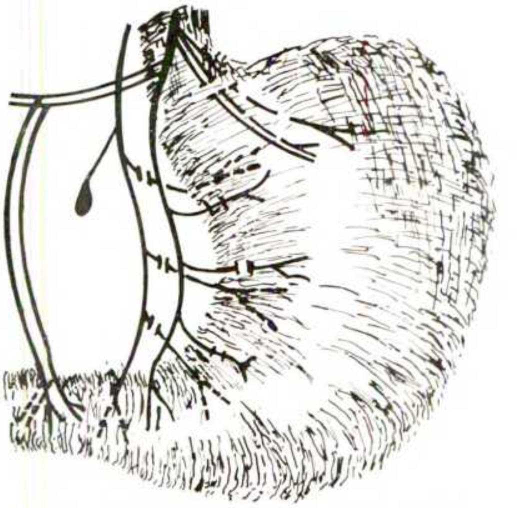

FIG. 1.—Diagram of the acid-fundic selective vagotomy.

Table I.—TYPE OF VAGOTOMY PERFORMED

Type of Vagotomy		*No. of Patients*
Truncal		198
Total selective	134	217
Acid-fundic selective	83	
		415

Table II.—GASTRIC DRAINAGE IN PATIENTS UNDERGOING VAGOTOMY FOR DUODENAL ULCER

TYPE OF VAGOTOMY	GASTRIC DRAINAGE	NO GASTRIC DRAINAGE	TOTAL	MORTALITY
Total selective	107	27 (2)	134	1
Acid-fundic selective	21	62 (7)	83	0
Total	128	89 (9)	217	1

Number of perforated duodenal ulcers is shown in parentheses.

Nine of the patients treated by selective vagotomy had a perforated ulcer of the anterior wall of the duodenum; a simple suture of the perforation was sufficient in these cases. The technique of total selective vagotomy has been described elsewhere (Natale, Marinaccio, and Pellegrino, 1969).

Operative Technique of A.F.S.V.—

Step 1.—The anterior nerve of Latarjet is demonstrated in the lesser omentum 1–2 cm. from the lesser curve up to its terminal branches to the antrum 6–7 cm. from the pylorus. The lesser curve is then separated from the lesser omentum leaving intact the nerve of Latarjet and its terminal branches on the antrum (*Fig.* 2); the dissection is begun near the incisura (*see arrow, Fig.* 2) and is continued upwards to the cardia; nerve-fibres arising from the nerve of Latarjet and blood-vessels are divided close to the stomach. The dissection is then continued to the cardia; the gastric fundus and the cardia are mobilized so that all the anterior nerve-fibres to the stomach are divided.

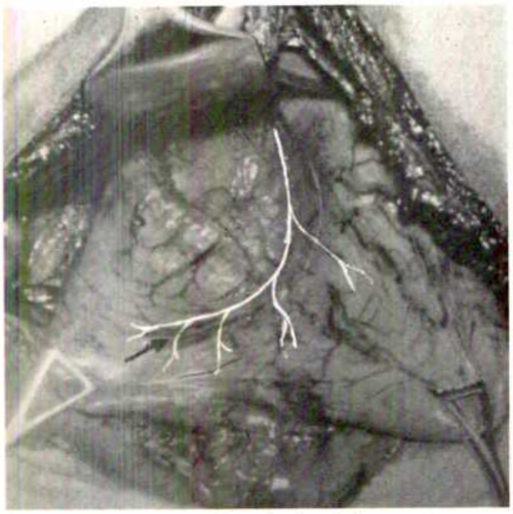

FIG. 2.—The course and distribution of the anterior nerve of Latarjet. The dissection begins at the point indicated with an arrow, leaving the antrum innervated.

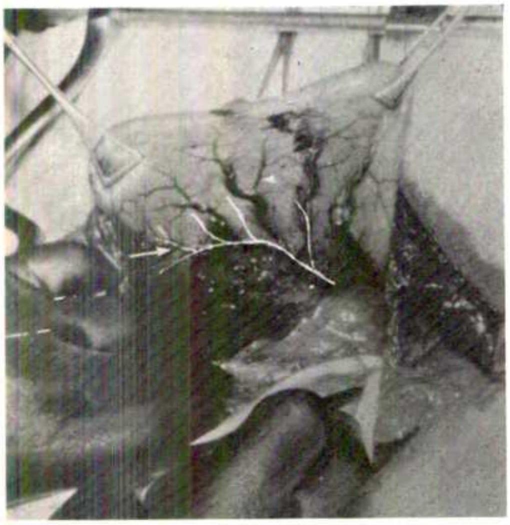

FIG. 3.—The course and distribution of the posterior nerve of Latarjet (the gastrocolic ligamant has been opened and the lesser sac penetrated). The dissection begins at the point indicated with an arrow.

Step 2.—The gastrocolic ligament is opened and the lesser sac is penetrated. The posterior walls of the stomach and of the lesser omentum are visualized and the posterior nerve of Latarjet demonstrated; its terminal branches to the antrum are preserved (*Fig.* 3).

The dissection begins near the incisura (*see arrow, Fig.* 3) and proceeds upwards. The lesser omentum is thus detached from the lesser curve. Finally, the cardia and the abdominal oesophagus are denervated.

RESULTS

1. Clinical Results.—The postoperative course of the patients who were treated by acid-fundic selective vagotomy has been very satisfactory. There was no mortality. The ulcer pain disappeared immediately after operation. Intravenous infusions were performed only during the first 24–36 hours. The patients had a liquid diet on the second and third postoperative days, and on the fourth day they were started on a solid diet. A small number (4·8 per cent) of patients had delayed gastric emptying (more than 300 ml. of resting juice after an overnight fast). In contrast delayed gastric emptying was present in 11·1 per cent of patients treated by total selective vagotomy without drainage (*Table III*).

Table III.—DELAYED GASTRIC EMPTYING AFTER SELECTIVE VAGOTOMY WITHOUT DRAINAGE (TUBE SUCTION)

Type of Vagotomy	*Patients with Delayed Gastric Emptying* (per cent)
Total selective	11·1
Acid-fundic selective	4·8

Long-term Results (3–10 months after surgery).—Eating tolerance (*Table IV*) was very good in 86·49 per cent and good in 13·51 per cent of the cases. Body-weight (*Table V*) had increased in most of the cases (86·49 per cent), was steady in 10·81 per cent, and had decreased in 2·70 per cent. The dumping syndrome (*Table VI*) did not occur in the patients who had undergone selective vagotomy without gastric drainage, but was present in 5·5 per cent of the patients who had had a gastric drainage operation.

Table IV.—EATING TOLERANCE 3–10 MONTHS AFTER ACID-FUNDIC SELECTIVE VAGOTOMY WITHOUT DRAINAGE

Eating Tolerance	*Percentage of Patients*
Very good (4/4)	86·49
Fairly good (3/4)	13·51
Poor (1/2)	0

Table V.—BODY-WEIGHT 3–10 MONTHS AFTER ACID-FUNDIC SELECTIVE VAGOTOMY WITHOUT DRAINAGE

Body-weight	*Percentage of Patients*
Increased	86·49
Steady	10·81
Decreased	2·70

Table VI.—PRESENCE OF THE DUMPING SYNDROME 3–10 MONTHS AFTER SELECTIVE VAGOTOMY

Gastric Drainage	*Percentage of Patients*
With gastric drainage	5·5
Without gastric drainage	0

According to Visick criteria the results in our series are as follows: grade 1 (very good), 86·49 per cent; grade 2 (good), 10·81 per cent; grade 3 (fairly good), 2·70 per cent (*Table VII*).

2. Gastric Secretion.—Gastric secretion was studied prior to surgery in all the patients. The tests were performed after an overnight fast. Gastric content was aspirated by means of a nasogastric tube, and some gastric juice was titrated with *N*/10 sodium hydroxide using phenol red as an indicator. The following data were evaluated: 1-hour basal acid output (B.A.O.); maximal acid output (M.A.O.) after pentagastrin stimulation (6 μg. per kg. body-weight i.m.) for 1 hour following the initial 30 minutes.

Average values obtained were: B.A.O., 8·8 mEq. per hour; M.A.O., 36·5 mEq. per hour. The B.A.O. and M.A.O. were re-evaluated 10 days after acid-fundic selective vagotomy of the stomach. At that time average values were 1·8 mEq. per hour for the B.A.O., and 11·4 mEq. per hour for the M.A.O. The reduction in B.A.O. was 80·5 per cent and in M.A.O. 68·5 per cent (*Table VIII*).

Table VII.—VISICK'S GRADES 3–10 MONTHS AFTER ACID-FUNDIC SELECTIVE VAGOTOMY WITHOUT DRAINAGE

Visick's Grade	*Percentage of Patients*
1	86·49
2	10·81
3	2·70
4	0

Table VIII.—ACID SECRETION BEFORE AND AFTER ACID-FUNDIC SELECTIVE VAGOTOMY

ACID SECRETION INDEX	ACID SECRETION		
	Before Operation (mEq. per hour)	10 Days after Operation (mEq. per hour)	Reduction (per cent)
B.A.O.	8·8	1·8	80·5
M.A.O.	36·5	11·4	68·5

Table IX.—INSULIN TEST (HOLLANDER) 3–10 MONTHS AFTER ACID-FUNDIC SELECTIVE VAGOTOMY

Test	*Percentage of Patients*
Negative	80
Late positive	20
Early positive	0

Table X.—GASTRIC EMPTYING 3–10 MONTHS AFTER ACID-FUNDIC SELECTIVE VAGOTOMY WITHOUT DRAINAGE

Gastric Emptying	*Percentage of Patients*
Within 4 hours	92·0
Within 6 hours	5·3
After 6 hours	2·7

3. Completeness of Vagotomy: Insulin Test.—To establish the completeness of vagotomy insulin tests were performed 4 months after surgery in the patients treated by acid-fundic selective vagotomy. Twelve 15-minute collections of gastric juice were made, 4 before and 8 after insulin administration (0·2 U. per kg.).

The secretory response to insulin was evaluated according to the Hollander criteria (Kallehauge and Amdrup, 1969); the vagotomy was considered complete if the insulin test was negative, adequate if the test was positive in the second hour (late positive test), and incomplete if the test was positive in the first hour (early positive test). In this series the test was negative in 80 per cent of the cases and late positive in 20 per cent (*Table IX*).

4. Gastric Emptying: Radiological Findings.—After acid-fundic selective vagotomy without gastric drainage radiographic examination 5 months after surgery (*Table X*) showed complete emptying of the stomach within 4 hours in 92 per cent of the patients, within 6 hours in 5·3 per cent, and after 6 hours in 2·7 per cent. These results were far better than those after total selective vagotomy without gastric drainage.

CONCLUSIONS

The clinical and secretory results in the present series support the following conclusions:—

1. Acid-fundic selective vagotomy achieves a complete denervation of the parietal cell mass and reduces basal and stimulated acid gastric secretion to the same extent as total selective (or truncal) vagotomy.
2. Acid-fundic selective vagotomy, preserving the vagal branches of the antrum, does not affect gastric emptying and makes gastric drainage unnecessary.

The clinical results, although after only a short follow-up, suggest that the procedure can be considered as the treatment of choice in most patients with an uncomplicated duodenal ulcer (76 per cent in our series). The gastric drainage procedure is required only in cases of stenosing duodenal ulcer with delayed gastric emptying. Pyloroplasty is also mandatory in the treatment of bleeding ulcer and of perforated ulcer (if the suture is stenosing).

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A RANDOMIZED PROSPECTIVE TRIAL COMPARING THREE ESTABLISHED METHODS OF GASTRIC DECOMPRESSION AFTER VAGOTOMY

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SUMMARY

One hundred and thirty-two patients who were about to undergo vagotomy and drainage were randomly allocated nasogastric tubes, gastrostomy tubes, or no decompression postoperatively. Significantly fewer patients with no decompression developed respiratory infections postoperatively. The role of smoking in the production of postoperative chest complications was again confirmed. Neither the choice of decompression nor its absence appeared to affect postoperative electrolyte control. Postoperative dysphagia was more common in the group with a nasogastric tube. Wound infections were commoner in the gastrostomy group. While most patients with gastrostomies expressed a preference for this type of decompression a proportion of those with nasogastric tubes expressed a preference for a gastrostomy.

IT is not generally agreed that gastric decompression is required after vagotomy with drainage, nor indeed do those who feel decompression to be necessary agree on the method of choice. Soon after the introduction of the nasogastric tube came reports of complications due to irritation, pressure, and disturbed function of the cardia. These have previously been summarized by Farris and Smith (1956).

Gastrostomy was suggested as a means of decompression over 30 years ago by Horsley (1939) and seemed to have several advantages in general use. Nasopharyngeal pressure and irritation were removed and there was no interference with function of the cardia. It was inevitable, however, that complications of gastrostomy should be reported, ranging from fistula formation to peritonitis. Barnes and Williams (1967) found that wound infections could be a problem particularly when the gastrostomy was sited near the main wound. When the gastrostomy was used for feeding purposes as well as for decompression deep venous thrombosis was noted and a curiously high incidence of dysphagia was recorded (Hamer, Wellwood, and Cox, 1969).

A retrospective review of 174 patients who had had a gastrostomy performed in the Victoria Infirmary, Glasgow, did not confirm this high incidence of dysphagia. Only 2 cases (1·2 per cent) were found. Four patients (2·3 per cent) were found to have developed deep venous thrombosis, 60 (34·5 per cent) had respiratory infections, and 34 (19 per cent) had identifiable electrolyte disturbances. No case of fistula formation was encountered. Although retrospective studies have been performed comparing gastrostomy and nasogastric decompression (Grant, Elliot, and Frederick, 1962; Hamer and others, 1969) no randomized prospective trial comparing nasogastric tubes, gastrostomies, and no decompression has been reported. The following study was therefore undertaken.

MATERIALS AND METHODS

A consecutive series of 132 patients who underwent vagotomy between August, 1969, and December, 1970, was studied prospectively. There were 100 males and 32 females with ages ranging from 16 to 74 years (mean 44·5 years). A duodenal ulcer was present in 127 cases, including 10 patients who were operated on because of bleeding, and 4 who had a perforated ulcer. The remaining 5 patients had a gastric ulcer which was excised by wedge resection in 3 cases and biopsied in 2.

Table I.—DISTRIBUTION OF COMPLICATIONS BETWEEN THE THREE GROUPS OF PATIENTS

COMPLICATIONS	TOTAL		NASOGASTRIC GROUP	GASTROSTOMY GROUP	NO TUBE GROUP
	No.	Per cent			
Electrolyte depletion	47	36	16	14	17
Chest infection	57	43	24*	21	12*
Wound infection	17	13	6	9*	2*
Dysphagia	9	6·9	6*	2	1*
Total No. of patients in each group	132		47	43	43

* Significant difference (*see Table III*).

Vagotomy was performed with a gastro-enterostomy in 103 patients and with a Heineke-Mikulicz pyloroplasty in 29. Four patients had, in addition, a hiatus hernia which was repaired during the operation.

The patients were divided into three groups by random selection based on the month of their birth. In the first group of 47 patients a nasogastric tube passed before operation was kept in place for 48 hours postoperatively. In the second group of 43 patients in place of the nasogastric tube a temporary gastrostomy was established using a Foley catheter which was removed after 8 days. The stomach was not fixed in any way to the parietal peritoneum. The remaining 42 patients were treated without decompression. A nasogastric tube could be passed whenever clinically indicated in this last group, but was required, because of paralytic ileus, by only 1 patient from the second to the ninth postoperative days.

Intravenous fluids were continued for a minimum of 48 hours after operation in all the cases. Electrolyte estimations were made before operation and twice in the first 4 days postoperatively. The patients were observed for evidence of chest or wound infection, a pyrexia of 37·3° C. or over, deep venous thrombosis, or pulmonary embolism. Before discharge from the ward the patients who had had nasogastric or gastrostomy tubes were asked to complete a questionnaire regarding the symptoms caused by the drainage tube. All the patients were asked both on discharge and 1–2 months after operation if they had experienced any postoperative dysphagia.

RESULTS (*Tables I, II, III*)

Electrolyte Depletion.—The serum-sodium level fell in several of the patients after operation and was accompanied by a less pronounced fall in serum chloride and potassium. For the purpose of comparison of the different groups a serum-sodium level of 133 mEq./l. or less was taken as evidence of sodium depletion. This was found in 47 of the 132 patients (34·6 per cent); 16 were in the nasogastric group, 14 in the gastrostomy group, and 17 among those with no drainage tube. As the differences between these groups are not significant the choice of drainage tube does not appear to affect the electrolyte depletion.

Table II.—PATIENTS' REACTIONS TO METHOD OF DECOMPRESSION

METHOD OF DECOMPRESSION	TOTAL	SYMPTOMS		CHOICE	
		Bearable	Distressing	Same	Change
Nasogastric tube	47	14	33	28*	19
Gastrostomy tube	43	36	7	40*	3

* Significant difference (*see Table III*).

Table III.—STATISTICAL ANALYSIS OF THE RESULTS

COMPARISON	χ^2	*P*
Chest infection	4·66	< 0·05 > 0·025
Wound infection	4·93	< 0·05 > 0·025
Dysphagia	5·84	< 0·025 > 0·0125
Patients' choice	13·60	< 0·001

Chest Infection.—Clinical signs of a chest infection with either a pyrexia of 37·3° C. or over, or a positive sputum culture, or radiological evidence were present in 57 of the 132 patients (43 per cent). Of these, 24 had had a nasogastric tube, 21 a gastrostomy tube, and 12 were in the group with no drainage tube. The difference in the rate of chest infection between the nasogastric group and those with no tube is statistically significant.

The number of patients who smoked cigarettes was 98 (74 per cent); 64 smoked 20 or more per day. Of the 57 patients with chest infection, 51 (89·4 per cent) were smokers and only 6 (10·6 per cent) were non-smokers. This is a significant difference confirming that smoking is a factor in producing postoperative chest infection.

Wound Infection.—Wound infection occurred in 6 patients of the nasogastric group, 9 of the gastrostomy group, and 2 of those without a tube, giving a total of 17 (12·9 per cent). There is a statistically significant difference between the rates of infection in the gastrostomy group and in the group with no tube.

Dysphagia.—Two patients who had had repair of a hiatus hernia complained of mild dysphagia as soon as oral feeding was commenced after operation. This temporary dysphagia appeared to be due to the operative procedure. Of the remaining 130 patients, 9 (6·9 per cent) developed post-vagotomy dysphagia

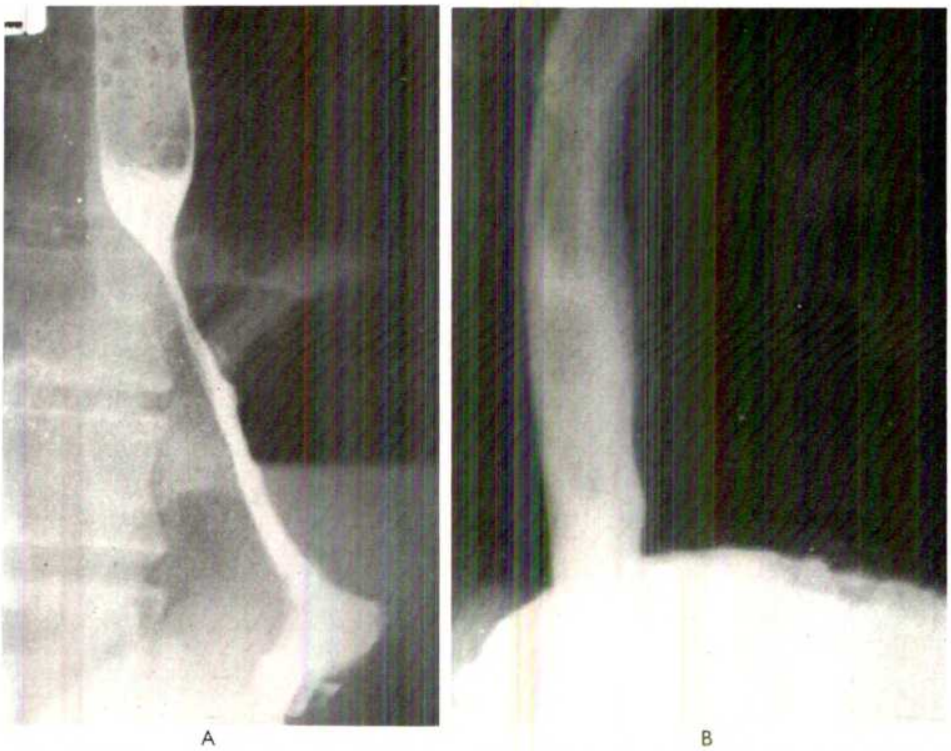

FIG. 1.—A, Barium-swallow film of a patient with troublesome dysphagia 4 weeks following vagotomy. B, Final appearance 4 months later.

between 12 and 28 days (mean 17 days) postoperatively. In 8 of the patients this lasted from a few days to 4 weeks until it settled spontaneously. The symptoms were distressing but varied in severity. In most cases the dysphagia occurred only with solid food, and in 1 case it was intermittent. These patients were symptom-free when seen at the outpatients' clinic and no treatment was required. The ninth patient developed more troublesome dysphagia and was readmitted 4 weeks after operation complaining of pain when swallowing food. A barium-swallow examination revealed a smooth stricture of the lower end of the oesophagus (*Fig.* 1 A) and on oesophagoscopy inflammation of the mucosa was seen at the site of the stricture. After bouginage the symptoms improved and eventually settled completely. A second barium swallow a few months later showed a normal oesophagus (*Fig.* 1 B).

Six of the 9 patients with dysphagia had had nasogastric intubation, while 2 came from the gastrostomy group and 1 had had no drainage tube. Pyloroplasty was the operative procedure in 4 of the 9 patients.

Other Complications.—There were no deaths in the series and none of the 132 patients developed clinical evidence of deep venous thrombosis or pulmonary embolism. Wound rupture occurred in 2 patients and 4 developed an incisional hernia. Two of the gastrostomy group were readmitted with pyrexia, possibly due to intraperitoneal infection, which settled with antibiotic therapy. In 2 patients a gastro-enterostomy was converted to a pyloroplasty because of obstruction at the stoma.

The Patients' Opinion of the Drainage Tube (*Table II*).—In the nasogastric group 14 of the 47 patients found the symptoms caused by the tube 'bearable', while the remaining 33 found them 'unpleasant' or 'distressing'. Nineteen patients in this group thought a gastrostomy would have been preferable if a choice were possible.

Of those with a gastrostomy tube, 36 of the 43 patients described the symptoms as 'bearable', and 40 would choose a gastrostomy again, only 3 electing to change to a nasogastric tube.

DISCUSSION

It is to be expected that the free drainage provided by a gastrostomy might lead to electrolyte depletion, and gastrostomy tubes have been devised with feeding limbs to allow gastric secretion to be returned to the duodenum (Kay, 1964). In our retrospective analysis we found only 19 per cent with depleted electrolytes. This was obviously a low percentage probably because of lack of information. Particular care, therefore, was taken in this prospective study to estimate electrolytes at the specified intervals. It is interesting that not only were the percentages of electrolyte deficiency in the gastrostomy and nasogastric tube patients the same, as found by Hamer and others (1969), but that a similar proportion of patients with no decompression should develop electrolyte abnormalities.

Grant and others (1962) stated that a gastrostomy tube reduces the incidence of chest infections, and this is advanced as a good theoretical indication for gastrostomy. The present trial offers good evidence that the choice of decompression does not influence the occurrence of postoperative chest infections. The low chest-infection rate in patients with no decompression is interesting and gives further weight to the suggestion that no decompression at all should be used until there is established evidence of paralytic ileus (Gunn, 1970). The effect of smoking is marked and underlines another hazard of this habit. As the period of the trial covered a whole year the seasonal variations in respiratory infections should have balanced.

It is not surprising that with such a potential source of infection nearby wound sepsis should occur after gastrostomy. We experienced a higher incidence of wound infection, even with gastrostomies placed well away from the main incision. Two patients developed evidence of peritoneal irritation following gastrostomy. Nevertheless, we do not feel that the wall of the stomach should be sutured to parietal peritoneum. Several patients from our retrospective series either underwent further surgery or came to post-mortem examination from other causes when it was noted that there was very little trace of the transomental gastrostomy. Furthermore, anchoring the stomach to the abdominal wall may carry the risk of future traumatic perforation (Grant and others, 1962).

As part of the present study the patients were questioned carefully about dysphagia both in hospital and after discharge. We found 9 patients (6·9 per cent) who developed dysphagia that could be attributed to their vagotomy. Six of these patients had had a nasogastric tube passed. The other 3 at no time had a nasogastric tube passed. The aetiology of the dysphagia, which usually appears 7–14 days after vagotomy, is uncertain. Three varieties have been described based on clinical signs and symptoms:—

1. *Dysphagia without Pain.*—The mucosa of the oesophagus appears normal on oesophagoscopy and a barium swallow reveals narrowing at its terminal part. There is thought to be a neural factor in its production following vagal section, particularly by the transthoracic route. Most of our cases were of this type.

2. *Dysphagia with Oesophagitis.*—In this group pain is associated with the dysphagia. Oesophagoscopy shows inflammation of the lower oesophagus and a barium swallow shows narrowing at the lower end of the oesophagus. *Fig.* 1 shows the barium-swallow film of the 1 patient in our series with marked dysphagia who appeared to fall into this group.

3. *Peri-oesophageal Cuff.*—The dysphagia in this group is more marked than group 1. Oesophagoscopy shows normal mucosa but with an appearance of extrinsic pressure. Barium swallow confirms the narrowing. In severe cases operation may be required to divide the cuff (Bruce and Small, 1956).

Whether these varieties are separate entities is open to doubt. They could all be features of a single process. The mildest form would be a little local oedema and damage to oesophageal muscle, and in the severe forms an organized fibrous cuff develops as a progression of the same progress. The occurrence of oesophagitis in some of the patients could well be related to nasogastric intubation. One possible factor could be that a diligent search for vagal fibres traumatizes the oesophagus against the nasogastric tube. Indeed we were impressed by the ease of performing vagotomy with no tube in place during the trial.

It is generally agreed that nasogastric tubes are uncomfortable. It seemed reasonable to seek the patients' opinion, particularly to determine if gastrostomies were better tolerated. There is no doubt that patients do find a gastrostomy more comfortable.

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INFLAMMATORY ANEURYSMS OF THE ABDOMINAL AORTA

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SUMMARY

Two hundred and seventeen patients presenting with abdominal aneurysms in the Department of Surgery at the Manchester Royal Infirmary between the years 1958–69 were surveyed retrospectively.

One hundred and eighty-seven of the patients underwent operation for resection of their aneurysms; of these, 19 (10 per cent) showed excessive thickening of the aneurysm walls and perianeurysmal adhesions at operation.

Subsequent histological examination of the walls of these unusual aneurysms showed extensive active chronic inflammatory changes, including plasma-cell infiltration.

This group of patients whose aneurysms we describe as 'inflammatory' presented with different clinical features in comparison with the atherosclerotic group.

Retrospective investigation has not yet revealed any aetiological factors. We feel that 'inflammatory' aneurysms are a discrete entity with significant differences from atherosclerotic aneurysms and previously described arteritis.

Two hundred and seventeen patients presented with abdominal aortic aneurysms at the University Department of Surgery at the Manchester Royal Infirmary over the period 1958–69 and of these, 187 underwent operative treatment with the intention of resection of their aneurysms.

One hundred and sixty-eight patients were found to have aneurysms of the atherosclerotic type. In the remaining 19 cases the aneurysms were unusually thick walled and surrounded by extensive fibrous adhesions which made operative procedures much more difficult. On 2 occasions aneurysms described at operation as 'surrounded by dense fibrous tissue' and 'densely adherent', respectively, were encountered before this investigation was undertaken. These 2 cases were probably of the 'inflammatory' type, but owing to the lack of histological verification have not been included in the series. Specimens of the aneurysm walls from this group of 19 cases were subjected to detailed histological examination and bacterial culture, the case records of all 19 patients were reviewed, and haematological, biochemical, and immunological investigations were carried out on the surviving patients.

Despite their striking operative appearance and significant incidence these aortic lesions, as far as we are aware, have not been previously described.

OPERATIVE APPEARANCE

In common with most abdominal aortic aneurysms the 'inflammatory' aneurysms are usually confined to the abdominal aorta between the renal arteries and aortic bifurcation; on only 1 occasion has there been involvement of the renal arteries.

The inflammatory aneurysm has a thick, firm, smooth wall which is shiny white in appearance although there is an obvious increase in the vascularity of the wall with multiple small vessels traversing it. The adjacent dense fibrosis is marked and may involve adjoining tissues and structures. In 1 case fibrosis was particularly marked in the tissues around the common iliac vessels, involving the ureters but not the vessels themselves. Resection of the aneurysm was not performed in this particular case because of the density of the fibrosis. This patient died 28 days after his laparotomy and autopsy showed bilateral hydronephrosis and hydro-ureter due to fibrosis in the retroperitoneal tissue.

On section the wall of the aneurysm is thickened up to 1·5 cm. and has a characteristic fleshy appearance with an increase in the vascularity. The dense fibrosis makes dissection of the adjacent structures, such as the sigmoid colon and duodenum, difficult. This may be particularly marked around the accompanying veins and separation of the inferior vena cava and left common iliac veins may be hazardous.

PATHOLOGY

Formalin-fixed tissue representing resected portions of the aneurysm walls was examined as paraffin sections after staining with haemalum and eosin, Victoria blue/Van Gieson for elastic tissue, the M.S.B. method of Lendrum, Fraser, Slidders, and Henderson (1962), the periodic acid-Schiff, and Mallory's phostungstic acid-haematoxylin techniques.

Sections from most specimens were also examined for bacteria and fungi. Frozen sections of fixed material were examined for neutral fat after Sudan IV staining and by polarized light for possible refractile content.

PATHOLOGICAL RESULTS

Macroscopic Appearances.—Specimens representing full-thickness strips or portions of aneurysm walls measured up to 7 cm. in length. Their most striking feature was the increased wall thickness which ranged from 0·5 to 1·5 cm. in cross-section.

Microscopic Appearances.—Thrombus was present on the luminal surface in all the cases, and significant atheromatous infiltrations were present in 6 and these showed disruption of their internal elastic laminae, occasionally with calcification.

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The media showed loss of smooth muscle, extensive loss or fragmentation of elastic fibres, variable inflammatory infiltration, and collagenization. In contrast with the usual atherosclerotic aneurysm the adventitial coats of all the specimens were markedly thickened (*Fig.* 1). In some instances medial and adventitial coats were fused to form a continuous fibro-inflammatory sheath densely infiltrated with lymphocytes, plasma cells, and histiocytes including occasional giant-cell forms and small granulomata. The inflammatory infiltrates varied in density and distribution: some as lymphoid aggregates or follicles (*Fig.* 2), and others as perivascular infiltrates with a high plasma-cell content around numerous adventitial vessels (*Fig.* 3) or diffused throughout the entire adventitial layer (*Fig.* 4). In 4 cases fibrin thrombi were present in the small penetrating vessels of the thickened adventitia (*Fig.* 5), and in 2 cases focal necrosis with polymorphonuclear infiltrations was present. The excess connective tissue was almost entirely collagenous; elastic fibres were absent or represented by trace fibres only. Transected nerves were prominent in the fibrous mass, and occasional penetrating lumbar arteries were either thrombosed and recanalized or occluded by endarteritis. Variable

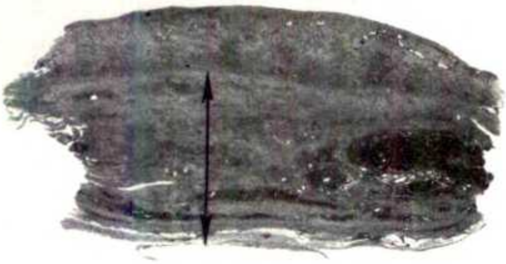

FIG. 1.—'Inflammatory' aneurysm showing thickening of the adventitia. H. and E. (× 3.)

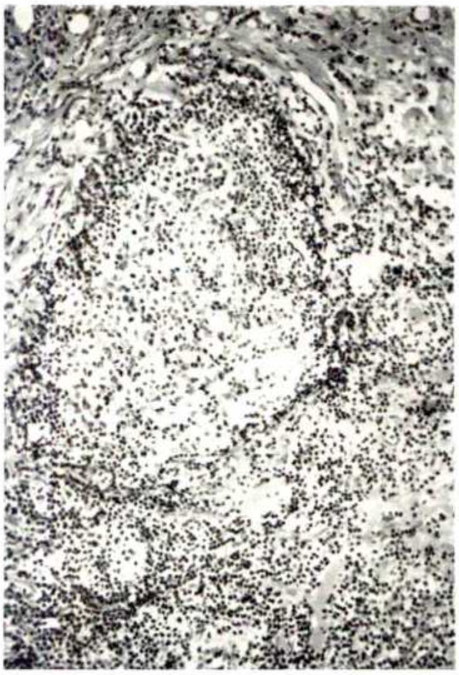

FIG. 2.—Lymphoid follicles in adventitia. H. and E. (× 75.)

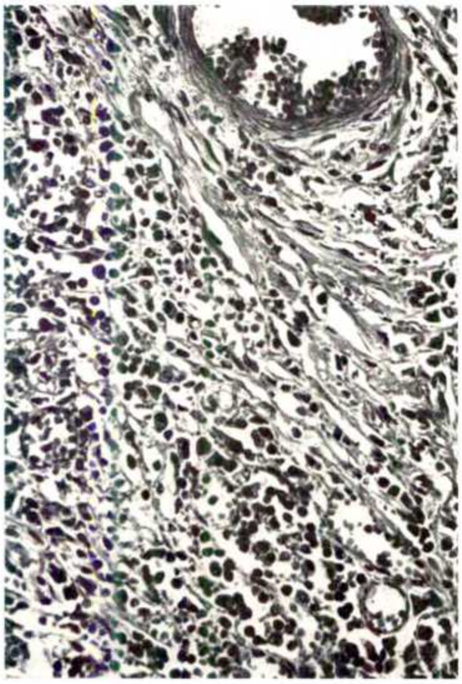

FIG. 3.—Perivascular lymphocytes and plasma-cell infiltrates in adventitia. Lendrum's M.S.B. (× 240.)

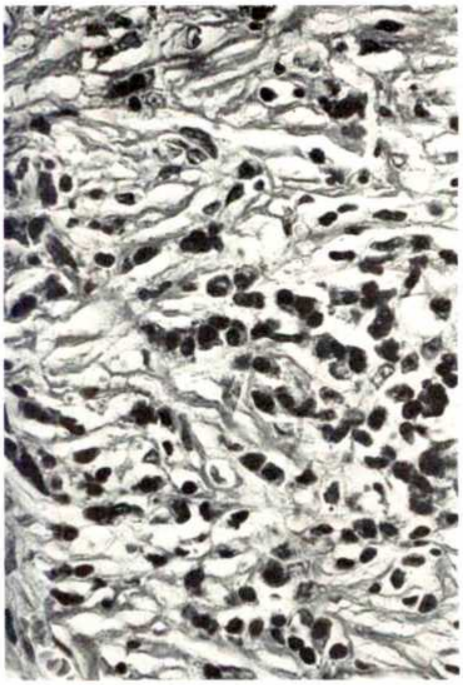

FIG. 4.—Prominent plasma cells in adventitial inflammatory infiltrates. Lendrum's M.S.B. (× 563.)

amounts of neutral fat diffusely infiltrated by inflammatory cells occurred throughout the fibrous tissue. No bacteria or fungi were identified and cultures of fresh aneurysm tissue failed to produce growth of micro-organisms.

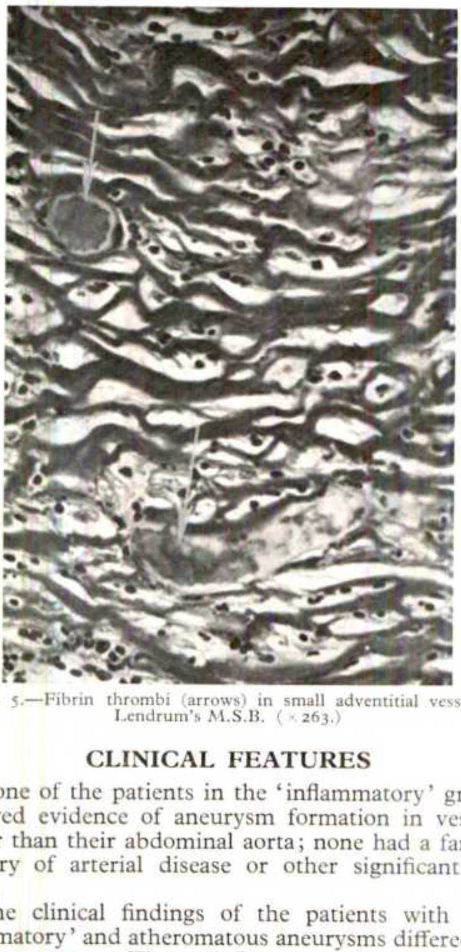

FIG. 5.—Fibrin thrombi (arrows) in small adventitial vessels. Lendrum's M.S.B. (× 263.)

CLINICAL FEATURES

None of the patients in the 'inflammatory' group showed evidence of aneurysm formation in vessels other than their abdominal aorta; none had a family history of arterial disease or other significant illness.

The clinical findings of the patients with 'inflammatory' and atheromatous aneurysms differed.

Age-range.—The 'inflammatory' aneurysms tended to occur in a younger age-group with an age-range of 42–71 years (average age, 62 years), as opposed to the atherosclerotic group where ages ranged from 55 to 86 years (average age, 72 years).

Incidence of Rupture.—The incidence of rupture in the two groups of aneurysms differed. Three of the 19 patients (15 per cent) of the 'inflammatory' group presented after rupture of their aneurysms, whereas in the atherosclerotic group rupture had occurred in 65 patients (40 per cent).

Sex.—Two of the patients with inflammatory aneurysms were females, an incidence of 10 per cent which also applied to this series as a whole and which conforms to the 1 : 9 female to male ratio for atherosclerotic aneurysms (DeBakey, Crawford, Cooley, Morris, Royster, and Abbott, 1964).

Peripheral Arterial State.—None of the patients with inflammatory aneurysms complained of intermittent claudication and a full complement of peripheral pulses was noted in 15 of the 19 cases. No record was made in 3 patients and 1 was noted to have absent popliteal and foot pulses. These findings suggest the absence of gross occlusive arterial disease. In the atherosclerotic group 16 (15·5 per cent) of those presenting without rupture complained primarily of intermittent claudication. Furthermore, 72 (70 per cent) were noted to have one or more peripheral pulses absent preoperatively.

Aortograms were not performed on any of the cases as we feel that this procedure is not necessary and may in fact be hazardous.

Hypertension.—Patients with a diastolic blood-pressure of more than 100 mm. Hg or a systolic blood-pressure of more than 170 mm. Hg were considered to be hypertensive. With these criteria hypertension was noted in only 3 of the 16 cases who presented without rupture of their aneurysms, an incidence of 19 per cent. In the series as a whole hypertension was noted in 65 (63·1 per cent) of the patients who had had a preoperative record made. This of course excludes the majority of the ruptured aneurysms.

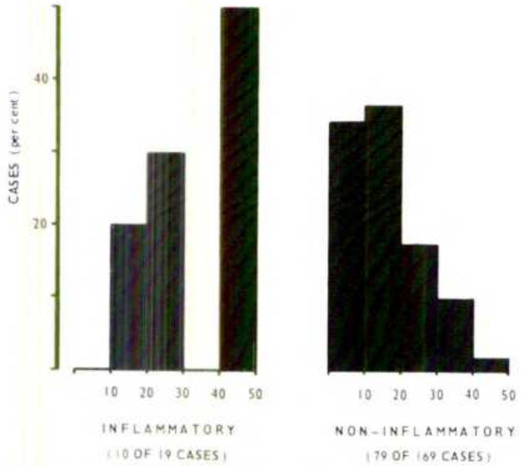

FIG. 6.—Comparative histogram of the preoperative E.S.R. in inflammatory and non-inflammatory cases.

Presentation.—In the 'inflammatory' group there were no unusual presenting features. Five patients presented with pulsatile abdominal masses, 4 with backache, and 4 with abdominal pain. One patient had duodenal obstruction and previous backache and 2 were asymptomatic.

The 3 remaining cases presented with ruptured aneurysms; of these, 2 had suffered backache, the third having been symptom-free.

Length of History.—This varied between 1 and 12 months. The patients showed no associated pattern of illness and were indeed surprisingly well considering the nature of their aortic lesions.

CLINICAL INVESTIGATIONS AND COURSE

Erythrocyte Sedimentation Rate.—Estimation of the preoperative erythrocyte sedimentation rate (E.S.R.) was performed by the Wintrobe method (Wintrobe and Landsberg, 1935) in 10 of the 19 cases (*Table I*); all were either at the upper limit of normal or above for their respective ages (Olbrich, 1948). In 5 cases the preoperative E.S.R. was above 40 mm. in the first hour, anaemia not being present in any. In contrast, the preoperative E.S.R. estimated in 79 of the 168 non-inflammatory cases was more than 20 mm. in the first hour in 23 cases (29 per cent) and below this rate in 56 (71 per cent).

Table I.—Preoperative E.S.R. in 10 Cases with 'Inflammatory' Aneurysms

Age and Sex of Patient	*E.S.R.* (mm. in first hr.)
67 M.	15
66 M.	19
66 M.	21
71 F.	21
60 M.	22
65 M.	41
64 F.	42
57 M.	43
69 M.	44
63 M.	46

In only 3 patients in this group was the E.S.R. above 40 mm.

A comparative histogram of the two groups (*Fig.* 6) shows that whilst patients with inflammatory aneurysms tend to have a raised E.S.R., those of the non-inflammatory group fall into lower values.

Calcification.—In the 'inflammatory' group calcification was noted on straight radiographs of the abdomen in 14 cases (87·5 per cent) and 2 (12·5 per cent) showed no evidence of calcification; 3 did not have a preoperative radiograph In the non-inflammatory group 119 patients had preoperative abdominal radiographs taken; 86 (71 per cent) showed evidence of calcification whereas 33 (29 per cent) did not. Thus there is no significant difference in the incidence of calcification between the two groups.

Operative Mortality.—One patient died during operation from hypotension, having ruptured his aneurysm preoperatively. There were 5 other postoperative deaths: 1 from pulmonary embolism at 12 days, 2 from graft thromboses associated with retroperitoneal abscess at 28 days and 40 days, respectively, 1 from cardiac failure at 10 days, and 1, previously mentioned, who had only a laparotomy and died at 28 days from causes not determined by post-mortem examination.

Postoperative Complications.—The only significant complication would appear to be the incidence of graft thrombosis associated with abscess formation. There has been 1 late death at 5 months from this cause in addition to the 2 in the immediate postoperative period. The abscess formation in 1 case was associated with perforation of the small bowel after attempts had been made to free small-bowel adhesions from the wall of the prosthesis 5 days after its insertion. No abnormality of the bowel was found in the other 2 cases. This abscess formation has not been seen in atherosclerotic aneurysms although graft thrombosis has occurred.

Wound dehiscence occurred in only 1 of the 17 cases who lived for longer than 14 days, an incidence (5·9 per cent) comparable to the series as a whole.

Late Mortality.—One patient died at 20 months of a myocardial infarct, and 1 at 2½ years of a cerebrovascular accident.

Table II.—Retrospective Investigations carried out in 11 Patients with 'Inflammatory' Aneurysms

Age and Sex	Pre-operative E.S.R.	Retrospective Tests									
		IgA 50–400	IgG 800–1800	IgM 50–200	Cholesterol 140–300	Albumin/Globulin	E.S.R.	Urea	Wassermann Reaction	Antinuclear Factor	Rheumatoid Factor
58 M.	—	330	900	170	185	4·0/2·4	10	56	-ve	-ve	-ve
66 M.	19	175	820	190	275	4·9/2·5	2	31	-ve	-ve	-ve
60 M.	22	410	1050	92	285	4·7/2·9	5	28	-ve	-ve	-ve
69 M.	44	165	1350	84	170	4·8/2·6	12	39	-ve	-ve	-ve
66 M.	21	290	1700	110	235	5·1/3·4	14	41	-ve	-ve	-ve
64 M.	—	260	1350	170	235	4·5/2·9	16	23	-ve	-ve	-ve
71 M.	21	280	1500	92	230	4·8/3·2	12	36	-ve	-ve	-ve
59 M.	—	360	1350	62	265	5·1/2·7	5	28	-ve	-ve	-ve
40 F.	—	216	920	100	285	4·9/2·8	8	36	-ve	-ve	-ve
63 M.	46	270	1060	110	250	3·1/3·7*	44	31	-ve	-ve	-ve
64 F.	42	180	1100	64	280	4·8/3·2	6	31	-ve	-ve	-ve

* This patient had a retroperitoneal abscess when investigations were performed, from which he later died.

Table III.—Comparison of Preoperative and Postoperative E.S.R. in 6 Patients

Age and Sex	Erythrocyte Sedimentation Rate	
	Preoperative	Postoperative
66 M.	19	2
66 M.	21	14
71 M.	21	12
60 M.	22	5
64 F.	42	6
69 M.	44	12

RETROSPECTIVE INVESTIGATIONS

Retrospective investigations were performed in all 11 survivors of the 19 patients at intervals varying from 4 months to 4 years after operation (*Table II*).

Erythrocyte Sedimentation Rate.—All the patients eventually reached the normal range (*Table II*). In 1 case this took several months to occur. This man's E.S.R. was 44 mm. preoperatively; 3 months after operation it was 47 mm.; 6 months postoperatively the value was 28 mm.; and after 12 months it had fallen to 12 mm. Comparison of preoperative and postoperative E.S.R. was available in 6 cases only (*Table III*). A postoperative E.S.R of 31 mm. (preoperative 44 mm.) was obtained from 1 patient who developed a retroperitoneal abscess which subsequently proved fatal.

Other Investigations.—The cardiolipin Wassermann reaction, Reiter protein complement fixation, and treponemal haemagglutination tests were negative in all 11 cases.

In view of the number of plasma cells in the inflammatory infiltrates we investigated the serum proteins both quantitatively and qualitatively (*Table II*). No abnormality was detected.

Qualitative and quantitative immunoglobulin assessments showed no abnormality. Quantitative immunoglobulin IgA, IgG, and IgM levels were all within normal ranges, viz., 50-400, 800–1800, and 50–200 mg. per 100 ml. respectively. Investigations for antinuclear factors were also negative (*Table II*).

Allowing for age and sex, all the serum cholesterol values were in the normal range, and the rheumatoid factor as defined by the sensitized sheep-cell and F 11 latex tests was negative in all cases.

DISCUSSION

We have previously noted the similarity in the extent of the 'inflammatory' aneurysms and the atherosclerotic aneurysms. This is, however, the only point of similarity.

From the surgical viewpoint the most striking difference between the two groups of patients was the gross appearance of their aneurysms. In the 'inflammatory' group the thickened aneurysm walls with their fleshy appearance and adjacent dense fibrosis were characteristic and striking. This fibrosis often made dissection at operation very difficult and the lumbar veins and arteries were liable to damage during mobilization of the upper end of the aneurysm. Similarly, the common iliac veins and inferior vena cava were solidly attached to the aneurysm wall and separation of them was particularly hazardous.

In addition, the duodenum may be so adherent to the anterior wall of the aneurysm that the plane of cleavage is completely obliterated. In 1 instance this was so marked as to have caused duodenal obstruction. Once mobilization of the proximal and distal ends of the aneurysm has been completed successfully the remainder of the operation carries no further special hazards, and indeed the anastomoses may be easier to perform as the adjacent aorta is relatively free from atheroma in comparison to the atherosclerotic aneurysm.

The aetiology of the 'inflammatory' aneurysm remains obscure. Atherosclerosis remains the most common cause of abdominal aortic aneurysm with an age-range between the fourth and the tenth decades with the highest incidence in the seventh decade (DeBakey and others, 1964). Other causes are rare, although Marquis, Richardson, Ritchie, and Wigle (1968) reported an aneurysm found at autopsy as due to 'idiopathic medial aortopathy' (*Case* 4), and other aortic aneurysms of uncertain aetiology have been reported by Abrahams and Cockshott (1962).

Specific causes of aortitis have long been known. Syphilis is still the commonest cause (Gore, 1960), involving mainly the thoracic vessel although the abdominal portion may also be affected. Aortitis has been described in rheumatic fever (Klotz, 1912; Reid, 1957; Heggtveit, Hennigar, and Morrione, 1963), rheumatoid disease, and ankylosing spondylitis (Schilder, Harvey, and Hufnagel, 1956; Ansell, Bywaters, and Doniach, 1958). In the present series serological tests for syphilis were uniformly negative and there was no evidence of a systematized collagen disorder.

Non-specific aortitis is rare. Cases of Takayashu's (pulseless) disease or of an allied aortitis have been described in countries other than Japan; for example, by Danaraj, Wong, and Thomas (1963) in Singapore, by Abrahams and Cockshott (1962) in Nigeria, and by Isaacson (1961) in South Africa. In these instances children or young adults were affected and secondary renal hypertension from involvement of a renal artery in the inflammatory process was common. Renovascular hypertension has also been reported in the aortitis syndrome in Japan (Committee Report, 1968).

In the present series of 19 patients with abdominal aortic aneurysms, 17 were males aged between 48 and 71 years; this contrasts with the male : female ratio of 1 : 7 in Takayashu's syndrome in a younger age-group (Committee Report, 1968), although in Western countries patients with aortic arch syndrome are often middle-aged or elderly (Thurbeck and Currens, 1959), and the disease is of mixed aetiology, involving atheroma and thrombosis, syphilis (Ross and McKusick, 1953), or idiopathic thrombosis (Lessof and Glynn, 1959).

We have referred to the present series of aneurysms as 'inflammatory' in type but this implies no specific aetiology or pathogenesis. From the pathological viewpoint the unusual feature was the grossly thickened aneurysmal walls resulting from active chronic inflammation and collagenization of the adventitial and medial coats. If these thick-walled aneurysms are of atherosclerotic origin they show an unusual form of a lesion which usually presents as a discrete, thin-walled fibrous sac or dilatation of the abdominal aorta. Adventitial cellular infiltration is a feature of atherosclerosis, particularly if complicated by recent thrombus (Schwartz and Mitchell, 1962), but the infiltrates seen are lymphocytic and homogeneous. The inflammatory response in the aneurysm described in this study was not only intense but heterogeneous, including polymorphonuclear leucocytes in areas of focal necrosis, lymphocytes in both follicular aggregates and diffuse infiltrates, large numbers of plasma cells, and occasional granulomata including giant-cell macrophages. Possibly this represents an exaggerated inflammatory response to fresh luminal thrombi which were present in all the specimens or to breakdown products of the thrombi permeating the aneurysm walls. The precise antigenic stimulus producing the intense phlogistic reaction is, however, unknown.

From the pathological viewpoint the condition of the aorta remote from the aneurysms is also relevant. To date 3 patients in this series have been autopsied. There has been no widespread aortic inflammation, the thoracic aorta showing moderate to severe atheroma but only insignificant inflammation of the media and no fibrosis of the adventitia. Degenerative medial changes with loss of elastic tissue were limited to an area immediately adjacent to the aneurysm.

In the absence of other significant disease processes one might assume that the raised E.S.R. is referable to the active inflammation within the aneurysm wall. However, this would not explain the postoperative drop in E.S.R. levels as the aneurysms were merely *incised and not excised in* preparation for the arterial graft, thus leaving most of the 'inflammatory' tissue in situ. Possibly surgical repair of the aneurysm is followed by reduction of the inflammatory process, but we have not yet had an opportunity of checking this by examination of further material.

In the first 9 months of 1970, 3 more cases of 'inflammatory' aneurysms have been seen; all had a raised E.S.R., 1 to a level of 87 mm. in the first hour.

It would appear, therefore, that the group of aortic aneurysms we have described differs from the more common arteriosclerotic form in both their clinical and structural characteristics.

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FEMORAL ANEURYSMS

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THE LONDON HOSPITAL

SUMMARY

Femoral aneurysms are a relative rarity in clinical practice. A series of 15 such aneurysms treated in a variety of ways is presented. The method of treatment did not appear to affect the outcome. Where the aneurysm was found to be infected at operation treatment was not successful. An alternative method of arterial reconstruction by endo-aneurysmorrhaphy is presented.

ALTHOUGH femoral aneurysms are relatively infrequently seen, even in specialist vascular units, the growing numbers of arterial vascular reconstructive procedures and the increasing age of the population have resulted in a gradual increase in the incidence of both false and atherosclerotic aneurysms since the condition was first recognized some hundreds of years ago. Despite the fact that more sophisticated methods of treatment have become available, femoral aneurysms still have an appreciable morbidity and mortality from their complications and following surgical treatment. This paper describes a series of femoral aneurysms of mixed aetiology treated in a variety of ways over the past 9 years at the London Hospital.

CASE MATERIAL

Fifteen aneurysms were treated in 13 patients, who had an average age of 59 years, the oldest being 76 and the youngest 47. All were male. Ten of the aneurysms were on the left side and 5 on the right. The most frequent presenting complaint was of a palpable, pulsating, occasionally painful mass in the groin. Two cases presented with preoperative symptoms attributable to thrombotic or embolic episodes with acute limb ischaemia and 1 had a spontaneous rupture of the aneurysm.

There were 7 true aneurysms, resulting from atherosclerotic degeneration of the vessel wall, and 1 primary mycotic aneurysm. Of the 7 false aneurysms, 5 followed previous surgical intervention, and 3 of these were infected. These operations had taken place from 9 years to 9 days before the appearance of the false aneurysms. Two of the false aneurysms resulted from direct trauma to the vessel wall. Eleven of the aneurysms involved the common femoral artery, 3 the superficial femoral artery, and 1 the profunda femoris artery.

MANAGEMENT AND OUTCOME

Four of the 7 atherosclerotic aneurysms were treated by endo-aneurysmorrhaphy (*Table I*). The profunda femoris aneurysm was treated by excision and autogenous vein replacement. The atherosclerotic superficial femoral aneurysm was treated by proximal and distal ligation of the artery with excision of the aneurysm. One patient who had an abdominal aneurysm in addition to a left common femoral aneurysm was treated by excision of both aneurysms, with a Dacron graft replacement. The primary mycotic aneurysm of the common femoral artery was initially treated by an autogenous saphenous vein by-pass. This subsequently developed a false aneurysm from the proximal suture line and was replaced by a Dacron iliofemoral graft. This was initially successful but later occluded, but with limb survival.

Table I.—DETAILS OF THE CASES IN THE PRESENT SERIES

CASE	DATE	AGE (years)	DIAGNOSIS	TYPE OF ANEURYSM	SITE OF ANEURYSM	PREOPERATIVE SYMPTOMS	TREATMENT	OUTCOME
1	1969	47	Atheroma, 1969	True atherosclerotic	Left common femoral	Claudication left leg	Endo-aneurysmorrhaphy	No symptoms
2	1967	63	Atheroma, hypertension, multiple aneurysms, 1969	True atherosclerotic	Left common femoral	Painful swelling left groin. Embolism to left calf	Endo-aneurysmorrhaphy	No symptoms
3	1965	59	Atheroma, ? arteritis, 1965	True atherosclerotic	Right common femoral	Painful swelling right groin. Claudication right leg	Endo-aneurysmorrhaphy	No symptoms
4	1970	70	Atheroma, 1969	True atherosclerotic	Left common femoral	Painful swelling left groin. Claudication left leg	Endo-aneurysmorrhaphy	No symptoms
5	1967	51	Atheroma, hypertension, 1967	True atherosclerotic	Right profunda femoris	Pulsating mass right groin	Excision and autogenous saphenous vein replacement	No symptoms
6	1962	70	Atheroma, 1962	True atherosclerotic	Right superficial femoral	Pulsating mass right groin	Ligation and excision	No symptoms
7	1969	66	Atheroma and abdominal aortic aneurysm	True atherosclerotic	Left common femoral	Pulsating mass left groin	Dacron aortofemoral graft	No symptoms
8	1970	59	Bilateral femoropopliteal grafts; left, March 1969; right, Dec., 1969	False mycotic anastomotic disruption	Right common femoral	Painful mass right groin and haemorrhage from groin	Simple closure of defect	Claudicating
9	1965	59	Right and left iliofemoral endarterectomies 7 years	False anastomotic disruption	Left common femoral	Pulsating mass claudicating	Revision arterioplasty	Claudicating
10	1968	59	Left superficial femoral endarterectomy 1 month previously	False mycotic anastomotic disruption	Left superficial femoral	Painful pulsating mass	Excision and saphenous vein replacement	Claudicating
11	1968	67	Atheroma—aortofemoral bifurcating graft, 1959	False anastomotic disruption	Left common femoral	Claudication	Iliofemoral Dacron by-pass	No symptoms
12	1967 and 1968	51	Primary atherosclerotic mycotic aneurysm, 1967. Subsequent false mycotic aneurysm, 1968	Primary mycotic False mycotic anastomotic disruption	Left common femoral Left common femoral	Painful pulsating mass and thrombosis left common femoral artery	Excision and saphenous vein replacement followed by Dacron iliofemoral by-pass	Claudicating
13	1965	49	Stab wound 9 days prior to appearance of aneurysm	False traumatic	Right superficial femoral	Painful pulsating mass right groin	Excision and saphenous vein replacement	No symptoms
14	1969	48	Mitral valve replacement and arterial puncture 1 month before aneurysm	False traumatic	Left common femoral	Pulsating mass	Evacuation and simple closure of defect	No symptoms

One of the 2 post-traumatic aneurysms was treated by lateral arterial repair, while the other was treated by excision of a segment of the damaged artery and replacement by an autogenous saphenous vein-graft.

Of the 5 false aneurysms resulting from prior surgical operations, the defect was found to occur at the site of the previous anastomosis or arterial repair in all cases. In these silk had been employed in 3 and Dacron suture material in 2 of the initial repairs. In only 1 of these cases had a Dacron graft been sutured end to side to the common femoral artery. All the false aneurysms which resulted from previous surgery were managed in different ways. One, following a femoropopliteal by-pass, was treated by simple closure, and another by a revision arterioplasty following a leak from a previous endarterectomy. Following an endarterectomy, 1 case developed an infected false aneurysm which was treated by an autogenous saphenous vein-graft. The fourth case had a second Dacron graft inserted more distally into the common femoral artery, and in the fifth case a long Dacron graft was used to circumvent the site of the previous infected false aneurysm.

There was no operative mortality and no limbs were lost. Of the 5 patients who had operations for false aneurysms resulting from previous arterial operations, 4 complained of intermittent claudication in the postoperative period, and 3 of these had been found at operation to be infected.

DISCUSSION

True postoperative aneurysms are comparatively rare in vascular practice and this group of 8 cases seen over a 9-year period agrees substantially with the numbers quoted in previous series (Tolstedt, Radke, and Bell, 1961; Bergan, Kaupp, and Trippel, 1969). Even in the largest reported series there were only 39 true atherosclerotic aneurysms out of a total of 150 peripheral aneurysms seen over an unstated period of time (Crawford, DeBakey, and Cooley, 1959). Multiple aneurysms are common in all the published reports and incidences ranging from 36 to 69 per cent are quoted (Pappas, Janes, Bernatz, and Schirger, 1964; Bergan and others, 1969). In the present small series only 2 patients had multiple aneurysms, 1 of these having no less than 4 aneurysms in the legs.

False aneurysms are also relatively rare, but this condition was much more common in the earlier published reports before it was realized that the use of absorbable sutures, woven grafts, and end-to-side anastomoses all contributed to the development of false aneurysms (Crawford, Edwards, DeBakey, Cooley, and Morris, 1961; Stoney, Albo, and Wylie, 1965; Sawyers, Jacobs, and Sutton, 1967; Spratt, Doran, and Baird, 1967).

Infection has also played a prominent part in the breakdown of graft anastomoses, and the incidence of such infected false aneurysms has been as much as one-third of the total numbers of the various reported series. By using non-absorbable sutures, knitted grafts, end-to-end anastomoses, and scrupulous aseptic technique it has, however, proved possible to reduce somewhat the incidence of infected false aneurysm formation, but 3 in the present series of 15 aneurysms resulted directly from dehiscence of an infected suture line.

Embolic episodes leading to peripheral gangrene are a well-recognized complication of untreated peripheral arterial aneurysms, and gangrene has been reported as occurring in over 50 per cent of patients in whom conservative treatment has been adopted (Crawford and others, 1959). No patient in these 15 cases suffered preoperative emboli resulting in limb death. Early treatment is, therefore, essential if this outcome is to be avoided.

Although the two standard methods of treatment by excision and either Dacron or autogenous vein replacement, or by-pass, were used, an alternative method of arterial reconstruction was used in 5 cases. This involved partial excision of the aneurysm with local endarterectomy and revision of the lumen to an appropriate size, the reconstruction of the artery being performed over a rubber catheter matched to fit the proximal vessel above the aneurysm. Although this procedure can be subjected to the criticism that under conditions of aneurysmal dilatation all the coats of the vessel wall are affected by the disease process, a substantial time has elapsed since these operations were performed and in no case has further arterial dilatation resulted. It is a simple surgical procedure under conditions where adequate substance remains following endarterectomy, and would appear to be preferable to the use of Dacron or an unsuitably small vein.

In 3 of the 4 cases in which treatment was not successful and the patients developed intermittent claudication postoperatively the aneurysms were infected preoperatively. This relationship between treatment, failure, and infection has been noted by others (Stoney and others, 1965; Sawyers and others, 1967; Spratt and others, 1967) and the presence of infection would seem to be an indication for 'radical and vigorous tratment, or complete avoidance of the infected area' (Sawyers and others, 1967) if treatment is to succeed.

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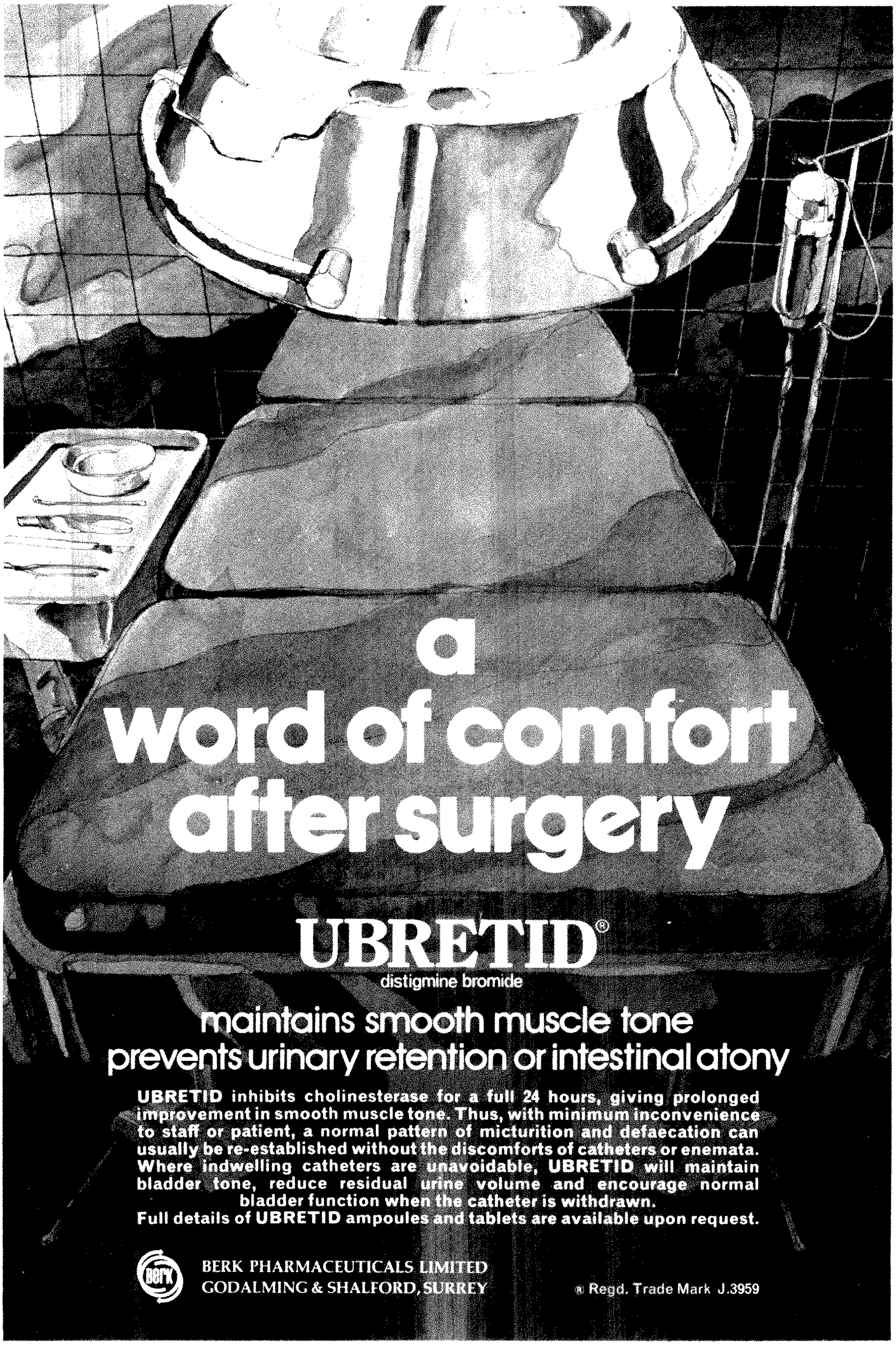

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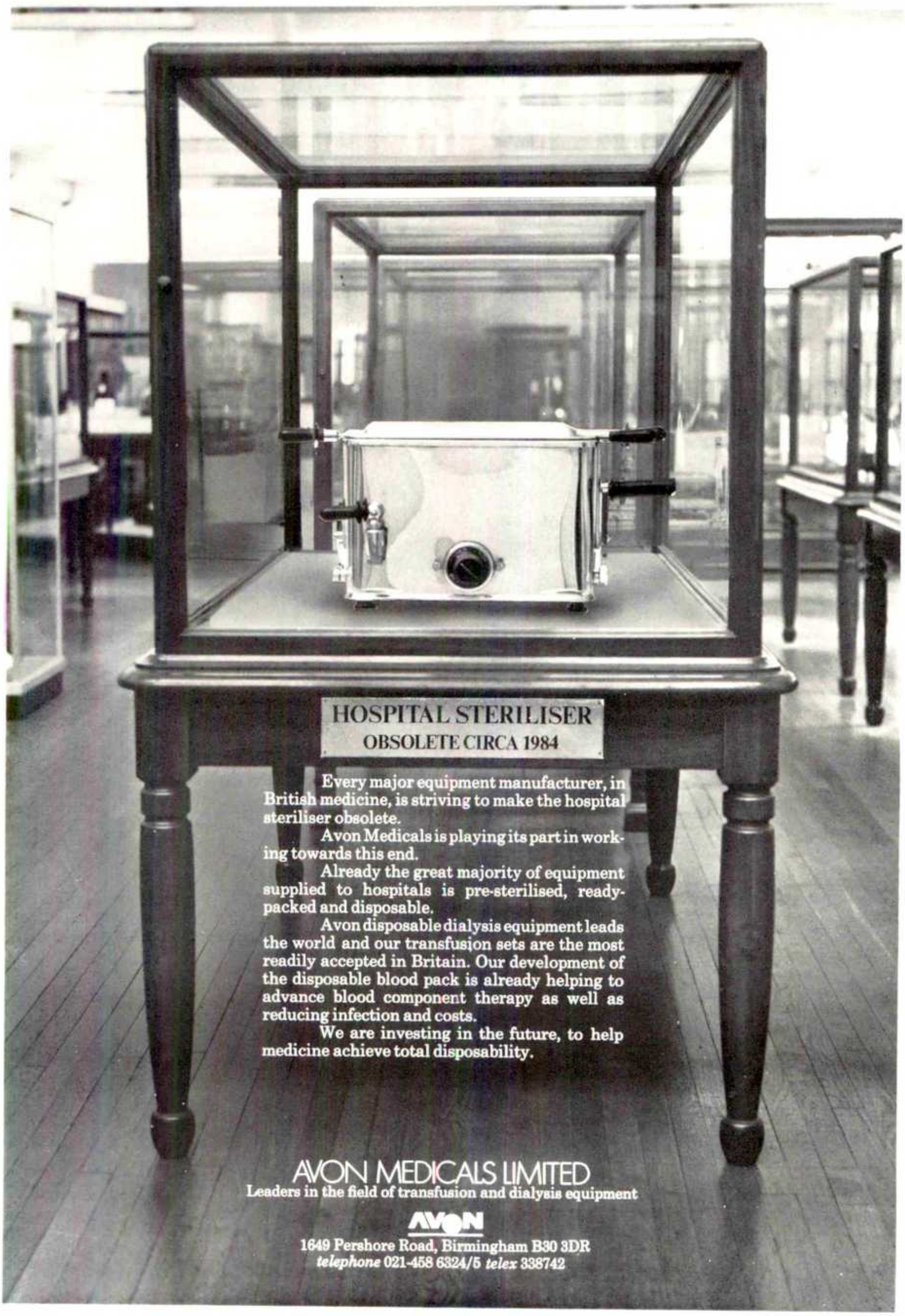

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THE HISTOPATHOLOGY OF SMALL VESSELS FOLLOWING MICROVASCULAR REPAIR

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SUMMARY

1. The histopathological findings following microvascular repair of 105 arteries and 89 veins in English-strain rabbits are reported.

2. The importance of (*a*) the accurate apposition of the vessel walls and (*b*) the avoidance of excessive medial necrosis is stressed.

3. The process of subintimal hyperplasia is described and the importance of its role in the repair of small vessels is discussed. Previously, the new formation of elastin tissue has been considered pathognomonic of vascular disease.

4. The appreciably slower rate of repair in veins is also reported.

5. From these observations suggestions have been made with regard to improved technique of surgical repair.

SINCE 1967 various microvascular surgical techniques have been developed in the Departments of Surgery (St. Vincent's Hospital) and Ophthalmology of the University of Melbourne. As part of this programme femoral vessels of the rabbit and the dog have been sutured with the aid of a special operating microscope (O'Brien, 1970). Direct anastomoses of arteries and veins and reversed arterial and venous grafts have been undertaken. Precise details of the special microvascular techniques have been described previously (O'Brien, Henderson, Bennett, and Crock, 1970; O'Brien, Henderson, Baxter, and Miller, 1971). All the operative specimens were subsequently removed for examination. In the present paper our attention will be confined to reporting in detail the histopathological changes observed in the vessels of the rabbit following direct suture. The features of repair which occur during the healing process have been studied and an attempt has been made to delineate those factors which are important in determining the early and long-term patency of the vessels.

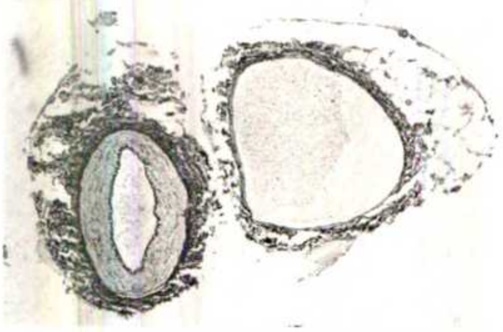

FIG. 1.—Transverse section of a normal femoral artery and vein of rabbit. Gomori aldehyde fuchsin (G.A.F.). (× 30.)

MATERIALS AND METHODS

This report is based upon histological examination of 105 arteries and 89 veins in English-strain rabbits, all of which had been repaired previously by direct suture. The vessels were measured with an ocular micrometer and their mean diameters were found to be 0·8 and 1·0 mm. respectively. The operative techniques and macroscopic assessment of the anastomoses of some of these vessels have already been reported (O'Brien and others, 1970). All the sutures used were of 0000000000 or metallized 28 μ nylon, interrupted, and inserted through the full thickness of the vessel wall. No attempt was made to strip the adventitia from the cut edges.

Excision biopsy of the anastomotic segments was performed at varying intervals following surgery until as late as the eighteenth postoperative week. The anastomoses were examined macroscopically and the histopathological features were studied by light and electron microscopy.

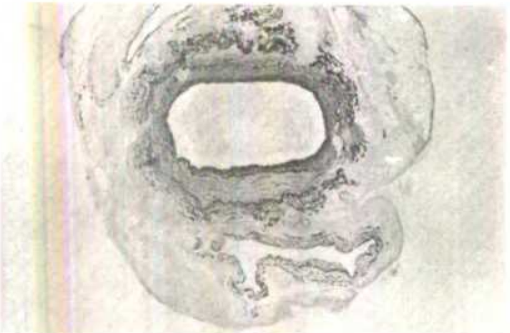

FIG. 2.—Transverse section of a patent artery and vein at the anastomosis, showing minimal subintimal hyperplasia in the artery. The vein is partly collapsed but patent, although the wall shows areas of necrosis (absence of internal elastic lamina and media) and a suture 'pull-through'. Biopsied 6 weeks after anastomosis. G.A.F. (× 30.)

The tissues were prepared by fixation in formol–saline (10 per cent) and serially sectioned (4 μ in thickness) proximal and distal to the lines of anastomosis. The sections were stained with haematoxylin and eosin, aldehyde fuchsin (Gomori, 1950), toluidine blue, and Verhoff Van Gieson.

Appropriate tissue was also selected for electron microscopy. The arterial segments were flushed with saline and fixed in 4 per cent buffered glutaraldehyde (approximately 4° C.) for 24 hours. Blocks of tissue from the level of the suture line and from regions proximal and distal to this were processed for transmission microscopy by post-fixing in chrome osmium (Dalton, 1955) and were embedded in Araldite. Sections were stained with lead citrate (Reynold, 1963) and uranyl acetate and viewed in a Siemens 1A electron microscope.

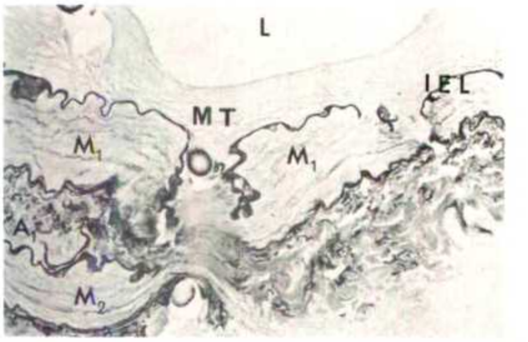

FIG. 3.—Transverse high-power section of an arterial wall at the anastomosis showing imperfect apposition of the cut vessel edges and the resultant tissue overlap. The media M_2 has been forced out of alinement with the media M_1 by excessive tension applied in tying of the suture. As a result the adventitia A_1 has been entrapped between the two layers of media M_1 and M_2. The necrotic tissue adjacent to the suture 'pull-through' is shown. The mural thrombus (MT) is seen between the lumen (L) and the ruptured internal elastic lamina (IEL). Biopsied 2 weeks after anastomosis. G.A.F. (× 240.)

RESULTS

Macroscopic Features.—Examination at the time of excision biopsy showed that 83 of 105 arteries (79 per cent) and 76 of the 89 veins (85 per cent) had remained patent. These findings were confirmed and an assessment of additional changes was made by microscopy.

Histopathological Features.—The histology of the normal femoral artery and vein of the rabbit is shown in *Fig.* 1. The following observations were made in both arteries and veins following suture. The arterial changes will be described first as these occurred earlier and to a more pronounced degree than those in the veins.

1. *Accuracy of Apposition of Cut Vessel Edges.*—In specimens with macroscopically patent anastomoses accurate apposition of all layers of the cut vessel edges had almost always been achieved (*Fig.* 2). However, even under these circumstances biopsies at 8–12 days showed coagulum between the opposing edges which was in continuity with a thin layer of mural thrombus which occupied the entire luminal perimeter. During the second week the thrombi underwent shrinkage and were invaded by smooth-muscle cells. Newly formed elastin fibrils and collagen fibres were also observed (*Fig.* 3). In addition during this period the luminal surfaces of the thrombi had become covered with endothelial cells.

Where accurate alinement of the cut vessel edges was not achieved more extensive thrombosis, either partial or complete, inevitably resulted. This was observed as early as 3 days postoperatively but may have occurred earlier. The mural tissue gaps were again filled by fibrinous coagulum which continued between the overlapping edges and became confluent with the luminal thrombus. Groups of fresh blood-cells were present in spaces which had developed within the luminal mass. After 7 days organization occurred by the ingrowth of small capillary loop from the adventitia at the cut edges and through suture perforations. Many fibroblasts were present throughout the thrombus and recanalization had commenced. However, when failure to achieve good apposition was accompanied by massive tissue disruption, especially when the media was extensively involved (*see below*), the resultant thrombus in the affected vessel segment failed to canalize for extensive periods, sometimes ranging from 8 to 18 weeks (*Figs.* 4, 5). In only 2 vessels, biopsied at 11 and 17 weeks respectively, were there small vessels containing medial tissue in their walls within the thrombi (*Fig.* 6).

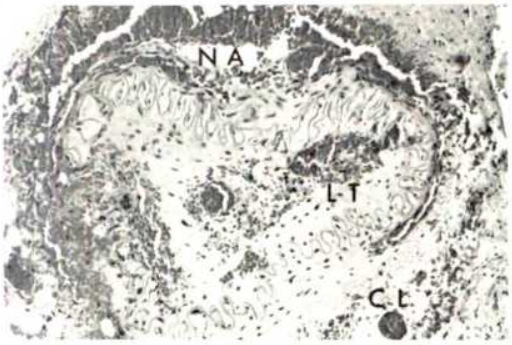

FIG. 4.—Transverse section of a thrombosed artery beyond the suture level showing blood-flow through spaces in the necrotic adventitia (NA) as well as through the luminal thrombus (LT). Small capillary loops (CL) are evident throughout the section. Biopsied 8 weeks after anastomosis. H. and E. (× 84.)

2. *Medial Disruption.*—The most important factors responsible for medial disruption were inaccurate apposition of the vessel edges (*Fig.* 3) and insertion of the sutures (*Fig.* 7). The number, placement, and tension of the sutures were all important as judged by the degree of tissue distortion. In some instances the sutures caused a scalloped or pinched effect in the wall (*Fig.* 8), whilst in others the suture pulled through the full thickness of the wall (*Fig.* 9). These necrotic pathways in the wall appeared to be due to excessive tension of the suture and frequently were associated with the failure of effective apposition of the cut edges.

The resultant associated cellular changes appeared to be of considerable significance in determining the degree of medial distortion. In the initial stages (up to 7 days) following vessel repair the sutures were surrounded by populations of cells of differing density in individual specimens, but consisting mainly of plump fibroblasts, smooth-muscle cells, and macrophages. These cells soon became less numerous, and after 14 days most of the sutures were surrounded by an area of hyaline necrosis (*Fig.* 9). However, in some specimens even at 4–8 weeks the cellularity was still more prominent than the associated necrosis. The amount of necrosis was greatest where there was suture crowding (*Fig.* 9) or where an excessive number of sutures had been inserted (*Fig.* 7). Under these circumstances the necrotic areas often became confluent and involved large areas of the vessel wall.

The extent of this mechanical disruption of the media largely determined its subsequent viability.

3. *Subintimal Hyperplasia.*—The degree of viability of the media appeared to be a critical factor in determining the success of the anastomoses (*Fig.* 2). Because the interrupted sutures traversed the full thickness of the wall at the anastomotic site the media was always penetrated and the continuity of the internal elastic lamina was invariably interrupted. Effective repair or reconstitution of these two components was only achieved by a hyperplastic response of the medial constituents, which response will be referred to as 'subintimal hyperplasia' (*Figs.* 2, 7, 10).

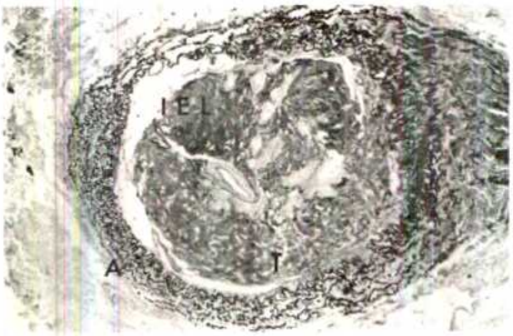

FIG. 5.—Transverse section of a thrombosed artery beyond the anastomotic site, showing small capillary loops and a developing vessel within a central thrombus (T). Small remnants of the old internal elastic lamina (IEL) are seen here. The original media is non-existent. The remaining tissue is adventitia (A) with its multilayered external elastic lamina. Biopsied 18 weeks after anastomosis. G.A.F. (× 72.)

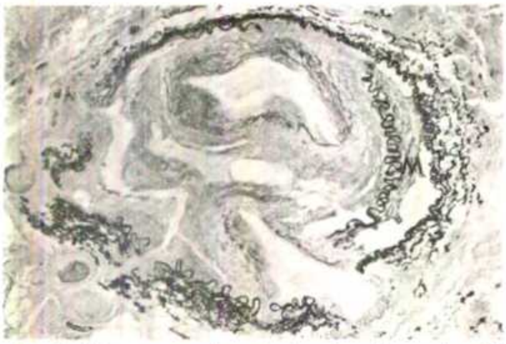

FIG. 6.—Transverse section of a thrombosed artery in which there is incorrect apposition of the cut vessel edges. Only a small amount of viable media (M) is present. Small vessels are forming within the thrombosed areas and the elastin fibrils of their developing media are clearly seen. Biopsied 17 weeks after anastomosis. G.A.F. (× 72.)

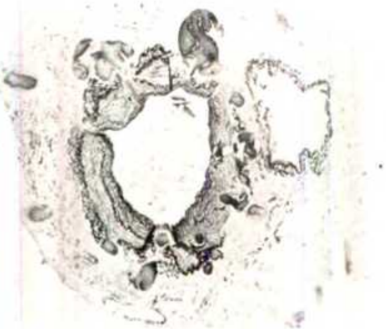

FIG. 7.—Transverse section of a patent artery and vein at the anastomosis showing uneven spacing of sutures in the artery as well as the 'pinched' appearance resulting from excessive suture tension. Subintimal hyperplasia is prominent. The vein, although patent, is collapsed and has a partly necrotic and broken wall. Biopsied 6 weeks after anastomosis. G.A.F. (× 30.)

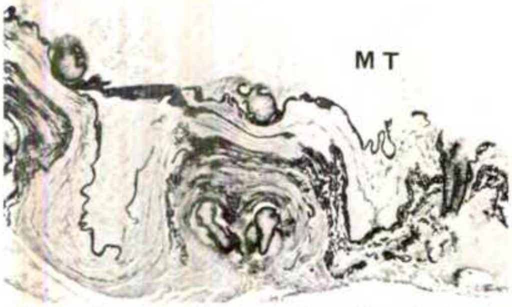

FIG. 8.—Transverse high-power section of the wall of a patent artery at the anastomosis, showing a mural thrombus (MT) and disruption of the arterial wall by the insertion of sutures, the tension of which has resulted in a 'scalloped' effect. Biopsied 1 week after anastomosis. G.A.F. (× 240.)

The speed and effectiveness of this restoration were directly dependent on the amount of surviving media following anastomosis. If at least one-third of the media was not viable the hyperplasia did not occur and invariably the vessel segment became thrombosed (*Fig.* 5). In the arteries which had thrombosed completely at the suture line viable media was not present and subintimal hyperplasia was never observed. On rare occasions, however, examination approximately 300 μ on either side of the thrombosed region showed subintimal hyperplasia in the patent segments where the media was not significantly damaged.

As early as 1 week in a patent vessel with a circumferential mural thrombus the luminal edge was already covered by immature endothelial cells. Medial cells, fibroblasts, elastin fibrils, and collagen fibres were present in the mural thrombus, the cells entering via the breaks in the internal elastic lamina. The cell population then consisted of longitudinally orientated smooth-muscle cells and fibroblasts. Fine elastin fibrils were recognizable with the Gomori stain (*Fig.* 3). Electron microscopy showed that the elastin elements first appeared as isolated clumps or as long microfibrils, 100–150 Å in diameter, in close proximity to smooth-muscle cells. Between 2 and 4 weeks the smooth-muscle cells gradually became more numerous than the fibroblasts and the elastin fibrils stained progressively more densely. The cells and fibrils spread circumferentially as well as along the vessel for varying distances (from 250 to 320 μ) to either side of the suture level. Simultaneously the fibrils became more concentrated immediately beneath the endothelium.

From 4 to 6 weeks the fibrils had usually reached a sufficient density to form a new internal elastic lamina. This was confirmed by electron microscopy which showed that the elastin clumps had coalesced to form elastic lamellae surrounded by typical peripheral microfibrils (*Fig.* 11). The new internal elastic membrane varied from 2 to 2·5 μ in width. The remnants of the original broken internal elastic membrane were always clearly visible (*Fig.* 7) and newly formed fibrils were more numerous where the breaks were widest.

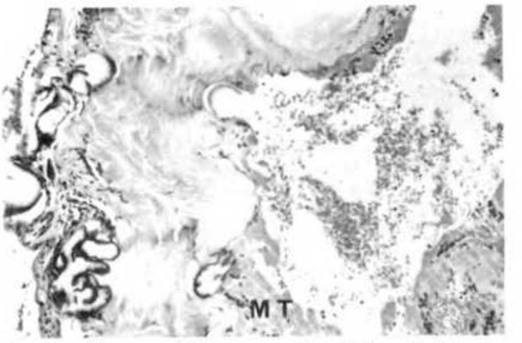

FIG. 9.—Transverse high-power section of the wall of a patent artery at the anastomosis, showing a mural thrombus (MT) as well as the suture crowding. As a result the hyaline areas of necrosis associated with the sutures have become confluent. Note the suture 'pull-through'. Biopsied 1 week after anastomosis. H. and E. (× 240.)

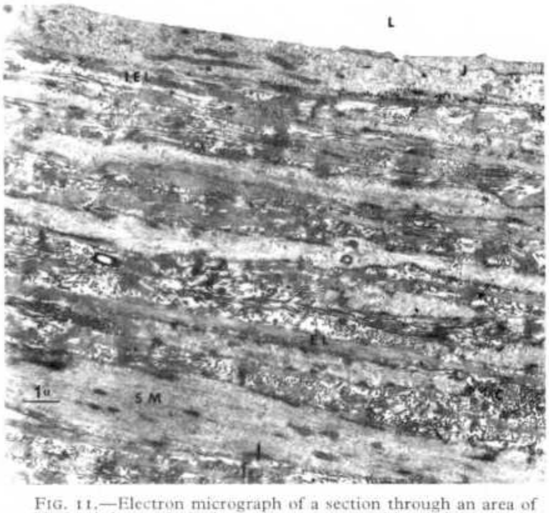

FIG. 11.—Electron micrograph of a section through an area of subintimal hyperplasia in a patent artery, biopsied 17 weeks after anastomosis. Beneath the lumen (L) is the endothelium with a tight junction (J) and several layers of longitudinally orientated smooth-muscle cells (SM), and newly formed elastic lamellae (EL), and collagen (C). A new internal elastic lamina (IEL) is seen deep to the endothelium.

In some vessels subintimal hyperplasia was not evenly distributed around the circumference and showed a higher concentration of the medial components at points where the disruption of the internal elastic lamina was greatest. Hyperplasia was occasionally more disorderly, forming papillary projections which encroached on the lumen, greatly reducing its internal diameter (*Fig.* 12.) Occasionally these papillae resulted in an interlacing meshwork so that the lumen of the vessel was divided into three or four separate channels, without any evidence of pre-existent thrombosis.

4. *Adventitial Damage.*—In addition to the trauma produced by the division of the artery prior to anastomosis, adventitial damage was caused by the insertion of sutures and the use of arterial clamps. No histological evidence was observed to suggest that adventitia was pulled into the lumen between the cut edges or along suture tracks.

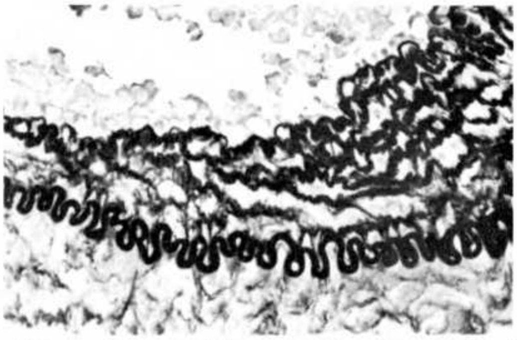

FIG. 10.—Transverse high-power section of an arterial wall, showing the high content of elastin in the subintimal hyperplasia and the 'condensation' of the fibrils at the luminal edge to form a new internal elastic lamina. This artery was sutured without cutting in order to observe the effect of sutures alone on the arterial wall. Biopsied 13 weeks after the placement of the sutures. G.A.F. (× 600.)

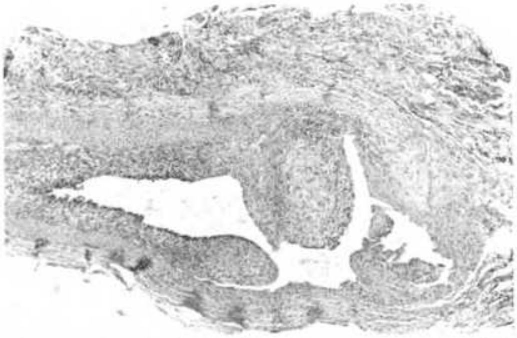

FIG. 12.—Longitudinal section of a patent artery beyond the anastomosis, showing disordered subintimal hyperplasia. This has resulted in papillary projections with considerable reduction of the lumen. Biopsied 2 weeks after anastomosis. H. and E. (× 48.)

To determine the effect of clamping on the vessel wall one artery was clamped for 1 hour without cutting and biopsied 1 week later. This vessel showed some degree of adventitial disruption and necrosis, and a small portion of the internal elastic lamina was reduplicated (*Fig.* 13), though the media appeared undamaged. At 7 days small capillary loops and many fibroblasts were observed entering the damaged adventitia to organize the necrotic areas. In the anastomosed arteries biopsies at 4–8 weeks usually showed the organization to be complete. However, where the damaged areas were extensive repair was often considerably slower.

Veins.—On the whole, repair following venous anastomosis proceeded along similar lines to that of arterial repair, with the same four factors being of prime importance. However, certain differences have been noted. These included:—

1. Accuracy of apposition of the vessel edges seemed to be more important with veins than with

arteries. Thrombosed veins which were biopsied after an interval of 1 week showed failure to achieve good apposition in every specimen.

2. Although the venous wall frequently appeared to be almost completely necrotic the vessel remained patent (*Fig.* 7).

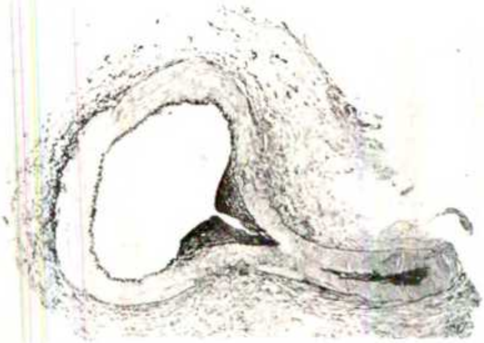

FIG. 13.—Transverse section of an artery (cut obliquely at one end) biopsied 1 week after clamping alone for 1 hour. Note the extensive adventitial damage and the subintimal hyperplasia where the internal elastic lamina has been disrupted. G.A.F. (× 48.)

3. Most veins exhibited some degree of narrowing. However, this did not appear to affect to any significant degree their ultimate patency (*Fig.* 2).

4. The rate of repair was appreciably slower. Endothelization of the mural thrombi was not evident until 4–6 weeks. Subintimal hyperplasia occurred subsequent to this time but was much less prominent than in arteries, consistent with the relatively small medial component in vein walls.

DISCUSSION

Although successful anastomosis of large blood-vessels has been possible for many years it is only recently that serious attempts have been made to overcome the problems associated with the repair of small vessels, particularly those with diameters in the region of 1 mm. Early work in this field was performed using relatively simple techniques and unsophisticated equipment (Seidenberg, Hurwitt, and Carton, 1958; Jacobson and Suarez, 1960). More recently a number of workers have become keenly interested in microvascular surgery because of the wide range of surgical applications which are made possible by the development of successful techniques (Krizek, Tani, Desprez, and Kiehn, 1965; Buncke, Daniller, Schulz, and Chase, 1967). More sophisticated equipment has been developed to provide for better magnification (O'Brien, 1970), suture material (O'Brien, Henderson, and Crock, 1970), and operative aids (Henderson, O'Brien, and Parel, 1970; Henderson, Pericic, and O'Brien, 1970). However, despite these advances if anastomoses of fine-bore vessels are to prove successful careful consideration must be given to the following points:—

1. The nature of the changes in the vessel walls subsequent to a technically successful anastomosis and the relevance of these changes to stenosis and occlusion.

2. The prevention of thrombosis produced by the action of platelets and related factors.

It has been the aim of this investigation to study the first of these important points by a careful histopathological examination of the sutured vessels. A number of pertinent factors have emerged.

It has been shown that the first requirement for successful anastomosis is correct apposition of the cut vessel edges. Repair then proceeds with the organization of both the coagulum between the cut vessel edges and the mural thrombi. Concurrently the thrombotic surfaces are endothelized by the proliferation of the intimal cells.

Organization is dependent upon medial activity and the findings demonstrate that minimal medial damage is the most important single entity concerned in successful vessel repair. It can be seen from the sequence of the histopathological processes that even with the most careful surgical techniques the vessel tissues suffer appreciable disruption.

It is worth re-emphasizing that correct apposition of the cut vessel edges is one of the most important factors in the prevention of thrombosis during the first week following anastomosis. Mural thrombi which cover the cut vessel edges are minimal where tissue overlap is avoided. Inaccurate apposition is more frequently associated with thrombosis in veins than in arteries, and this finding is probably related to the relative delicacy of the vein wall. The placing of the sutures and the tension with which they are tied must certainly be important factors in successful apposition.

In this series endothelium had commenced to grow over the luminal edges of the mural thrombi in the arteries at 8–12 days, but was not seen earlier than 4 weeks in the venous anastomoses. Other accounts of endothelial restoration during arterial repair vary considerably both with respect to rapidity and cellular origin. Times generally varied between 24 hours (Buck, 1961) and 2 weeks (Murray, Schrodt, and Berg, 1966). However, Poole, Sanders, and Florey (1958) reported that intimal lesions in the rabbit aorta were still not completely healed after 33 weeks. The two principal suggestions as to the origin of the new endothelial cells are (*a*) the intimal surface is restored by growth of the undamaged endothelial cells at the edges of the lesion, spreading into and covering the denuded area (Poole, Sanders, and Florey, 1959), and (*b*) the continuity of the luminal cells is restored by circulating mononuclear cells (Ghani and Tibbs, 1962). Alternative propositions are based on the fact that these early lining cells closely resemble macrophages (Buck, 1961) or smooth-muscle cells (Nomura, 1970). Zweifach (1959) adds further confusion to the problem by suggesting that cells possess diverse potentialities which vary with their particular location in the vascular system. In the present material the new endothelium appeared to arise and spread from the multiplication of the endothelial cells adjacent to the cut edges.

We regard the media as the most important mural component in the repair of small vessels. The medial reaction is comprised of hyperplasia of the cells and the production of elastin fibrils which reconstitute an internal elastic lamina. These processes are essential for successful repair. The term 'subintimal hyperplasia' is preferred to distinguish the process from any response which is of intimal or endothelial origin.

The hyperplasia is certainly medial in origin and when the formation of the new internal elastic lamina is complete both the cellular and the extracellular components are restored to a position beneath the intima.

At the end of 1 week the hyperplasia was well established, medial cells and elastin fibrils being conspicuous in the mural thrombi. These hyperplastic cells migrate through breaks in the internal elastic membrane and subsequently produce delicate elastin fibrils. The fibrils become more closely apposed and 'condense' beneath the endothelium, finally resulting in the production of a new elastic lamina. This medial response is proportional to the degree of tissue damage, provided always that medial disruption is not excessive. Hyperplasia was maximal where the discontinuity of the internal elastic lamina was greatest. These cells have been described as altered smooth-muscle cells, and by Buck (1961) as 'smooth-muscle cells which had undergone varying degrees of dedifferentiation'. Previous workers have reported the cellular proliferation as commencing at 10–14 days (Buck, 1961; Murray and others, 1966; Davies, Woolf, and Bradley, 1969), but only Buck referred to the production of elastin during this period.

Bunting (1939) put forward the view that if developing connective tissue was constantly subjected to 'alterations of tension and relaxation' elastic tissue formation would result. He based this conclusion on the dense elastic tissue observed in scars following myocardial infarction and in pleural adhesions. The work of Williams (1970) supported this concept. Following intimal damage of rabbit aortae Friedman and Byers (1965) observed that while transverse lacerations produced marked hyperplasia, longitudinal lacerations produced relatively slight cellular response. Bjorkerud (1969) attributed this difference to the fact that transverse lacerations were subjected to greater haemodynamic stress.

Murray and others (1966) were appreciative of the role of smooth-muscle cells in the reparative process, but the importance of elastin production appears to have been overlooked because previously new elastin production had been associated exclusively with vascular disease. Dible (1966) correctly observed that the term 'splitting' of the original internal elastic lamina inaccurately described the 'hypertrophied elastotic intima' because this was actually composed of newly formed elastica.

Our studies show subintimal hyperplasia to be part of the repair process and indeed that its occurrence is unavoidable. Furthermore, considerable disruption of the internal elastic lamina and media leads to excessive hyperplasia, which may result in either stenosis or subdivision of the vessel lumen. It is, therefore, obviously desirable to limit this response by avoidance of excessive damage to the above structures. This is best achieved by gentle handling, fine needles and suture material, restricting the number of sutures, and the careful adjustment of tension when the sutures are tied. The nature and strength of the arterial clamps are also of obvious importance and the time of their application should be limited.

These objectives are most likely to be achieved with adequate magnification and appropriate instrumentation.

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THE INCIDENCE OF RIGHT INGUINAL HERNIA FOLLOWING APPENDICECTOMY

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SUMMARY

A retrospective study of 549 patients who had undergone repair of an inguinal hernia is presented. It is noted that appendicectomy does not predispose to the development of a right inguinal hernia.

It has long been a clinical impression that the muscle-splitting incision in the right iliac fossa, commonly used for appendicectomy, renders the patient prone to develop an inguinal hernia on the right side (Aird, 1958) as a consequence of nerve and muscle damage weakening the inguinal canal. The purpose of the present study was to examine this relationship and to produce some statistical evidence either to refute or to confirm this hypothesis.

MATERIALS AND METHODS

The case records of 549 patients who had undergone inguinal hernia repair at Falkirk and District Royal Infirmary during the period 1967–9 were examined, referring particularly to a past history of appendicectomy performed through a right iliac fossa muscle-splitting incision or the presence of an appendicectomy scar.

Table I.—Incidence of Inguinal Hernia following Appendicectomy

	Right Side	*Left Side*
Total No. of inguinal hernia cases	301	248
No. with a previous appendicectomy	27	28
Percentage incidence ± 1 standard deviation	8·9 ± 1·7	11·2 ± 2·1

Among those who had undergone appendicectomy the number of cases coming to right inguinal hernia repair was noted, and as a control series the patients undergoing left inguinal hernia repair were documented. Cases being submitted to bilateral hernia repair were included in both the test and the control groups. No attempt was made to distinguish between direct and indirect herniae. Congenital herniae were discounted.

RESULTS

The results are summarized in *Table I.*

DISCUSSION

Lichtenstein and Isoe (1951) reviewed 576 patients with an inguinal hernia and found that a right-sided lesion was approximately twice as common following appendicectomy as was a hernia on the left side—clearly a significant relationship.

Cox (1961), describing a series of 252 cases of inguinal hernia, found that 12·4 per cent of right-sided hernia sufferers had previously undergone appendicectomy, compared with only 7·1 per cent of cases on the left side. In a statistical exercise, however, he concludes that these results do not support a relationship between right inguinal hernia and appendicectomy.

Scott (1960), in a study of 196 cases of inguinal hernia repair, was unable to establish a cause-and-effect relationship.

In the current study there was no statistical difference between the number of post-appendicectomy cases coming to right inguinal hernia repair and the number undergoing left-sided repair.

Clearly the limitation of a retrospective study of this nature is the inability to differentiate accurately between an uncomplicated appendicectomy and one which involves sepsis, drainage of the peritoneal cavity, and prolonged wound healing.

Taking the current study in combination with those of Scott (1960) and Cox (1961) it appears that there has been no evidence published since the review in 1951 of Lichtenstein and Isoe to support the belief that right inguinal hernia is a complication of appendicectomy.

It remains to explain why this relationship, noted by eminent observers in the past, has not held true. One possible explanation is that the advent of antibiotics has made appendicectomy a less infected procedure with quicker wound healing and fewer local long-term complications.

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VENTILATION IN AN ARTIFICALLY PRODUCED GAS CAVITY UNDER BASAL CONDITIONS

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SUMMARY

The left hemithoraxes of 150 SPF rats were transformed into stable skin-lined gas cavities which were opened to the exterior. Fifty-nine of 75 rats so exposed survived with the natural, unilateral lung receiving air from the trachea, and the skin-lined hemithorax (an artificially produced gas cavity) receiving air independently from a thoracostomy.

In the test rats the mean arterial *p*H, Po_2, and Pco_2 were 7·355 ± 0·17, 77·03 ± 2·56 mm. Hg, and 38·41 ± 2·41 mm. Hg respectively. The values were similar to those obtained for unoperated rats (7·349 ± 0·015, 80·18 ± 2·77 mm. Hg, and 38·24 ± 0·94 mm. Hg). Although the skin-lined hemithorax was functionally an open-ventilated gas cavity, its mean tidal volume (0·93 ± 0·07 ml.) and its mean minute-ventilation (271·6 ± 24·4 ml. per kg. per minute) were about half of normal.

In the test rats the mean rate of respiration and the mean tidal volume were 98·5 ± 4·3 per minute and 1·68 ± 0·04 ml. as compared with 76·1 ± 5·3 per minute and 1·94 ± 0·12 ml. in the unoperated rats. The differences were significant. However, the difference between the mean minute-ventilation (tidal volume × rate of respiration) in the two groups was not significant. The values obtained were 506·1 ± 36·2 ml. per kg. per minute (test rats) and 407·0 ± 50·4 ml. per kg. per minute (unoperated rats). This suggested further that under basal conditions the test rats achieved adequate ventilation by means of a compensatory rise in the rate of respiration.

BODELL, Head, Head, and Formolo (1965) have shown that it is feasible to implant prosthetic lungs, but their experiments were short-lived. Peirce (1966, 1967) described an implantable prosthetic lung which permanently occupied the pleural cavity and received its gas as air from the trachea as a result of natural breathing. Such a concept, however, presents many unsolved problems and the experiments described here have been performed in an attempt to provide possible solutions to two of them.

First, there was the difficulty of making the pleural cavity equal to the task of housing a functioning foreign body such as an implantable prosthetic lung. As a possible solution an experimental model has been produced in which the left hemithorax of SPF rats was lined with skin-grafts and opened to the exterior (Wosornu and Melrose, 1971).

Secondly, the route by which the prosthetic lung could receive air remained to be established. Peirce (1966) had suggested that the prosthetic lung might receive air from the trachea. However, such an arrangement would pose difficulties related to the different compliances and airway resistance of the natural lung and the contralateral implanted lung. Hugh-Jones, Macarthur, Cullum, Mason, Crosbie, Hutchison, Winterton, Smith, Mason, and Smith (1971) have emphasized the imbalance between the distribution of gas and blood as an important cause of early respiratory failure in lung transplantation.

It was thought that these difficulties could be circumvented if the two halves of the thorax were so partitioned that they functioned as separate ventilating chambers with the normal unilateral lung receiving air from the trachea and the prosthetic lung receiving air from a separate opening directly through the chest wall.

The experiments described here sought to explore and to quantify such a possibility. Ventilation in the skin-lined hemithorax in rats was measured and compared with ventilation in the unilateral lung on the opposite side. The arterial *p*H, Po_2, and Pco_2 of the test rats were also measured and compared with those of unoperated rats.

MATERIALS AND METHODS

Male albino SPF rats (purchased from Carworth, Huntingdon, England) were used. Their mean initial weight was 240 ± 30 g. They were kept under standard laboratory conditions in large cages which housed 5 rats each. A total of 150 rats had successful intrapleural skin-grafting; 132 survived the next 4 weeks or more. In 75 of these rats the skin-lined hemithorax was opened to the exterior and sutured to the skin. In this way an open artificially produced gas cavity was obtained in which the left hemithorax had been transformed into a skin-lined cavity bearing a skin-to-skin stoma directly through the chest wall. Fifty-nine of the 75 rats thus exposed survived. Details of the technique employed to prepare the experimental model have been described elsewhere (Wosornu, 1972).

OBSERVATIONS ON THE SKIN-LINED HEMITHORAX 24 HOURS AFTER THE CREATION OF THE PERMANENT STOMA

1. **Radiographic Demonstration.**—The rats were screened radiographically after the creation of the permanent stoma. (It was observed that there was no paradoxical respiration.) Chest radiographs were taken. Forty consecutive preparations were studied as follows:—

2. **Arterial *p*H, Po_2, and Pco_2** were measured with a Radiometer Type BMS/3. Blood-samples were obtained from the exposed abdominal aorta of 10 test rats and 10 unoperated SPF rats as controls. The rats were anaesthetized with intraperitoneal sodium pentobarbitone (2 mg. per 100 g.), and 2–3 ml. of blood were withdrawn slowly with a heparinized

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syringe, care being taken to exclude air-bubbles; the estimations were made immediately afterwards.

3. Measurements of Ventilation.—The minute-ventilation in the unilateral lung and in the skin-lined hemithorax was measured separately. Thirty test rats (mean weight 356·8 ± 20·1 g.) and 12 unoperated SPF rats (mean weight 394·3 ± 40·4 g.) as controls were used. A miniature Krogh spirometer filled with room air was employed; the maximum capacity of the air chamber was 25 ml. The output signal from the spirometer, a displacement transducer, was passed through a transducer converter into a direct current amplifier (Type SE 905) and recorded on an ultra-violet recorder (Type SE 3005).

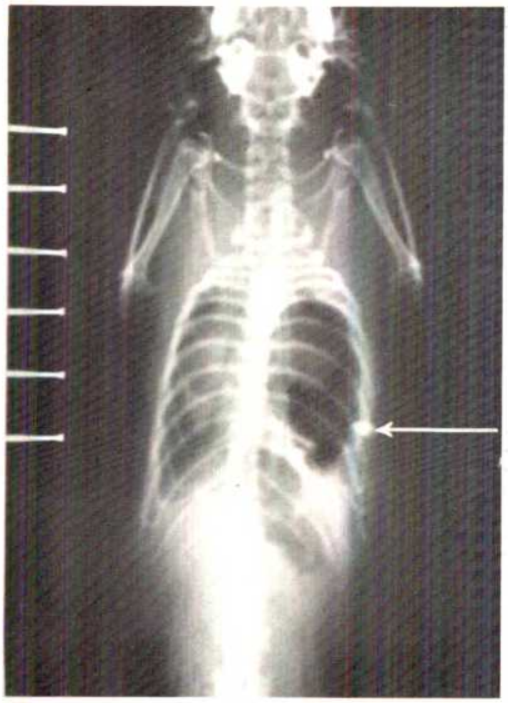

FIG. 1.—Radiograph of a test rat. The left hemithorax has been lined fully with skin-grafts and opened to the exterior to give the artificially produced gas cavity shown by the arrow. The markers, 1 cm. apart, were placed on the right-hand side.

TRACHEOSTOMY

The rats were anaesthetized with intraperitoneal pentobarbitone (2 mg. per 100 g.). A vertical midline skin incision was made in front of the neck, the trachea was exposed, delivered into the wound, and cannulated with a 3-cm. metal cannula (14 gauge) which was tied firmly in position. The stoma in the chest wall was fitted with a 3-cm. nylon connexion piece (internal diameter = 3·5 mm.); tissue glue was employed to obtain an airtight fit.

Before the tidal air was recorded the rats were allowed about 5 minutes to adapt to the tracheal cannula. The tidal air of the skin-lined hemithorax was recorded first. Recordings from the tracheal cannula were made continuously for about 45 seconds only because the system was closed and contained no agent to remove carbon dioxide. Three separate readings were made and the mean was accepted as the tidal air and rate of respiration.

RESULTS

Fig. 1 shows the radiograph of a test rat. The means of the arterial *p*H, Po_2, and Pco_2 of the test rats were similar to those of the unoperated rats (*Table I*).

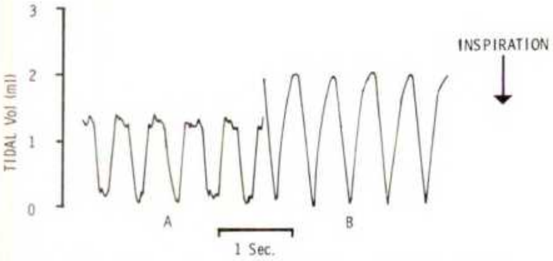

FIG. 2.—Tidal volumes recorded after the skin-lined pleural cavity had been opened to the atmosphere for 24 hours. A, Tracing from stoma in the chest wall. The stoma was created 4 weeks after intrapleural skin-grafting. B, Tracing from trachea of the same rat (280 g.).

Table I.—COMPARISON BETWEEN ARTERIAL *p*H, Po_2, AND Pco_2 IN UNOPERATED RATS AND IN TEST RATS

	*p*H	Po_2 (mm. Hg)	Pco_2 (mm. Hg)
Unoperated rats (10)	7·349 ± 0·015	80·18 ± 2·77	38·24 ± 0·94
Test rats (10)	7·355 ± 0·17	77·03 ± 2·65	38·41 ± 2·41
Statistical analyses (d.f. = 18)			
t	0·258	0·822	0·066
P	0·799†	0·433†	0·948†

† Not significant.

Values in the tables are given as the mean ± S.E.

Table II.—COMPARISON BETWEEN VENTILATION IN THE NATURAL UNILATERAL LUNG AND IN THE SKIN-LINED HEMITHORAX

	TIDAL VOLUME (ml.)	MINUTE-VENTILATION (ml. per kg. per minute)
Natural unilateral lung	1·68 ± 0·04	506·1 ± 36·2
Skin-lined hemithorax	0·93 ± 0·06	271·6 ± 24·4
Statistical analyses (d.f. = 29)		
t	10·6	8·98
P	< 0·001*	< 0·001*

* Significant.

$N = 30$; mean body-weight = 356·8 g.; mean rate of respiration = 98·5 per minute.

Functionally the skin-lined hemithorax was an open ventilated gas cavity (*Fig.* 2). The two ventilation variables measured were tidal volume and rate of respiration, and from the results the minute-ventilation per kg. body-weight was calculated. The three sets of values obtained were compared as follows: ventilation in the skin-lined hemithorax was compared with that in the natural unilateral lung, which in turn was compared with the ventilation of the unoperated rats.

In the test rats the mean tidal volume in the normal unilateral lung was 1·7 ± 0·04 ml. as compared with 0·9 ± 0·07 ml. in the skin-lined hemithorax. The respective minute-ventilations (tidal volume × rate of respiration) were 506·1 ± 36·2 and 271·6 ± 24·4 ml. per kg. per minute; the differences were significant (*Table II*).

Table III.—COMPARISON BETWEEN VENTILATION IN UNOPERATED RATS AND IN THE NATURAL UNILATERAL LUNG OF THE TEST RATS

	RATE OF RESPIRATION (per minute)	TIDAL VOLUME (ml.)	WEIGHT (g.)	MINUTE-VENTILATION (ml. per kg. per minute)
Unoperated rats (12)	76·1 ± 5·3	1·94 ± 0·12	394·3 ± 40·44	407·0 ± 50·4
Natural unilateral lung in test rats (30)	98·5 ± 4·3	1·68 ± 0·04	356·8 ± 20·11	506·1 ± 36·2
Statistical analyses (d.f. 40)				
t	2·96	2·59	0·923	1·51
P	0·005*	0·013*	0·361†	0·139†

* Significant. † Not significant.

The rate of respiration in the unoperated rats was 76 per minute as compared with 98·5 per minute in the test rats, and their respective tidal volumes were 1·9 and 1·7 ml. The differences were significant (*Table III*). However, the minute-ventilation in the unoperated rats (407·0 ± 50·5 ml. per kg. per minute) was not significantly different from the value obtained for the normal unilateral lung in the test rats (506·1 ± 36·2 ml. per kg. per minute) (*Table III*).

DISCUSSION

It has been possible anatomically to exteriorize the pleural cavity by relining it with skin-grafts (Wosornu, 1972). The next thing to consider was the function of the artificial gas cavity thus obtained. All normally or pathologically occurring or artificially produced gas cavities in the body may be divided into four functional types: closed non-collapsible, closed collapsible, open non-ventilated, and open ventilated gas cavities (Piiper, 1965). For example, whereas the normal paranasal air sinuses are open non-ventilated gas cavities the normal lungs are open ventilated gas cavities.

In the rats with a skin-lined hemithorax the two halves of the chest functioned as separate, open, ventilated gas cavities in phase. The natural unilateral lung received air normally through the trachea and the skin-lined hemithorax received air from an independent opening directly through the chest wall. However, the tidal volume and minute-ventilation in the skin-lined hemithorax were about half of normal.

In this investigation the values obtained for the mean tidal volume (1·9 ml.) and the mean rate of respiration (76 per minute) for the unoperated rats agreed closely with the mean values reported by others (Crosfill and Widdicombe, 1961; King, 1966; Binns, Clark, and Healey, 1971; McIntyre, 1971). Therefore, the values obtained for the test rats might be compared with those for the unoperated rats, since the experimental conditions were identical.

The test rats breathed significantly more rapidly than the unoperated rats ($P < 0{\cdot}005$) and there was also a significant difference between their tidal volume ($P < 0{\cdot}01$). However, there was no significant difference between their minute-ventilations ($P = 0{\cdot}1$; *Table III*). This suggested that the test rats achieved adequate ventilation by means of a compensatory increase in the rate of respiration.

King and Bell (1966) found that the mean arterial oxygenation in 35 normal SPF rats was 89·3 ± 2·9 S.D. and they commented also on the difficulty in obtaining arterial blood-samples from unanaesthetized rats. In the present study the test rats maintained normal arterial *p*H, Po_2, and Pco_2, which is a further indication that, under basal conditions, their respiration was adequate.

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POST-ANGIOGRAPHIC VERTEBRAL ARTERIOVENOUS FISTULAE

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SUMMARY

Four cases of arteriovenous fistula of the high cervical vertebral artery are presented as a complication of direct puncture of the vertebral artery using the lateral atlanto-occipital approach. One case is reported in detail. The management of such cases is discussed together with a brief review of the literature.

THE listed causes of arteriovenous fistula of the vertebral artery and veins are congenital or spontaneous (Ehrlich, Carley, and Kitrinos, 1938; Gooddy and Schechter, 1960; Svolos, Nomikis, and Tzouliadis, 1965; Markham, 1969), traumatic (Svolos and others, 1965), and as a complication of direct percutaneous puncture of the common carotid artery and the vertebral artery itself. This complication is very rare and has only been reported in a few cases. The literature reveals no previously reported case following vertebral artery puncture via the lateral atlanto-occipital route (Maslowski method) although Maslowski (1955) mentions this complication without providing details.

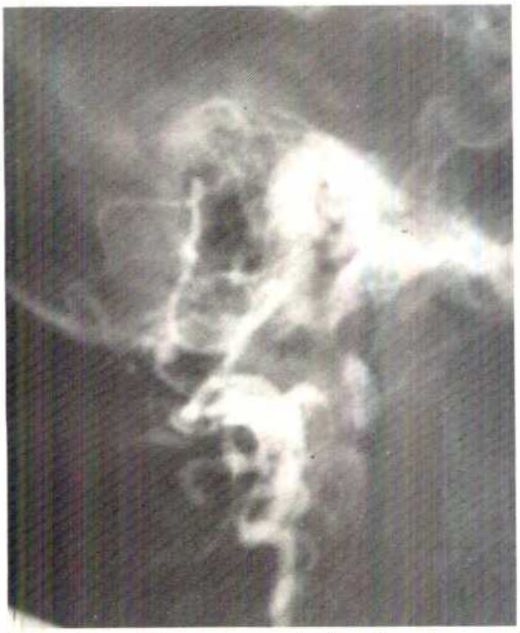

FIG. 1.—*Case* 1. The arteriovenous fistula of the right vertebral artery on 7 March, 1967.

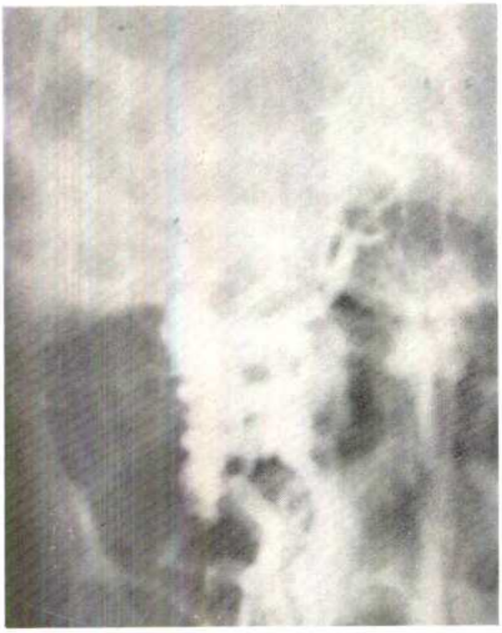

FIG. 2.—*Case* 1. The arteriovenous fistula of the right vertebral artery on 26 April, 1967, showing a larger venous drainage than before.

CASE REPORTS

Case 1.—The patient, a 42-year-old nurse, had been admitted previously with subarachnoid haemorrhage, and bilateral common carotid and bilateral vertebral angiography had revealed no definite lesion. Four weeks later she began to complain of noises in her head and was readmitted. A loud systolic bruit was audible over the right mastoid region. Percutaneous retrograde right brachial angiography on 7 March, 1967, showed an arteriovenous fistula of the right vertebral artery and the vertebral venous plexus in the region of the atlas at the site of puncture (*Fig.* 1). Following this procedure the noise became quieter and it was decided to defer surgery in the hope that the fistula would close by itself. A month later the patient returned complaining of dizziness and headache, whilst the noise in her head had been getting worse. Examination at that time showed no evidence of cardiac decompensation or enlargement, the pulse was 100 per minute and regular, and the blood-pressure was 120/80 mm. Hg. Neurological examination was normal apart from occasional nystagmus on looking to the right. There was a marked systolic bruit with a diastolic hum in the region of the mastoid. On 26 April a repeat percutaneous retrograde right brachial angiogram confirmed the existence of the fistula with, if anything, a larger venous drainage than before (*Fig.* 2). The bruit remained unchanged.

On 28 April, with the patient in the left lateral position, right side up, an incision was made just above and behind the right mastoid, curving somewhat transversely down to the midline in the region of C.V.2. A suboccipital craniotomy was performed with removal of the arch of the atlas. The vertebral artery was dissected completely free in its entire intradural and extradural course from the origin of the posterior inferior cerebral artery down to its emergence at the level of the foramen transversarium at C.V.2. The fistula could be seen joining a large conglomeration of veins overlying the vertebral artery at the arch of C.V.1 and at the old puncture site. The veins were all coagulated and stripped free of the artery, including the fistula.

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Postoperatively the patient has been asymptomatic and in good general health. At the time of the last review 3 years and 4 months after operation she had no recurrence of the bruit.

A further 3 cases of traumatic vertebral arteriovenous fistula have been observed in a total of approximately 2000 vertebral angiographies by the lateral atlanto-occipital route.

In each of these cases the patient complained of a loud bruit synchronous with the pulse on the affected side. The bruit appeared some weeks following the angiography in each case.

In 2 cases (*Cases* 2 and 3) the causal arteriovenous fistula was demonstrated radiologically by further vertebral angiography carried out by percutaneous puncture of the vertebral artery by the anterior route. In 1 of these cases the patient declared on waking after anaesthesia that the noise in his head had ceased and the bruit heard before angiography could no longer be detected. The bruit did not return. In the second case the patient noted that his bruit was much lessened on waking after anaesthesia and this disappeared completely within a few days. The bruit could not be heard on auscultation after the repeat angiography.

In the third case (*Case* 4) the fistula was demonstrated by angiography carried out by catheterization of the vertebral artery from the femoral artery. The bruit was unchanged by the procedure. Operative closure of the fistula was not successful. Repeat vertebral angiography by the anterior route 2 weeks after exploration demonstrated the fistula, although poorly because of arterial spasm at the puncture site. Following this procedure the bruit disappeared.

DISCUSSION

The most satisfactory way of obtaining a good vertebral angiogram is still by direct percutaneous puncture of the artery (Taveras and Wood, 1964). Traumatic arteriovenous fistula following direct puncture of the artery might be expected in a large number of cases since the venous plexus lies anteriorly and laterally close to the second and third parts of the vertebral artery. Sugar, Holden, and Powell (1949) commented on this possibility but stated that, although theoretically the possibility of traumatic arteriovenous fistula existed, they had not observed such a complication. They postulated that in the presence of a normal coagulative mechanism, and with the use of a sharp needle, the puncture sites should close automatically and quickly. In the present *Case* 1 the right vertebral artery was punctured by the lateral atlanto-occipital route. Initially the test injection of saline caused severe arterial spasm and the artery had to be repunctured on several occasions; these special and unusual circumstances might be the reason for the development of a fistula in this case.

The main clinical presentation of an arteriovenous fistula of the vertebral artery is a bruit over the site of fistula. This differs from an intracranial arteriovenous fistula which presents with a bruit in about 23 per cent of cases (Moody and Poppen, 1970). Other symptoms and signs of vertebral insufficiency, as were seen in *Case* 1, may not occur.

Patients have been managed in many ways—conservatively (Maslowski, 1955; Gooddy and Schechter, 1960; Robles, 1968), by proximal ligation (Orlson, Baker, and Svien, 1963), by proximal and distal ligation (Elkins and Harris, 1946), and by exposure and ligation of the fistula (Chou and French, 1965). In the present *Case* 1 the fistula was successfully closed by direct exposure and coagulation. It is interesting that in 3 out of the 4 cases presented here the bruit disappeared after repeat angiography by the anterior route although in 1 of these, *Case* 4, indirect vertebral angiography did not affect the bruit. In *Case* 1 only indirect angiography (percutaneous retrograde brachial angiography) was used to demonstrate the fistula. Direct surgical closure of the fistula can be a formidable procedure and may not be successfully completed (*Case* 4). Vertebral angiography by the anterior route may be a simpler alternative.

Acknowledgement.—We are grateful to Mr. J. F. Shaw for permission to report *Case* 4.

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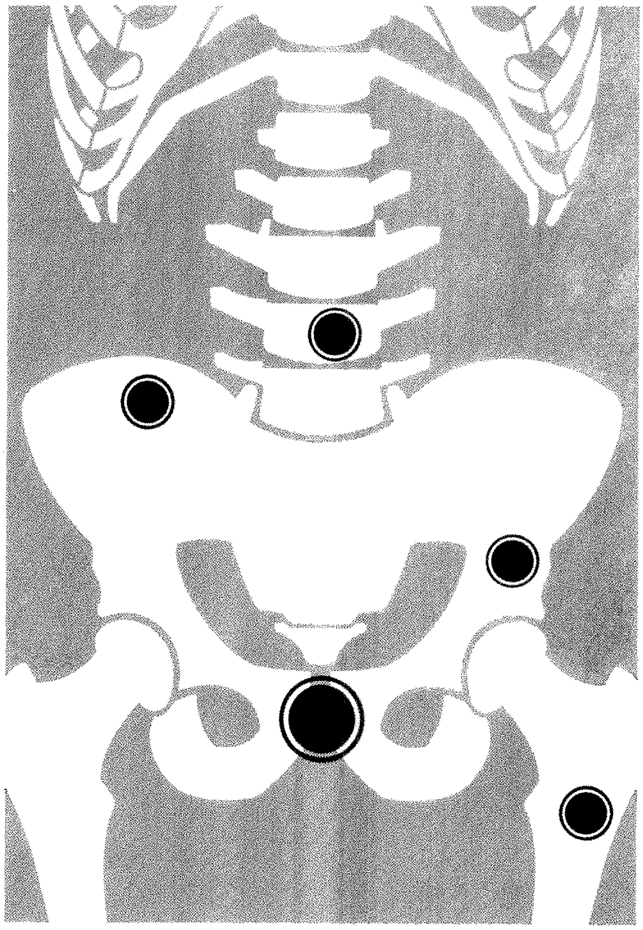

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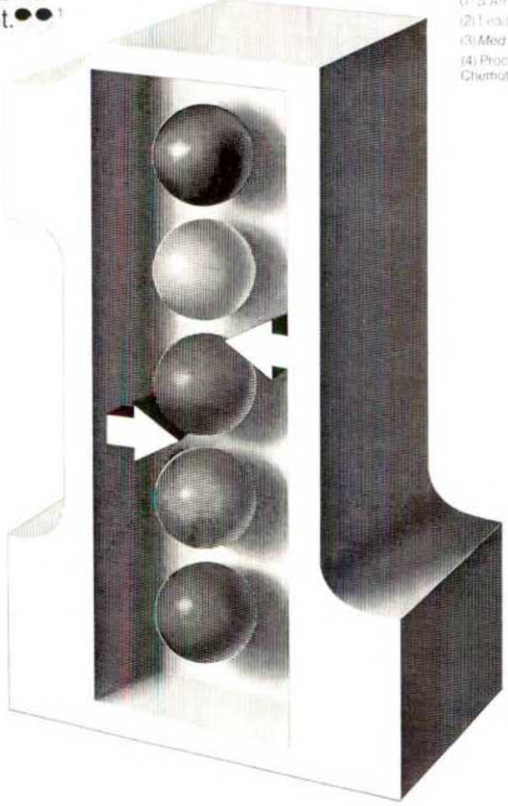

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POSTOPERATIVE CHANGES IN BLOOD VISCOSITY AND THE INFLUENCE OF HAEMATOCRIT AND PLASMA-FIBRINOGEN

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SUMMARY

The blood of 25 patients undergoing surgery has been investigated for levels of whole-blood and plasma viscosity, haematocrit, and plasma-fibrinogen before and after operation.

The whole-blood viscosity diminished by between 14 and 23 per cent after operation. The haematocrit fell from a mean preoperative level of 42·3 per cent (S.D. ± 5·2) to a mean postoperative level of 36·3 per cent (S.D. ± 5·5). When the effect on viscosity of this reduction in haematocrit was removed the blood viscosity rose after operation by 9–14 per cent.

The level of plasma-fibrinogen rose from a mean preoperative level of 360 mg. per cent (S.D. ± 78) to a mean postoperative level of 714 mg. per cent (S.D. ± 155), an overall increase of 98 per cent. This postoperative rise in the plasma-fibrinogen concentration exerted an effect on the blood viscosity opposite to that of the haematocrit.

The deleterious effects of a rise in blood viscosity on tissue perfusion and oxygenation are outlined, and the relevance of the reported findings to the maintenance of an adequate microcirculation in the postoperative period is discussed. Attention is drawn to the benefits of a slight fall in haematocrit during this period.

In patients undergoing surgery it is becoming increasingly clear that the maintenance of an adequate flow of blood through the microvasculature is as vital to life as that through the heart and great vessels.

In the postoperative period there are rapid changes in the haematocrit and in the plasma-fibrinogen, two factors which affect viscosity (Godal, 1962; Litwin, 1968). This period therefore provides an ideal time in which to measure the effects of these factors on blood viscosity.

The rate of blood-flow depends partly on the blood viscosity. Many factors affect viscosity; the effect of flow-rate or shear rate* is shown in *Fig.* 1. Reemsta and Creech (1962), using fresh heparinized blood from dogs, showed that at a constant temperature blood viscosity increased with increasing haematocrit. This effect was most marked when the haematocrit rose above 40 per cent, when the increase in viscosity became exponential (Rand, Lacombe, Hunt, and Austin, 1964) (*Fig.* 2).

The purpose of the present study was to determine, solely within the range of change occurring in patients, the alterations which occur in blood viscosity following operation, and to relate these to alterations in haematocrit and in plasma-fibrinogen.

MATERIALS AND METHODS

Blood-samples were taken by venepuncture from 25 patients (16 male and 9 female) undergoing major operations; these were mostly abdominal, such as prostatectomy, colectomy, abdominoperineal resection, and cholecystectomy. Samples were collected between 9 and 10 a.m. on the day before operation and on subsequent postoperative days up to the tenth day.

Blood was drawn into disposable plastic syringes through a No. 1 needle and was immediately transferred into plastic tubes containing 24 mg. E.D.T.A. (Stayne Laboratories).

Haematocrits were determined by the Hawksley microhaematocrit method. Blood for reconstitution to a haematocrit of 47 per cent was centrifuged at 700 *g* for 20 minutes and the plasma was pipetted off. Packed cells and plasma were then mixed in the proportion of 1 : 1, and the resultant haematocrit of 47 per cent was confirmed by the microhaematocrit method. Preliminary experiments confirmed that no alteration in viscosity readings resulted from centrifugation of the blood-samples.

Viscosity of whole blood, of blood reconstituted to a haematocrit of 47 per cent, and of plasma was determined using a Wells Brookfield viscometer, Model LVT, at six shear rates—5·75, 11·5, 23, 46, 115, and 230 sec.$^{-1}$ (Wells, Denton, and Merrill, 1961). The temperature was maintained constant at 37° C. by a Radiometer Thermostat VTS 13 waterbath. The viscometer measures torque developed in the fluid between a rotating cone and a plate. The torque produced is a function of the shear stress. The fluid, 1·2 ml., to be investigated was introduced between the cone and the plate. Provided that the quantity introduced did not exceed 0·4 ml. either side of this value, no alteration was produced in the viscometer readings. Shearing was started at 230 sec.$^{-1}$ and the readings were taken when the needle reading stabilized, usually within 3 minutes. An average of two readings was taken at each shear rate.

Plasma-fibrinogen Concentration.—Plasma-fibrinogen concentration was estimated using a gravimetric method (Hickman, 1971). Duplicate 1-ml. samples of plasma were added to plastic test-tubes containing 2 ml. of phosphate saline buffer,

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* Shear rate expresses how fast one plane or film of blood moves against its adjacent plane. It is expressed in cm. per second divided by unit distance between the films (in cm.), i.e., 1/sec. or sec.$^{-1}$.

Shear stress is the tangential force per unit area applied to a fluid plane to cause it to slide over its adjacent plane, thus producing flow. It is measured in dyn per cm.^{2}

Viscosity is defined as shear stress divided by shear rate in dyn per cm.^{2} or poise (P). 1 P = 100 cP.

*p*H 6, and 40 NIH units of thrombin (Leo Pharmaceuticals Ltd., Denmark). The samples were allowed to stand at room temperature for a minimum of 2 hours and the clot was then extracted using a steel needle (Regoeczi, 1967). After successive washes for 30-minute periods in 0·9 per cent saline and distilled water, the clot was removed from the needle using pointed forceps and placed in acetone for a further 30 minutes. The acetone was then drained from the clot, which was baked in a constant temperature oven at 90° C. for 15 hours. Clots were weighed immediately after removal from the oven using a Mettler, type H16, spring balance.

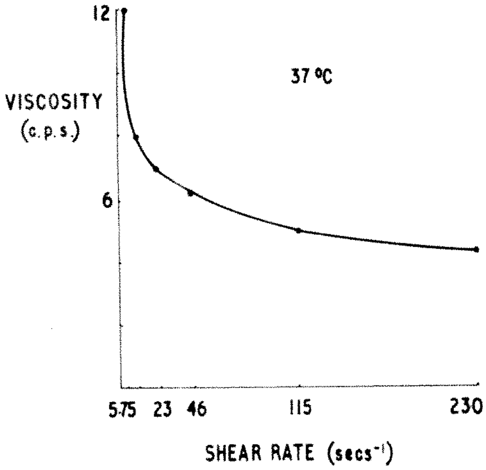

FIG. 1.—The relationship between shear rate and blood viscosity.

Table I.—THE PERCENTAGE DECREASE IN WHOLE-BLOOD VISCOSITY OCCURRING AFTER OPERATION MEASURED AT DIFFERENT SHEAR RATES

Shear Rate (sec.$^{-1}$)	*Percentage Decrease in Viscosity after Operation*
5·75	19·0
11·5	18·7
23·0	16·4
46·0	15·8
115·0	23·3
230·0	14·4

The mean fall in haematocrit after operation was 14·2 per cent.

Using this method, the mean percentage error in 80 such duplicate samples selected at random was 2·07 per cent (S.D. ± 1·85), and the mean value obtained in a study of 70 healthy young adults aged 20–35 years was 264 mg. per 100 ml. of plasma (S.D. ± 43·89).

RESULTS

The haematocrit fell from a preoperative mean of 42·3 per cent (S.D. ± 5·2) to a postoperative mean of 36·3 per cent (S.D. ± 5·5). This was significant ($P < 0{\cdot}001$).

The level of plasma-fibrinogen rose from a preoperative mean of 360 mg. per cent (S.D. ± 78) to a postoperative mean of 714 mg. per cent (S.D. ± 155). The peak of this rise varied from the first to the tenth postoperative days, but occurred most frequently on the third, fourth, or fifth day.

Whole-blood viscosity not corrected to constant haematocrit diminished after operation compared with the preoperative level. The decrease was between 14·4 and 23·3 per cent (varying with shear rate) after operation. At all shear rates the fall from preoperative to postoperative levels was significant ($P < 0{\cdot}005$). The percentage at each shear rate is shown in *Table I.*

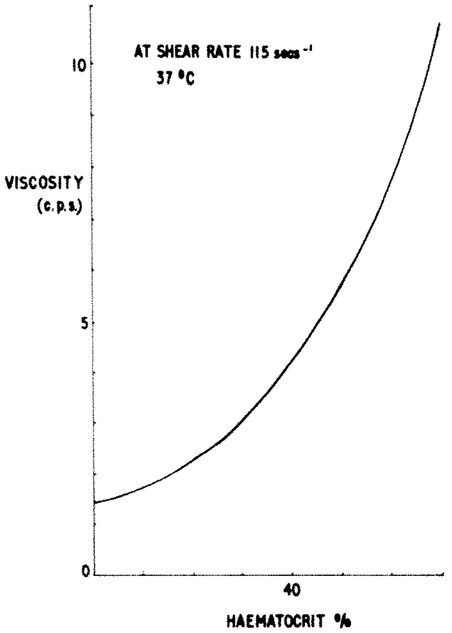

FIG. 2.—The relationship between the viscosity of whole blood and the haematocrit. Increase in the haematocrit above 40 per cent produced a marked increase in the blood viscosity.

Table II.—THE PERCENTAGE INCREASE IN VISCOSITY AFTER OPERATION WHEN THE HAEMATOCRIT IS MAINTAINED AT 47 PER CENT

Shear Rate (sec.$^{-1}$)	*Percentage Decrease in Viscosity after Operation*
5·75	13·7
11·5	13·8
23·0	11·5
46·0	10·7
115·0	11·2
230·0	9·4

The plasma-fibrinogen rose during this period by a mean of 98·3 per cent.

Whole-blood viscosity measured at a constant haematocrit of 47 per cent rose after operation compared with the preoperative level. This increase was significant at all shear rates ($P < 0{\cdot}001$). The increase varied from 9·4 to 13·8 per cent (varying with shear rate). The figures are shown in *Table II.*

When whole-blood viscosity was correlated at each shear rate with the haematocrit it was found that a rise in the haematocrit was associated with a rise in viscosity, and further that the correlation was significant (*Table III*).

When the effect of changes in the haematocrit was excluded by measuring blood viscosity at a constant haematocrit it was found that all shear rates changes in blood viscosity correlated with the change in plasma-fibrinogen and again this correlation was significant (*Table IV*). The results are shown graphically in *Fig.* 3.

Plasma-samples were investigated for the determination of their fibrinogen content and viscosity at shear rates of 230, 115, and 46 sec.$^{-1}$ Measuring the viscosity of each plasma-sample at these three shear rates did not alter the viscosity by more than 0·1 cP. This confirmed the Newtonian behaviour of plasma. There was a close correlation between plasma viscosity and plasma-fibrinogen ($P < 0·001$).

Table III.—THE CORRELATION BETWEEN THE BLOOD VISCOSITY AND THE HAEMATOCRIT AT THE DIFFERENT SHEAR RATES

SHEAR RATE (sec.$^{-1}$)	CORRELATION COEFFICIENT	SIGNIFICANCE
5·75	0·3461	$P < 0·01$
11·5	0·4870	$P < 0·001$
23·0	0·4687	$P < 0·001$
46·0	0·4234	$P < 0·001$
115·0	0·5201	$P < 0·001$
230·0	0·5471	$P < 0·001$

Table IV.—THE CORRELATION AT A CONSTANT HAEMATOCRIT (47 PER CENT) BETWEEN BLOOD VISCOSITY AND PLASMA-FIBRINOGEN AT DIFFERENT SHEAR RATES

Shear Rate (sec.$^{-1}$)	*Correlation Coefficient*
5·75	0·4022
11·5	0·5064
23·0	0·4184
46·0	0·4098
115·0	0·3369
230·0	0·4027

All these correlations are significant ($P < 0·001$).

The increase in the plasma viscosity from a preoperative mean of 1·5 cP to a postoperative mean of 1·7 cP failed to reach significance.

DISCUSSION

The range of shear rates used in this study probably includes the shear rates which are found in the main arteries, arterioles, and veins. Shear rate is a function of the flow rate and the radius of the vessel. The shear rate at the wall of the aorta has been estimated at 100 sec.$^{-1}$, and in an 'end-arteriole' of the order of 10 sec.$^{-1}$ (Wells and Merrill, 1962).

An increase in the fibrinogen concentration increases the blood viscosity because fibrinogen induces the aggregation of red cells (Rosenblum, 1969). Other plasma proteins have very little or no effect on viscosity except in the presence of fibrinogen, with which they act synergistically (Merrill, Filliland, Lee, and Salzman, 1966). Fibrinogen is a long fibrillar molecule with a length : width ratio of 15 : 1, and with a net change most dissimilar to that of the red cell. At concentrations of fibrinogen of 500–800 mg. per cent erythrocyte aggregation is marked. Albumin, on the other hand, with a length : width ratio of 3 : 1 and a highly electronegative charge inhibits aggregation (Ditzel, 1959; Wells, Gawronski, Cox, and Perera, 1964).

If the viscosity of defibrinated blood is determined there is very little change in viscosity with change in shear rate, such blood behaving virtually in a Newtonian fashion. Further, as shown in this study, plasma does behave in a Newtonian fashion. The non-Newtonian characteristics of whole blood are due therefore to the presence of both red cells and fibrinogen, and changes in their concentration in the blood are the main factors which influence blood viscosity. The postoperative period is characterized by changes in both these factors, so that any change in blood viscosity in this period will be the resultant of the two factors. The results of the investigations reported here allow the effect of changes in the concentrations of red cells (i.e., the haematocrit) to be separated from that of changes in the concentration of fibrinogen, and show that after operation a fall in the haematocrit counteracts the effect of the rise in fibrinogen, resulting usually in a slight fall in the viscosity of the blood.

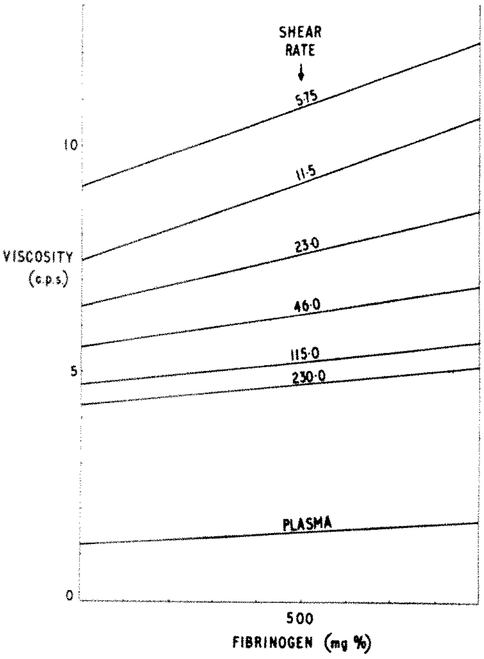

FIG. 3.—When blood-samples were measured at a constant haematocrit increase in the fibrinogen concentration was associated with an increase in the viscosity, the changes being greatest at lower shear rates.

Godal (1962) showed, as confirmed in this study, that after operation an increase in the level of fibrinogen in the plasma to as much as double or treble its preoperative value is normal. If the haematocrit remained constant throughout this period an increase in the blood viscosity of the order of 11 per cent would occur; if the haematocrit should also rise, as for instance as the result of an acute extracellular fluid deficit, the effect of this would be synergistic, with a further rise in blood viscosity and adverse effects on tissue perfusion and oxygenation.

Seligman, Frank, and Fine (1946) have shown, in studies on dogs, that increased blood viscosity aggravates haemorrhagic shock by reducing blood-flow. When the blood viscosity is high, the cardiac output becomes critically low at blood-pressures higher than those observed in haemorrhagic shock in which the blood viscosity is normal. Repogle, Kundler, and Cross (1965) have also shown that the cardiac output falls as the haematocrit and blood viscosity increase. In addition, the systemic peripheral resistance rises as the viscosity rises (Halmagyi, Starzecki, and Horner, 1965). Case, Berglund, and Sarnoff (1955) have demonstrated that while keeping the left ventricular work load of the vagotomized canine heart constant an increase in haematocrit from 32 to 55 per cent results in a decrease in the left coronary artery blood-flow from 193 to 83 ml. per minute. The same increase in haematocrit results in an increase in the coronary resistance from 0·6 to 1·7 mm. Hg per ml. per minute.

In the dog the consumption of oxygen by the tissues increases as the haematocrit increases up to a haematocrit value of 42 per cent, and then falls as the haematocrit continues to rise. At haematocrits of less than 42 per cent the increasing oxygen carriage of the blood more than compensates for the increasing blood viscosity (and hence decreasing cardiac output), but at values greater than 42 per cent the viscosity factor becomes the more significant (Crowell, Ford, and Lewis, 1959).

Any rise in blood viscosity which occurs as a result of the increase in plasma-fibrinogen postoperatively therefore tends to reduce cardiac output, reduce coronary blood-flow, and increase coronary and systemic peripheral resistance. It may also increase the liability to deep-vein thrombosis. In the postoperative period a modest drop in the packed-cell volume to offset this effect is beneficial to the patient, for the detrimental effect of the reduced oxygen carriage in the blood is more than offset by the improved circulatory effects.

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MALIGNANT MELANOMATA: AN AID TO PREOPERATIVE DIAGNOSIS

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SUMMARY

The use of the Zeiss operation microscope in the preoperative diagnosis of malignant melanomata has given an overall accuracy rate of 85 per cent. The method is quickly and simply carried out, and is without risk to the patient and the operator. The machine is portable and can therefore be used at the bedside in a patient who is not ambulant. Only a normal domestic power supply is required. The use of this machine in the assessment of such cases is therefore advocated.

THE clinical diagnosis of an advanced malignant melanoma (the malignant tumour arising from the melanocyte cells of the epidermis) seldom offers a diagnostic problem. In the early case, however, clinical diagnosis can be difficult, and as the patient's greatest hope of a cure lies in the early treatment of the lesion by wide excision and skin-grafting it is a problem of considerable significance. On the one hand lies the risk of failing to diagnose a malignant melanoma and delaying definitive treatment, and on the other there is the possibility of wrongly labelling a benign pigmented naevus as malignant and instituting unnecessary extensive surgery.

Published figures in the literature lend support to the need for assistance in this diagnosis; Sverdlow (1952), reporting on 27 histologically proved malignant melanomata, states that only 16 (57 per cent) had been accurately diagnosed preoperatively, and Becker (1954), reporting on 151 specimens which were subsequently confirmed as malignant melanomata, states that 72 (48 per cent) were received at the laboratory with the correct clinical diagnosis.

It is in view of these figures that a study has been carried out over the past 5 years with the aim of evaluating the use of the Zeiss operation microscope for surface examination of suspected malignant melanomata at low magnifications. It was anticipated that surface features of malignant melanomata could be identified in this way, and could offer a guide to the surgeon in his preoperative assessment of the lesion.

MATERIALS AND METHODS

The machine used for this study was the Zeiss operation microscope (*Fig.* 1). This is a binocular microscope with a 35-mm. camera mounted on a side-arm. The magnifications obtainable are × 6, × 10, × 16, × 25, and × 40. The lesions referred for assessment are first washed thoroughly and then covered with a light oil to increase the epidermal translucency. Olive oil has been found to be satisfactory for this purpose. As it has been shown that melanocytes are not stimulated to mitotic activity by skin stripping with adhesive tape (Lessard, Wolff, and Winklemann, 1968) this procedure is used in lesions with a thick epidermal layer.

Every lesion is examined at all available magnifications and then photographed using Kodachrome II colour film and flash illumination. The most satisfactory magnifications for photography are × 10 and × 16, as above this magnification small movements such as transmitted abdominal pulsation become troublesome. All the lesions included in this report were removed surgically and the histology of each lesion was studied.

RESULTS

The accuracy of this method of assessment is shown in *Table I*. It can be seen that a total of 72 histologically confirmed malignant melanomata have been studied and that the preoperative accuracy rate was 85 per cent. The surface features which were commonly found to be present in these lesions and which proved a pointer to the diagnosis were, first, extensive variation in colour and in pigment density within any one lesion. Thus, although a blue naevus may have a characteristically blue-black appearance the colour is uniform, whereas a malignant melanoma may at one point have pigment very similar to that of the naevus but other areas may show dark- or light-brown areas of pigmentation and also areas of erythema. Another important feature has been found to be the relative distribution of pigment within the lesion, as a malignant melanoma frequently shows dark pigment deposits at its lateral margins whereas the tendency in benign pigmented naevi is for the lesion to show peripheral pigment loss with the greatest density of pigment centrally. Malignant melanomata frequently have dilated and abnormal capillaries clearly visible on the surface of the lesion and such capillaries have never been observed in a benign junctional or compound naevus. A feature which has been noted to be present in a high proportion of lesions showing junctional activity as a component of their histological features, namely malignant melanomata and junctional and compound naevi, is the presence of a very regular, delicate, superficial pigmentary pattern, not unlike a spider's web. This pattern would appear to indicate areas of active melanocyte proliferation, and although by itself this feature is not diagnostic for malignant melanoma its presence in conjunction with marked pigment variation, peripheral pigment increase, or dilated capillaries is virtually diagnostic of malignant melanoma as none of these other features has been observed in junctional or compound naevi.

Table I.—ACCURACY OF PREOPERATIVE ASSESSMENT USING SKIN MICROSCOPY AS CONFIRMED BY SUBSEQUENT HISTOLOGICAL EXAMINATION

TYPE OF LESION	NO. CORRECTLY DIAGNOSED	NO. INCORRECTLY DIAGNOSED	PERCENTAGE ACCURACY
Malignant melanomata	61	11	85
Junctional naevi	29	3	91
Compound naevi	92	13	91
Blue naevi	7	1	87
Basal-cell papillomata	34	8	81
Angiomata	12	2	86
Multifocal basal-cell carcinomata	7	3	70

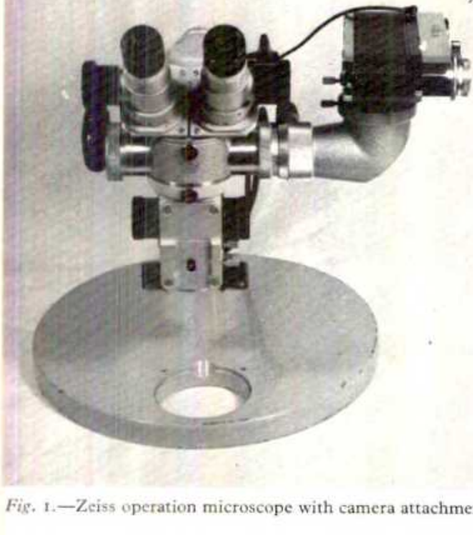

Fig. 1.—Zeiss operation microscope with camera attachment.

The amelanotic melanoma is commonly felt to be an extremely difficult diagnostic problem, but in the present series only 2 lesions, both in the subungual area, were found to be completely devoid of melanin pigmentation. This observation is in keeping with Olsen's (1966) comment, based on a series of 500 cases of malignant melanoma, that truly achromatic malignant melanomata are rare and that in the majority of cases labelled as amelanotic lesions one can observe a rim of melanin pigment at the lateral limit of the lesion.

DISCUSSION

The differential diagnosis of a malignant melanoma commonly includes other benign tumours of melanocyte origin such as junctional, compound, and blue naevi. Vascular lesions such as cavernous haemangiomata may on occasion have a very deeply pigmented surface and have also to be considered. Pigmented basal-cell papillomata and pigmented basal carcinomata of the adenocystic type may also at times give rise to confusion. *Table I* shows the accuracy of skin microscopy for differentiating these lesions preoperatively. The detailed magnified surface appearance of these lesions is reported elsewhere (MacKie, 1971).

Other methods of assisting preoperative assessment of malignant melanomata have been advocated in the past, but none has as yet won general acceptance. In 1955 Bauer and Steffen advocated the use of intravenous radioactive phosphorus using the isotope ^{32}P. This was based on their finding that the radioactive uptake over the malignant melanoma was 3·85 times higher than that over contralateral normal skin. Brauer, Kopf, Witten, Berman, and Cave (1960) also used this technique for studying 145 lesions and found 20 per cent false-positive and 37 per cent false-negative results. A comparison of the radioactive uptake over benign pigmented skin tumours is not included in this series and this method would not appear to be one which could be quickly or routinely undertaken in a busy ward or out-patients' department.

In 1962 Venkei and Bakos advocated the use of thermo-differentiation in the diagnosis of malignant melanoma. This suggestion was based on their findings that the skin temperature over a primary malignant melanoma is 1° C. or more higher than that over contralateral normal skin. In this series of 80 cases of histologically proved malignant melanomata 61 (76 per cent) gave positive results. Again a comparison with benign pigmented skin tumours is not included. A disadvantage of this method is the fact that consistent skin temperatures are extremely difficult to obtain, and usually require several hours' adaptation in a thermostatically controlled room.

The most recent method for preoperative assessment of pigmented lesions was advocated in 1968 by Andreev, who suggested incisional biopsy of the suspected malignant melanoma under cover of a dose of radiation to the tumour of 4000–5000 rad. In view of the work of Olsen (1967), who has shown that the natural progression of malignant melanoma treated by radiation is initial regression followed by early and widespread metastases, the wisdom of this procedure would seem to be debatable.

The use of frozen section in cases where clinical doubt as to the histological nature of the lesion exists is much debated. The chief problem is that only one portion of the lesion is sampled which may well show only active junctional change whereas an area only 1 or 2 mm. distant may show definite malignant activity. This fact is the reason for the many discrepancies which exist between the frozen-section report on a pigmented lesion and the report based on paraffin sections. The technique of frozen section in suspected malignant melanomata requires careful attention as the cells are easily distorted and the differentiation between junctional activity and early malignant change can thus be made extremely difficult (Rook, Wilkinson, and Ebling, 1968).

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HAEMANGIOMATA OF SKELETAL MUSCLE

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SUMMARY

Two cases of skeletal muscle haemangiomata are described.

All previous cases of this condition are reviewed and a brief account is given of the important facets of aetiology, diagnosis, and treatment.

Wherever a soft-tissue swelling presents in the region of skeletal muscle the possible diagnosis of a haemangioma should be considered and may frequently be confirmed pre-operatively with the aid of radiography.

Local excision remains the treatment of choice wherever possible.

Two new cases of haemangiomata arising in muscle are described. They fall into the rare group of skeletal muscle haemangiomata which provide interesting problems of diagnosis. The present cases are discussed in the light of previously reported cases with special reference to aetiology, diagnosis, and management.

CASE REPORTS

Case 1.—The patient, a 28-year-old married woman, was admitted to Westminster Hospital in September, 1970, with a swelling of the right upper arm which had been progressively enlarging over the past year. She was a professional 'cellist and had attributed the swelling to muscle hypertrophy resulting from over-zealous practice. Apart from occasional aching in the upper arm she complained of no other symptoms and her general health was excellent. Photographs of the patient as a young girl revealed no visible swelling at that time.

Examination revealed a normal, healthy young woman with no cutaneous haemangiomata, although she was suffering from an acute episode of pityriasis rosea at the time of admission. The lump in the arm measured 7 × 3 cm., was firm, mobile, and separate from the vascular bundle, but appeared to arise from the biceps muscle (*Fig.* 1). There was no skin attachment and no palpable axillary lymph-nodes could be felt. Fluctuation could not be demonstrated and there was no bruit.

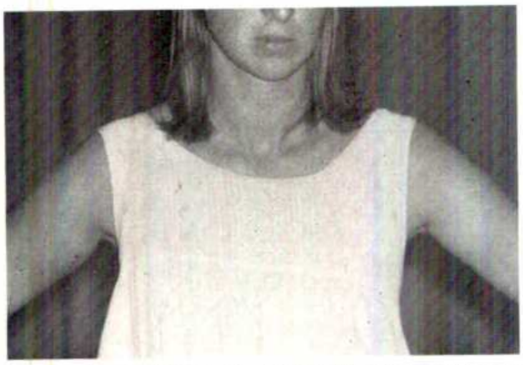

FIG. 1.—*Case* 1. Patient after biopsy but prior to definitive excision, showing site of tumour over right biceps brachii.

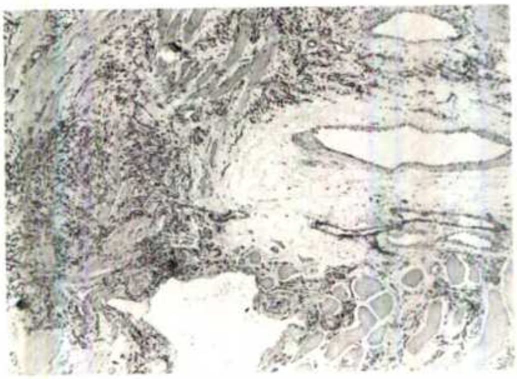

FIG. 3.—*Case* 1. Break up of muscle-bundles by blood-vessels of varying size. H. and E. (× 60.)

A radiograph of the chest and a full blood-count were normal. A preoperative diagnosis of fibrosarcoma was made, and the patient was given a single treatment of radiotherapy preoperatively, producing a centre dose of 1000 rad. At operation (18 Sept., 1970) an incision was made over the swelling and a highly vascular fibromuscular mass was found within the epimysium of the right biceps brachii. A biopsy was taken and the wound was closed. The biopsy report was as follows: 'The lesion is made up of vasoformative tissue of capillary type. In many areas the lesion consists of solid islands of endothelial cells devoid of lumina (*Fig.* 2). The vascular process is infiltrating through muscle-bundles (*Fig.* 3). The appearances are those of a vascular hamartoma and not a true neoplasm. Apparent growth of these lesions is said to be due to the opening up of vascular channels already present in a collapsed state. I have been able to match this case with one removed from the biceps of a young woman in 1964 at the Royal Marsden Hospital. In that case local excision was carried out and the patient had no further trouble.' With this information a right subclavian arteriogram was performed (*Fig.* 4). This showed a highly vascular lesion in the middle third of the upper arm on its medial aspect. It derived its blood-supply from a number of small branches of the brachial artery.

Further surgery was planned to remove the lesion. At operation on 25 Sept. a 10-cm. incision was made down the medial border of the upper arm, excising the biopsy scar. The tumour was seen to derive its blood-supply from obviously dilated branches of the brachial artery in the groove between the biceps and the coracobrachialis. There was no clear delineating plane between the tumour and biceps muscle-fibres. The musculocutaneous nerve was identified and preserved. The feeding vessels to the tumour were ligated, causing visible shrinkage of the mass. The tumour was excised together with superficial fibres of the biceps brachii which underlay it.

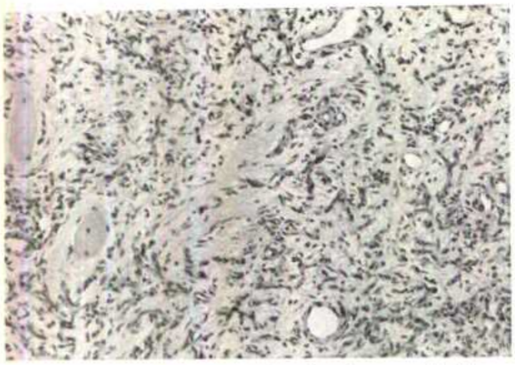

FIG. 2.—*Case* 1. Proliferating but largely uncanalized vasoformative tissue. H. and E. (× 62.)

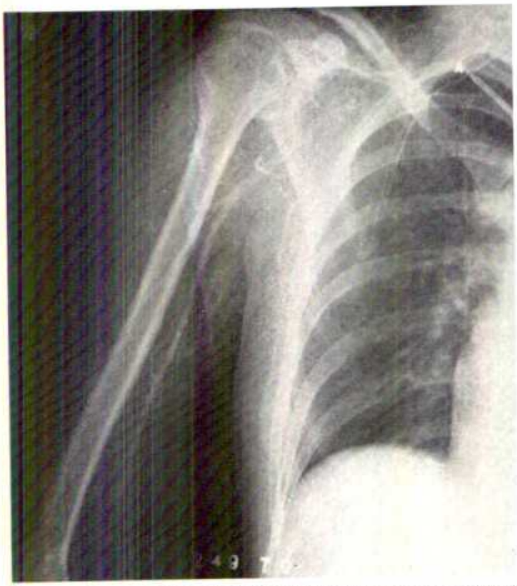

FIG. 4.—*Case* 1. Right subclavian arteriogram showing a highly vascular lesion over the medial aspect of the upper arm.

Postoperative recovery and healing were uneventful. The patient was last seen on 7 Jan., 1971, when the wound was well healed with slight keloid deformity. She had no residual motor or sensory deficit and was once again playing the 'cello professionally.

PATHOLOGY.—The macroscopic appearance was of a strip of biceps muscle measuring 11 × 3 cm. Within the muscle there was a small area of haemorrhage related to the biopsy. The surrounding muscle showed a speckled white appearance presumably due to the vascular component.

The microscopic appearance confirmed the diagnosis of vascular hamartoma. The histological appearances were modified in some areas by the biopsy, but there was no sign whatsoever of neoplasm of any kind. The muscle from the cut ends of the specimen was normal.

Case 2.—The patient, a 29-year-old fireman, was admitted to Westminster Hospital in February, 1971, with a large lump in the centre of his back. He had first noticed the lump 3 months previously, at which time he had felt a pain in the back on stretching forward. The lump had apparently become slightly smaller in the intervening 3 months. The patient was otherwise in good health with no past medical history apart from the excision of a branchial cyst 2 years previously.

Examination revealed a healthy man with no other palpable lumps and no cutaneous haemangiomata. The lump in the centre of his back was flat and tender. It measured 4 × 2·5 cm. and had an ill-defined border. There was no skin fixity but there was some deep attachment. Fluctuation could not be demonstrated and there was no bruit.

Radiographs of the chest and spine were normal, as was a full blood-count.

A provisional diagnosis of neurofibroma was made. At operation (23 Feb., 1941) an extensive ill-defined haemangiomatous mass was found extending from the latissimus dorsi muscle. Biopsies were taken and the incision was closed. A firm pressure dressing was applied. The post-operative course was uneventful.

PATHOLOGY.—Histological examination showed a cavernous haemangioma in which thrombosis had occurred in some of the vascular spaces. There was no evidence of neurofibromatosis.

DISCUSSION

Liston (1843) is generally accredited with the first description of a skeletal muscular haemangioma. His case was of a tumour of the popliteal space which was found to arise from the semimembranosus muscle. Since then excellent and comprehensive reviews have appeared on the subject, notably by Davis and Kitlowski (1930), Jenkins and Delaney (1932), Swallow, Eger, and Wagner (1944), Bonvallet (1950), Jones (1953), Bendeck and Lichtenberg (1957), Scott (1957), and La Sorte (1960).

Scott (1957) collected 393 histologically proved cases, to which may be added 9 cases collected by La Sorte (1960) and 16 cases collected by Stock (1953), but not included in previous reviews. Since then 9 further cases have been reported, including the present 2 (*Table I*), bringing the current total to 437 cases.

Most authors believe that these tumours are congenital in origin and they have frequently been described as vascular hamartomata. Most of them are discovered in childhood or adolescence, and over 85 per cent of the reported cases occurred in the first three decades of life. Willis (1960) reported a known congenital case. Scott (1957) described them as arising in abnormal embryonic sequestrations which retain their embryonic characteristics. Excessive muscle contraction and minor trauma probably play a part in stimulating blood-flow into pre-existing vascular malformations. The present *Case* 1 arose in the right arm of a professional 'cellist, and *Case* 2 on the back of a fireman.

The tumours show an almost equal sex incidence with a marginal preference for women. They mainly arise from a single muscle (66 per cent of the reported cases) although in some instances as many as five muscles have been involved (La Sorte, 1960). It seems likely that all races may be affected with reported cases in Asians, Americans, Europeans, and Indians. As already stated, the age of presentation is greatest in the under-30 age-group (85 per cent), with less than 5 per cent occurring after the age of 50.

Table I.—DETAILS OF 9 RECENTLY REPORTED CASES OF SKELETAL MUSCLE HAEMANGIOMATA

AUTHOR	AGE AND SEX	SITE	TREATMENT
Das (1959)	21 F.	Vastus medialis	Excision
	17 M.	Deltoid	Excision
	25 F.	Calf muscles	Biopsy and radiotherapy
	9 M.	Sternomastoid	Excision
	46 M.	Vastus medialis	Excision
Ghosh (1959)	22 M.	Quadriceps	Biopsy and compression bandage
Band and Khan (1967)	11 F.	Vastus medialis	Excision
Fergusson (1972)	28 F.	Biceps brachii	Excision
	29 M.	Latissimus dorsi	Biopsy and compression bandage

Ninety-eight per cent of cases present with a soft-tissue swelling which has been apparent for between 1 month and 20 years. Sixty per cent of cases have associated pain from pressure on local nerves. The overlying skin was normal in 39 per cent of cases, but was frequently warm and bluish-red; ulceration of the overlying skin has been reported. The swelling is smooth and mobile in the transverse axis of the muscle-fibres. It may be any size and the dimensions in an individual tumour may vary. For instance, when situated in a limb muscle the swelling will become smaller with elevation of the limb, and greater if a proximal tourniquet is applied occluding the venous return. La Sorte (1960) reports a bruit in 1·8 per cent and pulsation in 3 per cent of cases. Functional impairment with deformity, limitation of movement, and muscle weakness are common when extensive muscle involvement has occurred.

Skeletal muscle haemangiomata are misdiagnosed in over 90 per cent of cases, although in the 9 recently reported cases (*Table I*) 4 had a correct preoperative diagnosis. The most common erroneous diagnoses are lipoma, fibrosarcoma, lymph-nodes, and hernia. Radiological evidence has proved useful in making a correct diagnosis. Soft-tissue films may show the appearance of dilated vessels, and also the presence of phleboliths which Wakeley described as characteristic in 1921. More recently, arteriograms have proved invaluable in many suspected cases. Aspiration of blood and biopsy are the most conclusive diagnostic tests.

In situ the tumours appear red with a bluish tinge; they may be spongy or firm, and some contain patchy calcification. They are more often diffuse than circumscribed and appear to infiltrate local muscle-bundles. They progressively enlarge locally but never metastasize. On excision the vascular part of the specimen tends to shrink to a small piece of ragged tissue. Microscopically, arterial, venous, capillary, and cavernous elements may be found infiltrating between muscle-fibres in various degrees of degeneration. Skeletal muscle haemangiomata accounted for 0·8 per cent of 1308 assorted haemangiomata reviewed by Watson and McCarthy (1940).

The treatment of choice is local excision of the tumour which may shell out or may necessitate excision of a cuff of the surrounding muscle. Where excision is impracticable because of extensive infiltration or the likelihood of risking permanent deformity, then radiotherapy may be beneficial.

Carbon-dioxide snow, of use in skin lesions, is quite unsatisfactory for the diffuse skeletal haemangiomata. Injection of sclerosant fluids has been tried by Stock (1953) without great success. Partial excision with the risk of recurrence is to be avoided wherever possible. In very rare cases of large painful tumours causing deformity or loss of function, amputation may be necessary.

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NASOGASTRIC TUBE MANAGEMENT

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Although the routine use of a nasogastric tube after abdominal operations is contentious (Earle, Metheny, and Lundmark, 1955) there are those who consider that tube decompression of the upper gastro-intestinal tract has contributed much to the relative safety of abdominal surgery (Wells and Tinckler, 1962).

The purpose of utilizing a nasogastric tube in postoperative management or for preoperative preparation of patients with intestinal obstruction is to evacuate fluid and gas from the upper gastro-intestinal tract; by so doing tension on recent suture lines is lessened, bowel distension is reduced with benefit to the vascularity and nutrition of the bowel wall, drag is reduced on vulnerable suture lines as in oesophagojejunal anastomosis, patients are relieved of a bloated feeling in the abdomen, and reduction of bowel distension eases strain on the patient's abdominal parietal wound.

Investigation of gastro-intestinal motility after abdominal operations has shown that while small-bowel tone and movement persist, gastric tone and motility either decrease or disappear for approximately 24–48 hours postoperatively, depending on the nature of the operation (Tinckler, 1960).

HISTORICAL REVIEW

In 1790 John Hunter, in a way one would expect of him, was one of the earliest to intubate the stomach (Hunter, 1841). His tube was a fresh eel skin drawn over a probang for introduction and was used for feeding a patient unable to swallow because of bulbar palsy.

Alexander Munro (1797) claimed that his father in 1767 used a flexible tube of coiled wire covered with leather to remove fluid and gas from cattle's stomachs in which there had been excessive fermentation.

A Philadelphia surgeon, Philip Physick, in 1800 advocated the use of a tube to wash out the stomach of poisoned patients.

Although Kussmaul (1869) revived clinical interest in stomach tubes, their development and routine application paralleled advances in abdominal surgery in this century.

The principal use which was made of gastro-duodenal tubes initially was the examination and analysis of gut secretions for diagnostic purposes. Later under the impetus of people like Wangensteen and Paine (1933) such tubes began to be more frequently applied for aspiration in the management of gastric and intestinal distension by decompression. Long before then, however, came isolated reports of utilizing gastroduodenal tubes for aspiration. Westerman in 1910 reported 15 cases of paralytic ileus due to peritonitis which were treated by siphon drainage of the stomach with a nasogastric tube, and Meyer (1926) used gastroduodenal tubes after gastric operations for aspiration and administration of fluids.

Matas (1924) advocated the use of siphon drainage of the stomach postoperatively whenever there was gastro-intestinal stasis.

Continuous suction aspiration of duodenal tubes originated with Ward of San Francisco (1925) but

Wangensteen (1932) popularized the application of this principle in the management of mechanical intestinal obstruction. Wangensteen and Paine (1933) showed that continuous suction was much more efficient than siphon drainage in decompressing the gastro-intestinal tract.

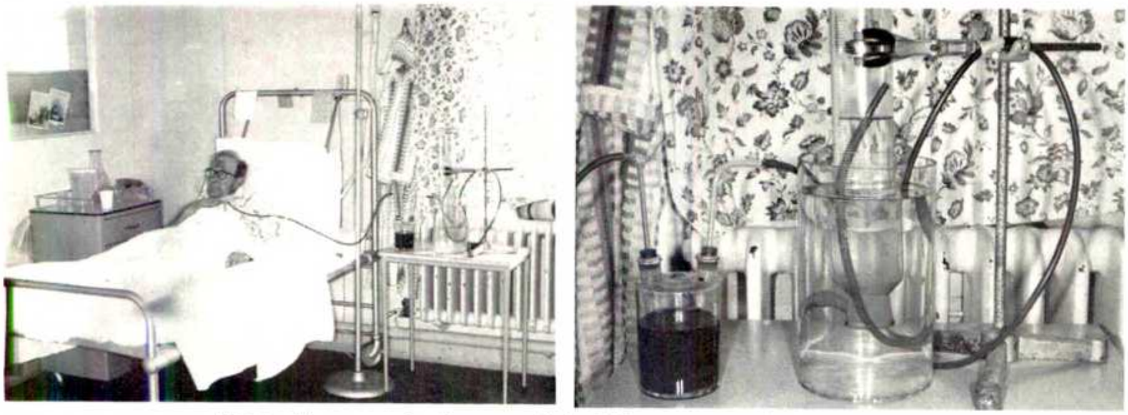


FIG. 1.—The nasogastric tube connected via a fluid trap to a gas-collecting apparatus.

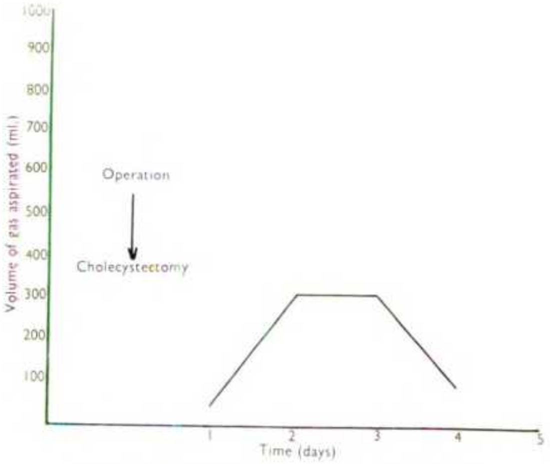


FIG. 2.—*Case* 1. Nasogastric tube gas collection.

NASOGASTRIC TUBE MANAGEMENT

The most commonly employed method of nasogastric tube management is to secure the tube in position with a turn of strapping applied to the patient's nose and to aspirate the tube at intervals.

The main advantage of adopting an intermittent aspiration policy is that it ensures that the patient is visited at prescribed intervals and the patency of the tube tested, giving an opportunity to flush the tube and adjust its position if it is found to be blocked or displaced.

It cannot be denied that the presence of a nasogastric tube causes the patient some discomfort. If then a tube is to be used it should obviously be used to the greatest possible effect and discomfort mitigated as much as possible. It is pointless to subject the patient to nasogastric intubation if no attempt is made to ensure that the tube accomplishes its purpose. This means ensuring that the tube does not become blocked and that it lies at all times in the optimum position for evacuating fluid and gas from the stomach. The question remains how best to service these tubes to maximum advantage. The options are intermittent aspiration, spigoting in the interval, as appears to be standard practice, to leave the tube open to drain spontaneously into a receptacle, or a combination of intermittent aspiration and open drainage.

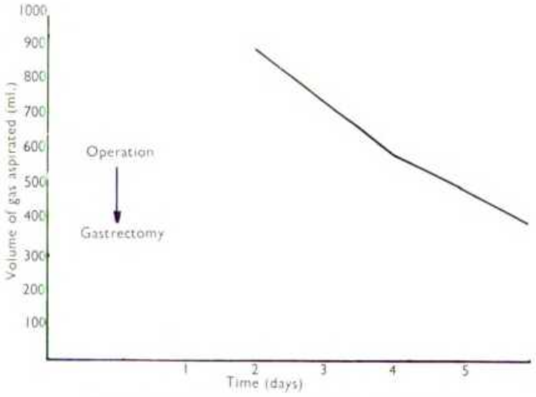


FIG. 3.—*Case* 2. Nasogastric tube gas collection.

METHODS AND THE AIM OF THE INVESTIGATION

In the patients investigated the nasogastric tube was connected by tubing led under water to a gas-collecting apparatus placed at the bedside (*Fig.* 1).

By this means gas passing from the stomach up the nasogastric tube was collected and measured during successive 24-hour periods.

A fluid trap was interposed between the patient and the gas collector in which accumulated gastric contents which siphoned over from time to time; in the patients investigated this spontaneously siphoned fluid amounted to volumes up to as much as 500 ml. in a 24-hour period.

The stomach was aspirated intermittently, disconnecting the nasogastric tube from the gas-collecting apparatus for the purpose.

The object of the investigation was to determine how much gas spontaneously vented from the stomach via the nasogastric tube if it was left on open drainage in between aspiration as an indication as to the possible advantage of open drainage which would justify recommending its routine adoption.

RESULTS

The results for 6 patients investigated are portrayed in *Figs.* 2–7 and featured in *Table I.*

It is to be noted that the peak of gas collection was reached in general on the second postoperative day and thereafter tailed off, presumably as gastric motility returned following the immediate transient postoperative loss of stomach activity.

DISCUSSION

The results of this investigation revealed that by spigoting nasogastric tubes between aspirations in order to avoid soiling the bed linen a substantial

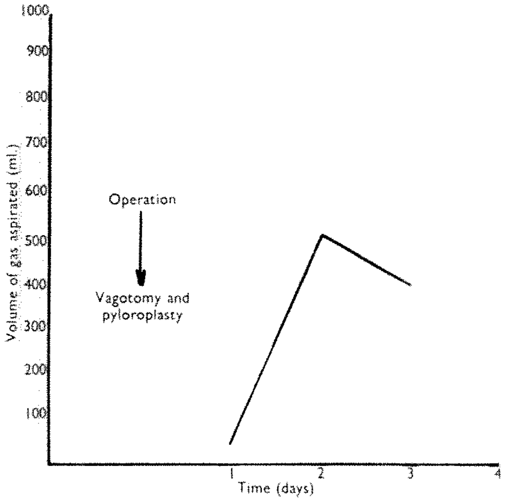


FIG. 4.—*Case* 3. Nasogastric tube gas collection.

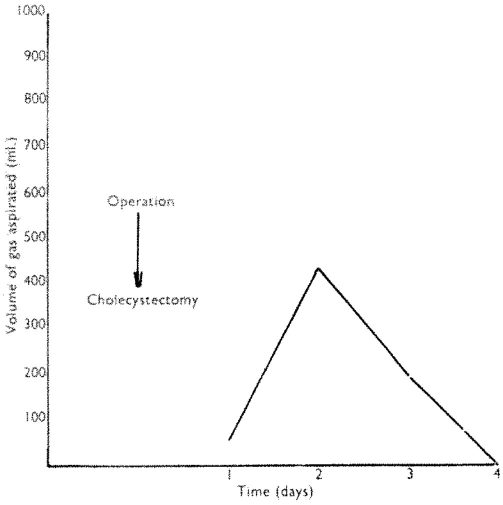


FIG. 5.—*Case* 4. Nasogastric tube gas collection.

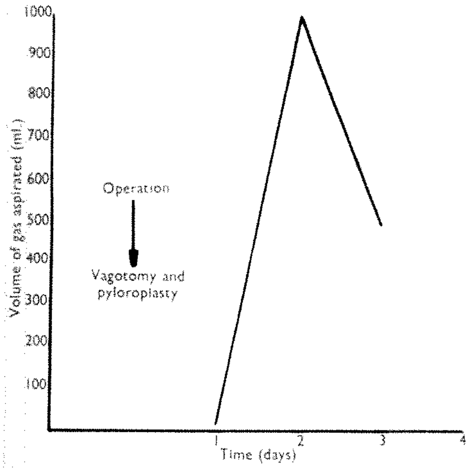


FIG. 6.—*Case* 5. Nasogastric tube gas collection.

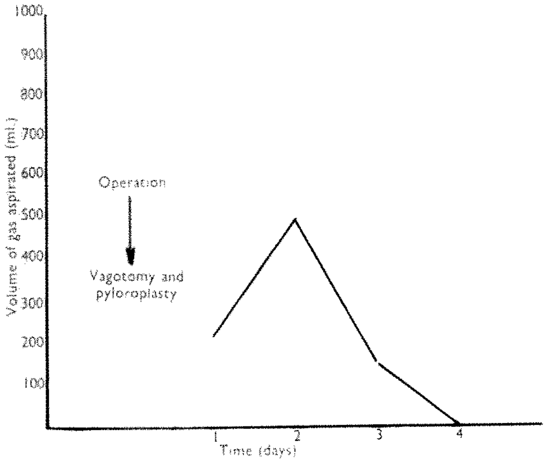


FIG. 7.—*Case* 6. Nasogastric tube gas collection.

Table I.—THE VOLUME OF GAS COLLECTED VIA A NASOGASTRIC TUBE IN BETWEEN ASPIRATION

CASE	OPERATION	GAS COLLECTED (ml.)					
		1st Day	2nd Day	3rd Day	4th Day	5th Day	6th Day
1. H.	Cholecystectomy	50	410	160	—	—	—
2. J.	Partial gastrectomy	—	900	—	560	—	350
3. T.	Vagotomy and pyloroplasty	40	480	400	—	—	—
4. H.	Cholecystectomy	40	300	300	90	—	—
5. V.	Vagotomy and pyloroplasty	—	960	480	—	—	—
6. M.	Vagotomy and pyloroplasty	200	460	110	—	—	—

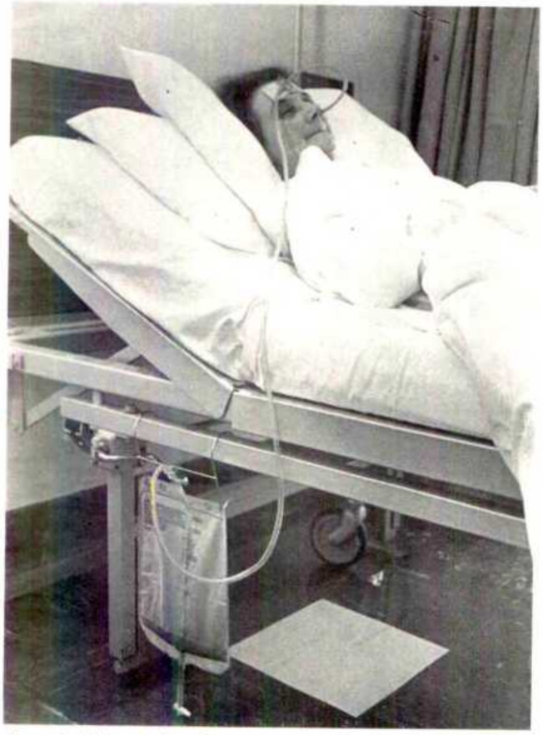


FIG. 8.—Nasogastric tube managed with continuous drainage into a disposable polythene bag.

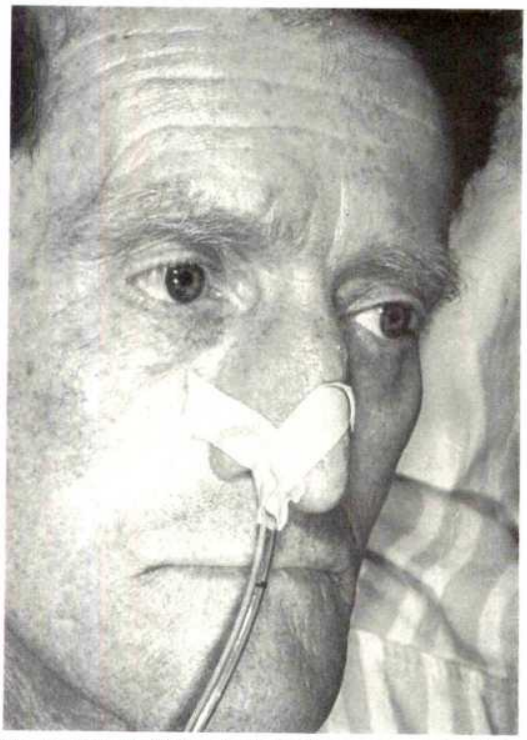
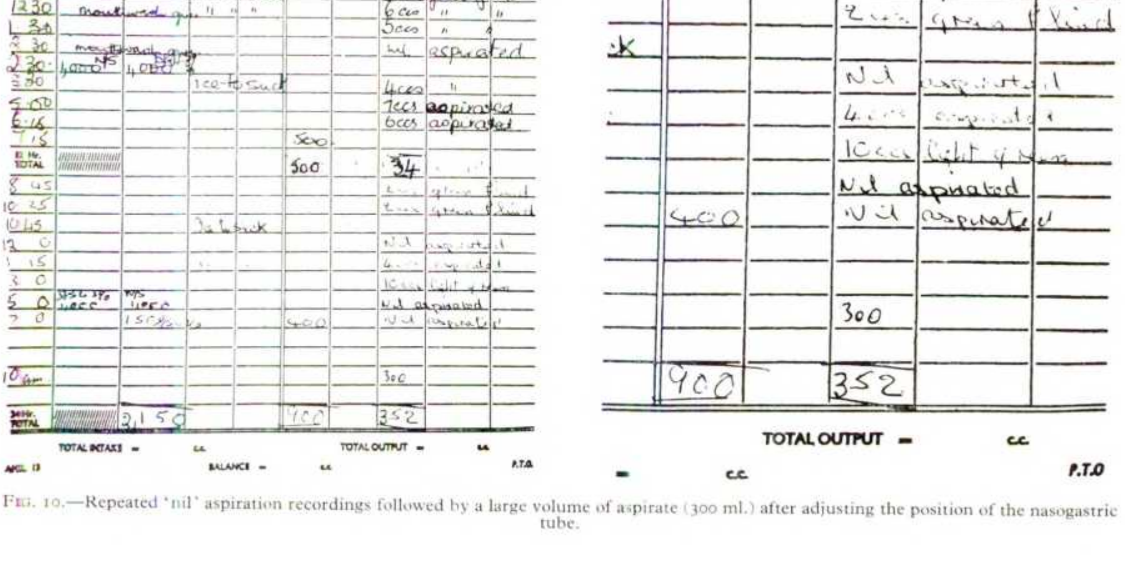


FIG. 9.—The standard method of fixing a nasogastric tube in position.



FLUID BALANCE CHART HOSPITAL

Date :

Name Age

Address Hourly aspiration — Ice to suck

Case Note No.

Day No.

1 ounce = 28 c.c.

20 ounces = 1 pint

1 pint = 560 c.c.

URINARY CHLORIDE: Time / Gms. %

SERUM ELECTROLYTES: Na / K / Chloride / CO_2

	INTAKE				OUTPUT				
TIME	I.V. FLUID SET UP	I.V. FLUID GIVEN	ORAL	OTHER	URINE	VOMIT	SUCTION	NATURE OF ASPIRATION	OTHER
7.15	[illegible] 3%						3ccs	green fluid	
8 45									
10 0	[illegible]						2ccs	green fluid	
1 AM			Ice to suck				2ccs	green fluid	
12 30	mouthwash given		" " "				6 ccs	"	"
1 30							5ccs	"	"
2 30	mouthwash given						Nil	aspirated	
2 30	1,000 N/S	1,000 [illegible]							
3 30			Ice to suck				4ccs	"	
5.00							7ccs	aspirated	
6.15							6ccs	aspirated	
7 15					500				
12 Hr. TOTAL	▨				500		34		
8 45							2ccs	green fluid	
10 25							2ccs	green fluid	
10 45			Ice to suck						
12 0							Nil	aspirated	
1 15							4ccs	aspirated	
3 0							10ccs	light green	
5 0	[illegible] 1,000cc	N/S 1,000cc					Nil	aspirated	
7 0		1,500 [illegible]			400		Nil	aspirated	
10 pm							300		
24 Hr. TOTAL	▨	2,150			400		352		

TOTAL INTAKE = c.c. TOTAL OUTPUT = c.c.

APG. 13 BALANCE = c.c. P.T.O.

uck		4ccs	"	
		7ccs	aspirated	
		6ccs	aspirated	
	500			
	500	34		
		2ccs	green fluid	
		2ccs	green fluid	
k				
		Nil	aspirated	
		4ccs	aspirated	
		10ccs	light green	
		Nil	aspirated	
	400	Nil	aspirated	
		300		
	900	352		

TOTAL OUTPUT = cc.

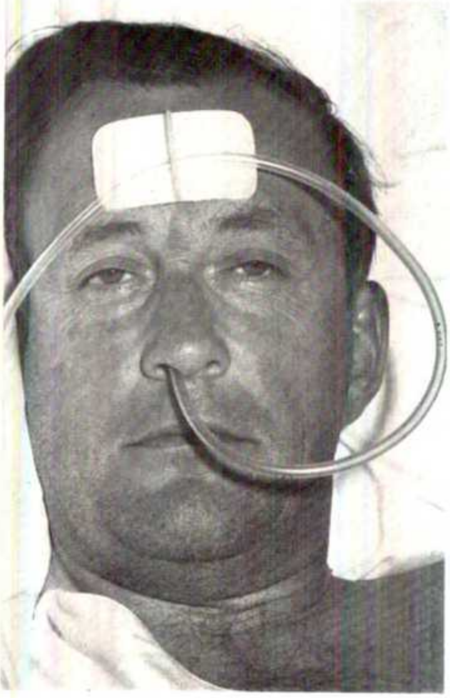
= cc. P.T.O

FIG. 10.—Repeated 'nil' aspiration recordings followed by a large volume of aspirate (300 ml.) after adjusting the position of the nasogastric tube.

opportunity is lost to decompress further the upper gastro-intestinal tract. Full utilization of the tubes is, therefore, not being exploited.

On the basis of this investigation it would appear justifiable to recommend that nasogastric tubes should be managed by continuous drainage into a suitable, convenient receptacle such as a disposable polythene bag (*Fig.* 8). Disposable bags suitable for open-drainage management are available from Simpla Plastics Ltd., Phoenix Estate, Caerphilly Road, Cardiff.

Experience with this type of management has repeatedly shown that substantial quantities of gas and fluid eruct and siphon over into the collecting bag, thus contributing to the comfort and well-being of the patients.



ADDENDUM

A Nasogastric Tube Retaining Device.—The standard method of retaining a nasogastric tube in position is to fix it to the patient's nose with a piece of zinc-oxide strapping. This method, which is simple and effective if rather crude, has the disadvantages that it is uncomfortable for the patient and deters easy adjustment of the tube's position as to do so necessitates pulling the strapping off the patient's face and detaching it from the tube, which manœuvre requires a good deal of manipulation and causes some discomfort (*Fig.* 9).

Notwithstanding that a nasogastric tube is positioned correctly on its insertion, it cannot be assumed that that position will remain the correct one throughout the period of its utilization as kinking of the tube may occur; also change of position of the patient, retching, and alterations of gastric tone may subsequently prevent the tube coming into contact with the stomach contents. A nil gastric aspiration result recorded repeatedly on the balance chart is the 'give-away' of the situation and indicates the necessity for adjusting the tube's position (*Fig.* 10).

An alternative means of retaining a nasogastric tube in position which meets the dual requirements of being comfortable for the patient and enabling ready adjustment of position has been designed and has proved its worth in practice. It is made of plastic, is disposable, and consists of a flange 4 × 6 cm. bearing at right-angles to it a fenestrated blade with slots of graduated size to accommodate the several gauges of nasogastric tubing.

The flange of the device is stuck to the patient's forehead with a double-sided plaster (Chiron); the correctly positioned tube is threaded through the fenestrated blade which acting with a cleat action grips it and holds it in position without occluding its lumen which remains clear for intermittent aspiration and open drainage (*Fig.* 11).

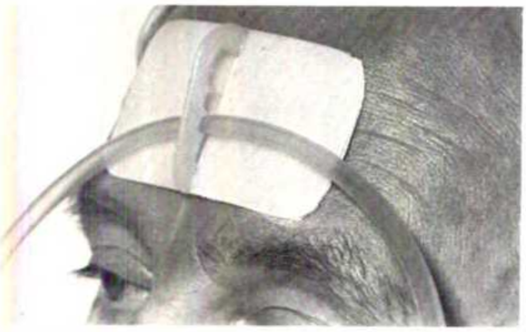


FIG. 11.—The disposable nasogastric tube-holding device in use.

Adjustment of the tube's position is readily accomplished by liberating it from the cleat until the new position is obtained and then cleating the tube again.

These devices can remain in position for several days and are well tolerated by patients who quickly become unaware of their presence. They are available from Down Bros., Mayer & Phelps Ltd., Church Path, Mitcham, Surrey.

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TREATMENT OF PERITONITIS WITH PER- AND POSTOPERATIVE IRRIGATION OF THE PERITONEAL CAVITY WITH NOXYTHIOLIN SOLUTION

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SUMMARY

The present paper describes a technique for irrigating the peritoneal cavity in severe peritonitis, both at the time of laparotomy and in the immediate postoperative period, with a solution of noxythiolin. A consecutive series of 9 cases with fulminating peritonitis of various causes treated by this method is presented together with the operative findings, a discussion of the postoperative progress, and the bacteriological studies of the irrigating device. A full review of the literature of peritoneal lavage in the management of peritonitis is included in the discussion.

PERITONITIS, of whatever origin, still presents an extremely common and dangerous problem in emergency surgery. In all age-groups it carries a high morbidity and mortality, but particularly in middle and advanced years.

Conventional methods of management include preoperative resuscitation, operative treatment, followed by a period of nasogastric suction, intravenous therapy to maintain adequate hydration and to correct the electrolyte imbalance until the period of paralytic ileus has resolved, the use of systemic antibiotics, and in the more severe cases showing evidence of circulatory collapse the judicious use of blood transfusion and systemic steroids.

The work of such eminent authorities as Fine, Lillehei, Filler, and Sleeman (Filler, Sleeman, Hendry, and Phlaski, 1966; Filler and Sleeman, 1967) leaves very little doubt that the chief factor leading to circulatory collapse and death in peritonitis is the absorption of Gram-negative organisms and their associated endotoxins from the peritoneal cavity, and that, furthermore, as soon as viable organisms are eliminated from the peritoneal cavity the danger of circulatory collapse diminishes rapidly.

It would seem desirable in the management of peritonitis that, in addition to the supportive measures outlined above, as much as possible is done both at the time of operation and in the immediate postoperative period to sterilize the peritoneal cavity of contaminating organisms, and thus to attack the problem at source. Failure to do this will inevitably lead to loculated collections of pus gathering in between coils of intestine and in rather more defined anatomical spaces such as the pouch of Douglas, which will obviously lead to a situation jeopardizing the recovery of the patient.

This paper consists of a relatively short series of 9 patients, all operated on personally, and presenting acute surgical emergencies with symptoms and signs of widespread peritonitis with associated signs suggestive of Gram-negative bacteriaemia, i.e. tachycardia, very poor peripheral perfusion, and low central venous pressure (with the exception of *Case* 5). All the patients were treated by conventional measures, but in addition the peritoneal cavity was thoroughly lavaged with a dilute noxythiolin (Noxyflex) solution, and furthermore a similar solution was dripped into the peritoneal cavity postoperatively for periods varying from 24 to 72 hours.

The leading paper on this subject is that of Browne and Stoller (1970), who used noxythiolin at the time of operation but did not perfuse it into the peritoneal cavity postoperatively, and who present a very impressive series of 23 patients with exclusively faecal peritonitis, with a mortality of 3 patients, 2 of whom were thought to have died from pulmonary embolus.

The present paper presents the methods of per- and postoperative lavage employed in a variety of types of peritonitis, and in the last part gives a full historical review of the place of peritoneal lavage in the management of life-threatening peritonitis.

PATIENTS AND METHODS

The patients with the exception of *Case* 5 presented with severe generalized peritonitis and all were operated on. Conventional methods of postoperative management were adhered to, i.e., nasogastric suction, intravenous fluids, blood transfusion where indicated, and monitoring the central venous pressure. As regards antibiotic therapy, all the patients received penicillin (2 MU. 6-hourly) and streptomycin (0·5 g. b.d.), except where indicated to the contrary.

At the time of operation about 5 g. of noxythiolin powder were dissolved in 500 ml. of normal saline and liberally lavaged around the peritoneal cavity until the fluid returning was completely clear; if contamination was severe another 500-ml. aliquot was prepared. It was interesting to note that the solution seemed to be very effective at detaching fibrinous plaques from the bowel wall. When the operative treatment had been concluded, a large sterile Ryle's tube was inserted via a stab wound into the peritoneal cavity, the tip of the Ryle's tube being adjusted to lie in the position where maximal sepsis would be expected to occur, i.e., in the pouch of Douglas where a low large-bowel anastomosis had been carried out for either perforated diverticulitis or carcinoma. Two corrugated drains were usually introduced by separate stab incisions to permit free egress of the drainage fluid—ileostomy bags could always be fitted around these. While the main operation wound was being closed the assistant gently poured in more diluted noxythiolin solution.

During the postoperative period the Ryle's tube was connected to a conventional drip arrangement, and noxythiolin solution, again in the concentration of 5 g. of noxythiolin to 500 ml. of normal saline, was dripped in continuously every 12 hours; the drainage fluid was collected in loosely attached ileostomy bags around the drain sites. The total period of postoperative irrigation varied from 24 to 72 hours depending quite empirically on the estimated degree of contamination. When it was decided to conclude the irrigation, the Ryle's tube was withdrawn from the abdomen in the usual way and the tip was cut off and sent for culture.

The selection of cases for this method was fairly discriminatory, all the patients included in this series being desperately ill and in real danger of perishing. Furthermore, the patients were all aged 45 years or over. As the studies of intraperitoneal noxythiolin seemed to be rather limited at the time when the present series was undertaken, although no untoward effects have been recorded so far, it was felt unjustifiable to use this agent on young people, and in particular no children with peritonitis complicating appendicitis were treated by this method.

The choice of the dosage régime was rather empirical, and it may in future be possible to use larger doses. No untoward effects were noted in this series.

CASE REPORTS

Case 1.—Mrs. G. A. aged 56 years, was admitted on 26 Feb., 1970, with signs of a generalized peritonitis. The patient had had little previous medical history except an anterior colporrhaphy operation carried out in 1964. She also had had a peri-urethral abscess.

Laparotomy (26 Feb.) revealed a generalized peritonitis which appeared to be primary, as no other pathological lesion could be found in the abdomen. The abdominal cavity was irrigated with noxythiolin. Postoperatively the noxythiolin solution (1 per cent) in normal saline was run in via the Ryle's tube in the peritoneal cavity for 24 hours.

Swabs of the peritoneal cavity at operation grew haemolytic *Streptococcus*, and the tip of the Ryle's tube when sent for culture was sterile.

The patient did extremely well postoperatively, there being no wound infection and no significant postoperative pyrexia.

Case 2.—Mr. C. C., aged 73 years, was admitted in March, 1970, with a 72-hour history of lower abdominal pain which was getting progressively worse, associated with severe anorexa and vomiting and also symptoms of tenesmus. On examination the patient appeared to be rather 'toxic' with a temperature of 37·8° C. with signs suggestive of peritonitis in the lower abdomen. In particular he was extremely tender per rectum.

Laparotomy through a lower right paramedian incision revealed a gangrenous appendix in the rectovesical pouch and a very severe pelvic peritonitis, with multiple loops of small bowel in a pool of pus. Appendicectomy was carried out and the loops of bowel were liberated from the pelvic sepsis, the pelvic cavity being washed out liberally with large quantities of noxythiolin solution. A Ryle's tube was inserted through a stab wound and the tip was left in the rectovesical pouch which was irrigated for 48 hours postoperatively. The patient had no serious postoperative pyrexia and recovered extremely quickly. Culture of the tip of the irrigating catheter was sterile.

Case 3.—Mr. R. H., aged 48 years, was seen urgently in the surgical clinic on 2 July, 1970, with intense pain in the left iliac region which had developed over the preceding 48 hours. On examination he was found to be tender in the left iliac fossa, but there was nothing to suggest either obstruction or generalized peritonitis. Straight radiographs of the abdomen in the erect film revealed a small quantity of gas under the right diaphragm, and it was concluded that the patient had had an attack of acute diverticulitis with possible localized rupture of either an abscess or a diverticulum. He was treated conservatively to begin with, but a barium-enema examination revealed an unequivocal carcinoma at the lower sigmoid area.

Laparotomy (14 July) through a left lower paramedian incision revealed a carcinoma of the lower sigmoid which had perforated locally, and numerous loops of small bowel were adherent to it. The loops of bowel were dissected free but with spillage of a great deal of pus from the larger pericolic abscess around the growth. A formal resection was carried out with end-to-end anastomosis, the peritoneal cavity being liberally irrigated with noxythiolin solution and a Ryle's tube being left down to the rectovesical pouch. The patient was irrigated for 72 hours postoperatively. He did extremely well, pyrexia was not a problem, and the wound healed cleanly.

The swab from the abscess grew a heavy colony of *Escherichia coli* organisms, but the Ryle's tube which had been left in the rectovesical area was sterile when withdrawn.

Pathology of the specimen revealed a deeply infiltrating carcinoma.

Case 4.—Mrs. G. S., aged 62 years, was admitted on 29 July, 1970, with signs and symptoms suggestive of advanced pelvic peritonitis. This had appeared very quickly in the space of about 48 hours. She did, however, give a history of some bowel irregularity for 3 months.

This patient was explored immediately because of the severity of her signs and a perforated carcinoma of the rectosigmoid area was encountered with very severe faecal peritonitis. An immediate resection of the neoplasm was carried out with end-to-end anastomosis and a Ryle's tube was left down to the area of the anastomosis after irrigating the peritoneal cavity with noxythiolin. The patient was irrigated for 48 hours postoperatively with noxythiolin solution. The tip of the Ryle's tube was sent for culture and grew coliform bacilli in rather scanty numbers.

Histology of the resected specimen showed the presence of a deeply infiltrating carcinoma.

Case 5.—Mr. T. O'D., aged 48 years, had been investigated at the surgical out-patients' department for some time with abdominal pain and some evidence of chronic gastro-intestinal blood-loss; barium studies had been equivocal.

The patient was admitted on 14 Aug., 1970, with evidence of haematemesis and melaena and was initially treated conservatively. Forty-eight hours later he had a fresh attack of haematemesis and it was noted that the vomit smelt faeculent. He was explored through a left paramedian incision, when a huge fungating carcinoma of the splenic flexure was encountered which had invaded the greater curvature of the stomach. The main tumour, which was the size of a pineapple, was mostly outside the bowel and the stomach, but was obviously the cause of a malignant gastrocolic fistula which accounted for the patient's faeculent vomiting.

The tumour was dissected free from the retroperitoneal parietes which it had invaded and the attached spleen was removed. A Billroth-I gastrectomy and a large segmental resection of the splenic flexure of the colon were also carried out to achieve clearance. During the dissection there was wholesale spillage not only of faeculent material but also of masses of polypoid malignant tissue.

Postoperatively the patient had a rather stormy course with a high swinging pyrexia (the only patient in this series to do so). The Ryle's tube was left in the left subphrenic space as this was thought to be the area of maximum contamination. The perfusion was run for 72 hours at the usual rate of 500 ml. per 12 hours, with 5 g. of noxythiolin in each bottle, and the effluent drained from two quite large flank drains (*Figs.* 1, 2).

The indwelling Ryle's tube was removed after 72 hours and the tip was amputated and sent for culture. This grew a heavy growth of coliform bacilli. The patient was put on large doses of penicillin and streptomycin for the first 8 days postoperatively but was still running a high pyrexia and was 'switched' to intravenous cleporin (500 mg. 4-hourly). On the tenth postoperative day he developed sudden pain in the right side of the chest and it was assumed that he had sustained a pulmonary embolus. He was accordingly put on anticoagulants.

The patient made slow and steady progress and was eventually discharged 3 weeks after admission, with a slight discharging sinus where the Ryle's tube had been inserted which still grew coliform bacilli. Screening of the diaphragm had not revealed a subphrenic abscess and at the time of discharge his temperature had completely settled down.

Case 6.—Mr. S., aged 66 years, was admitted in August, 1970, with physical signs of a very advanced and severe peritonitis. The history was that he had had a partial gastrectomy carried out 15 years previously for a duodenal ulcer. He had suddenly developed cramping abdominal pains in the epigastrium about 6 hours prior to admission. On admission he showed signs of poor peripheral circulation with a tachycardia of 110 beats per minute and a blood-pressure of 100/50.

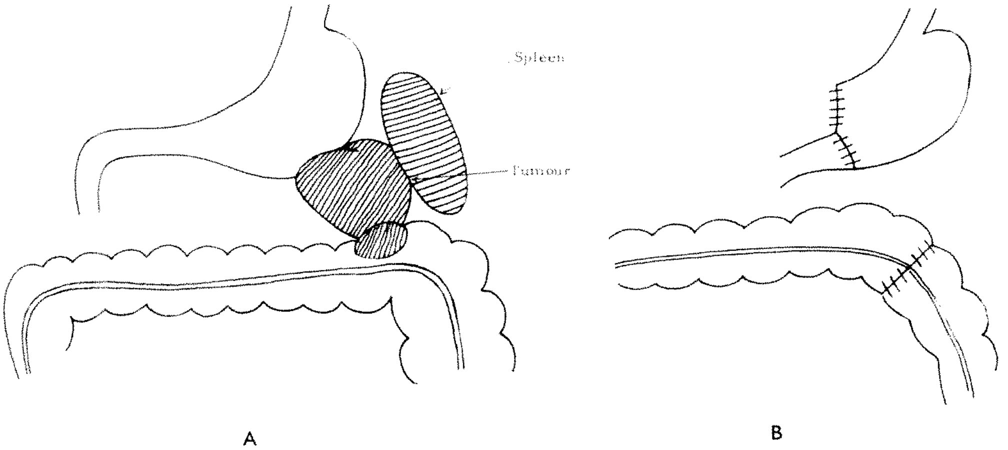

FIG. 1.—*Case* 5. A, Malignant gastrocolic fistula. B, After Billroth-I gastrectomy and left-sided large-bowel resection.

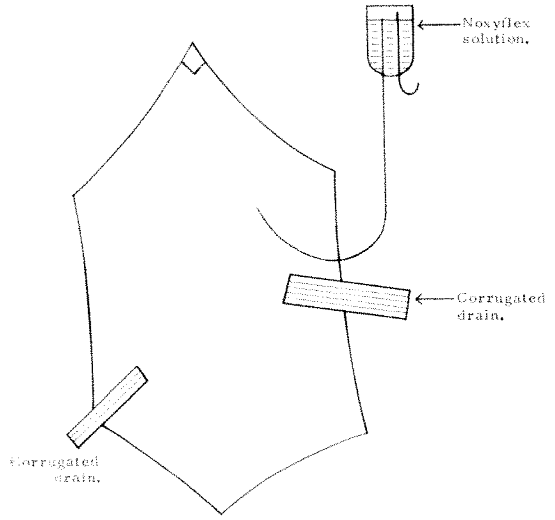

FIG. 2.—*Case* 5. Diagram of the irrigation of the peritoneal cavity using a sterile Ryle's tube inserted under the left cupola of the diaphragm. Two corrugated drains are inserted in the flanks bilaterally.

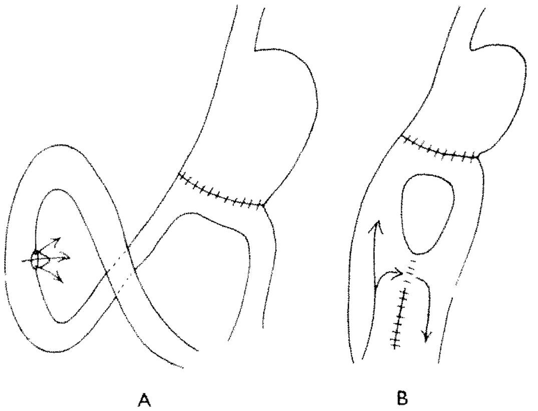

FIG. 3.—*Case* 6. A, The volvulus of the afferent loop of the gastrectomy with perforation of the bowel and consequent biliary peritonitis. B, Reduction of the volvulus with a wide entero-anastomosis between the afferent and efferent loops.

The radiographs of the abdomen were not particularly helpful and only showed a slightly 'ground-glass' appearance suggestive of free fluid in the abdomen.

After preliminary resuscitation, the patient was operated upon, and on opening the abdomen a very severe and profuse biliary peritonitis was encountered. The mechanism of this was found to be a volvulus of the afferent loop of the antecolic Polya gastrectomy around a band. The volvulus had obviously raised the intraluminal pressure in the afferent loop to such an extent that it had 'blown off' a perforation in the mesenteric border of the small bowel thus liberating the afferent loop contents into the peritoneum. The bowel comprising the volvulus was very oedematous and bruised but perfectly viable. The perforation was oversewn in two layers, the band was divided and the volvulus was reduced. In order to prevent this happening again the afferent loop of the bowel was sutured to the efferent loop of the gastrectomy and a wide entero-anastomosis was constructed. Noxythiolin was instilled at the time of operation and dripped in postoperatively for 48 hours (*Fig.* 3).

The patient did extremely well, and in the morning following the operation was reading a newspaper and showed no signs of toxicity.

The tip of the Ryle's tube when sent for culture was sterile.

Case 7.—Mrs. M. G., aged 88 years, had been treated in the out-patients' department for some considerable time for severe diverticulitis proved by repeated barium-enema examinations. Because of her generalized decrepitude it was decided to try to treat her conservatively.

Because of a recent exacerbation of her symptoms she had been admitted at the end of August, 1970, for a period of conservative management and assessment. At 8.00 a.m. on 4 Sept., whilst in hospital, she obviously developed a perforation of her diverticular bowel, with signs of gross peritonitis and poor peripheral circulation. After a period of intensive resuscitation she was operated on approximately 3 hours after the onset of her symptoms. Through a left paramedian incision it was found that she had a gross faecal peritonitis. The peritoneal cavity was washed out with noxythiolin solution and a badly perforated sigmoid colon was encountered, the perforation being through a large diverticulum pointing laterally. An immediate sigmoid colectomy was carried out with end-to-end anastomosis, and a Ryle's tube was left down to the pouch of Douglas and was brought out through a small stab incision. In addition two corrugated drains were also inserted.

The patient had a reasonably smooth postoperative progress to begin with, her ileus settling down after about 72 hours, at which time the noxythiolin infusion was stopped. The tip of the Ryle's tube was sent for culture and was sterile.

On the fourth postoperative day the patient was passing one motion per rectum and was drinking very well. However, her cardiovascular state was not very good and she developed a congestive cardiac state which gradually got worse and she died on 21 Sept. from general decrepitude and a bad heart, but there was no indication of any further abdominal trouble.

Histology of the resected specimen of sigmoid colon confirmed the original diagnosis of severe diverticulitis.

Case 8.—Mr. J. R., aged 61 years, was admitted on 8 Jan., 1971, at 12.30 p.m. with a history that at 7 a.m. he had been straining at defaecation and had suddenly developed a very severe pain in the 'pit of his stomach'. He had gone to work as a dispensing chemist's assistant but had found it quite impossible to carry on working. He denied any significant previous abdominal or bowel symptoms, but was on anticoagulants for a deep venous thrombosis in his left leg. On examination he had a completely rigid abdomen with absent bowel-sounds, a tachycardia of 120 beats per minute, and a blood-pressure of 110/70. His peripheral circulation was very poor, with a dense peripheral cyanosis.

After preliminary resuscitation and checking his prothrombin time he was operated on within an hour of admission.

At operation a fulminating faecal peritonitis was encountered. The sigmoid colon was quite severely affected with diverticulitis, and a perforation, 1·5 cm. in diameter, was encountered at the apex of the sigmoid loop. An immediate sigmoid colectomy was carried out with end-to-end anastomosis and the appendix was removed. The peritoneal cavity was irrigated with noxythiolin solution and a Ryle's tube was left down to the site of the anastomosis and brought out through a stab drain site. Noxythiolin was dripped into the peritoneal cavity for 72 hours postoperatively. The tip of the Ryle's tube was sent for culture and found to be sterile, as was a wound swab. The patient did extremely well postoperatively, never developing a temperature of above 36·7° C. By the fourth day his ileus had settled down and he was passing flatus per rectum, and he started passing a motion on the fifth day quite normally.

His wound healed perfectly and he was discharged 12 days after operation. Histology confirmed the original diagnosis of diverticulitis.

Case 9.—Mr. J. F., aged 35 years, was admitted on 2 April, 1971, from another hospital with a 2-year history of recurrent severe attacks of pancreatitis. On examination he was found to have evidence of a mass in the left hypochondrium which was felt to be an inflammatory pseudocyst of the tail of the pancreas. He was explored on 14 April when a huge collection of fluid was found in the tail of the pancreas overlapping the left kidney which was drained and found to contain a mixture of blood-clot and pancreatic juice. This was drained externally via a large Malecot catheter.

Postoperatively the patient complained of recurrent upper abdominal discomfort which suddenly became worse on the morning of 29 April at 7.00 a.m. when he presented with an obvious upper abdominal peritonitis. A provisional diagnosis of a perforated stress ulcer was made, and he was resuscitated and operated on as quickly as possible.

At the second laparotomy a large perforated duodenal ulcer was encountered with evidence of widespread peritonitis. There was also evidence of continued pancreatitis, all the tissues in the gastroduodenal area having the consistency of friable wet cheese. With extreme difficulty a tag of omentum was secured and sutured across the perforation with interrupted atraumatic thread sutures. Because of the very grave mixture of a perforated duodenal ulcer in the presence of an active pancreatitis it was decided to irrigate the peritoneal cavity with noxythiolin, both by lavage at operation and by a postoperative drip. The Ryle's tube was left in Rutherford Morrison's pouch and irrigation was carried out for 72 hours postoperatively.

It had been noted before the second laparotomy that the contents of the drainage-tube from the pancreatic pseudocyst were growing a mixture of coliforms, anaerobic streptococci, and *Pseudomonas*. The tip of the Ryle's tube was sent for culture when removed on the third day and was found to be sterile. The patient's condition improved dramatically after the second laparotomy and apart from several episodes of quite severe abdominal pain, which were thought to be due to recurrent minor bouts of pancreatitis, he made steady progress and showed no signs of continued intra-abdominal sepsis. His wound became slightly infected but this settled down quite quickly and he was eventually discharged on 2 June, 1971.

DISCUSSION

The use of per- and postoperative lavage of the peritoneal cavity in a systematic attempt to eradicate infection from the peritoneal cavity in the case of fulminating peritonitis does not appear to have attracted the attention it deserves.

Historically the first reference found in the literature was that of Joseph Price of Philadelphia (1905), who used sterile water in large amounts at the time of laparotomy. In 1910 Deaver argued that this was not indicated, and in fact was frankly dangerous as it might very well spread the infection elsewhere in the peritoneal cavity. Franz Torek (1911) in the period 1911–14 appears to have been very much in favour of peroperative irrigation, and is recorded as making long incisions in cases of peritonitis and using very large quantities of water to irrigate the peritoneal cavity. It is interesting to note that he did not permit the use of sponges or swabs in the peritoneal cavity whilst this was going on. He is reported to have reduced the mortality of diffuse peritonitis at that time from a uniform 100 per cent to approximately 40 per cent incidence.

There the matter appears to have remained dormant until the classic paper of Burnett, Brown, Rosemond, Caswell, Buchor, and Tyson (1957) from Philadelphia. They record the case of a young man seen by them in 1942 with a catastrophically severe peritonitis complicating a neglected appendicitis. At that time they washed his peritoneal cavity out with 500 ml. of normal saline containing 0·8 per cent sulfanilamide and left a metal sump drain down to the pelvis. This young man recovered very quickly and his maximum postoperative temperature was not above 37·4° C. Burnett and others were very much impressed by this case and they treated a series of 3 cases of severe peritonitis by this method, but substituting antibiotics for the sulphonamide that they had employed of necessity in 1942. In their cases the lavage was carried out at the time of operation but no attempt was made to carry out irrigation in the postoperative period. They proceeded to perform experimental studies in animals with severe experimental peritonitis and found that the best results were achieved by lavage of the peritoneal cavity with a saline solution of penicillin and streptomycin with the exhibition of these antibiotics intramuscularly for 48 hours postoperatively.

Table I.—DETAILS OF THE PRESENT SERIES

CASE NO.	AGE (years)	OPERATIVE FINDINGS	PROCEDURE	POSTOPERATIVE PYREXIA AND PROGRESS	WOUND	ANASTOMOTIC LEAK	CULTURE OF CATHETER
1	56	Peritonitis (haemolytic *Streptococcus*)	Irrigation with noxythiolin	Nil Excellent	Very clean	None	Sterile
2	73	Peritonitis (perforated appendicitis)	Appendicectomy with irrigation with noxythiolin	Nil Excellent	Very clean	None	Sterile
3	48	Perforated carcinoma of the sigmoid colon	Sigmoid colectomy and noxythiolin irrigation	Nil (significant) Excellent	Very clean	None	Sterile
4	62	Perforated carcinoma of the rectosigmoid colon	Anterior resection and noxythiolin irrigation	Nil (significant) Excellent	Clean	None	Scanty growth of coliforms
5	48	Malignant gastrocolic fistula (carcinoma of the colon; splenic flexure) (*see Figs.* 1 and 2)	Billroth-I gastrectomy; resection of splenic flexure; splenoid growth completely removed	Very severe (but no subphrenic abscess) Stormy progress but survived	Very infected	None	Heavy growth of coliforms
6	66	Volvulus of afferent loop of gastrectomy with severe biliary peritonitis (*see Fig.* 3)	Reduction of volvulus; suture of perforation; fixation of afferent to efferent loop; entero-anastomosis	None Excellent	Very clean	None	Sterile
7	88	Faecal peritonitis and perforated diverticulitis	Sigmoid colectomy	Nil, but died from heart failure	Clean	None	Sterile
8	61	Faecal peritonitis (from a perforated diverticulitis)	Sigmoid colectomy	Nil Excellent	Clean	Nil	Sterile
9	38	Pancreatitis and perforated stress duodenal ulcer	Closure of perforation with great difficulty	Nil (significant) Slow progress but made a complete recovery	Troublesome wound infection, grew coliforms	Nil	Sterile

Artz, Barnett, and Grogan (1962) point out the magnitude of the problem that severe peritonitis presents, and indicate that the mortality from peritonitis in the Mississippi University Medical School in the period 1955–60 was 34·5 per cent. Artz and others carried out an extremely extensive experimental survey in dogs with faecal peritonitis and showed that the best results were obtained with early irrigation of the peritoneal cavity in combination with antibiotic therapy. They quote the experimental work of Schatten and Abbott (1953), who used a dog model of appendiceal peritonitis and showed that under these circumstances intravenous Terramycin produced a mortality rate of 100 per cent, whereas when it was instilled intraperitoneally the mortality rate was 41·1 per cent.

Other studies of intraperitoneal antibiotics include that of Cohn and Cotlar (1962), who showed the beneficial effect of intraperitoneal kanamycin on experimental peritonitis in dogs, and went on to use this in a large series of 128 patients with peritonitis (the majority of whom were suffering from either appendicitis or perforated peptic ulcer), with an overall mortality of 8·9 per cent. They employed a dose of 1·9 g. of kanamycin suspended in 50 ml. of normal saline in their patients, but they do not lay very great stress on intraperitoneal lavage in the postoperative period.

Two rather more important papers in recent years have demonstrated the potential value of supplementing peroperative lavage with postoperative irrigation of the peritoneal cavity. First, Schumer, Lee, and Jones (1964), in a largely experimental study, demonstrated the value of intermittent postoperative irrigation with antibiotic solutions in guinea-pigs with peritonitis. Secondly, McKenna, Currie, McDonald, Mahoney, Finlayson, and Lawsham (1970) studied two matched groups of 25 patients each suffering from fulminating peritonitis over a 3-year period. The first group was treated by purely conventional measures, i.e., fluid and electrolyte replacement, antibiotics, and laparotomy to define and treat the precipitating lesion. The mortality in this group was over 50 per cent. In the second group the patients were treated in exactly the same manner but, in addition, the peritoneal cavity was irrigated at the time of the laparotomy with up to 4 litres of a balanced salt solution. Two infusion cannulas were left in the subhepatic spaces at the termination of the laparotomy, and two large sump drains were also left in each iliac fossa to drain off the fluid. In the postoperative period the peritoneal cavity was irrigated with large amounts of a balanced salt solution (up to 16 litres in the first 8 hours) which contained 25 mg. of kanamycin and 1 MU. of penicillin in each litre. By these measures the mortality in this group was reduced by 40 per cent and the morbidity by an estimated 50 per cent. Of great interest in this very thorough piece of work was the fact that peritoneography with Conray 60 was carried out in the postoperative period in 5 patients and showed that there was free perfusion to all the recesses of the peritoneal cavity.

The experimental work of Filler and others (1966) and Filler and Sleeman (1967) leaves very little doubt that one of the principal lethal factors in peritonitis is the continuance of infection in the peritoneal cavity. By using very elegant labelled-dye experiments they demonstrated that the presence of haemoglobin and its derivatives seems to block the absorptive 'pores' of the peritoneal lining. By the same token, residual loculated infection in the peritoneal cavity, particularly in association with haemoglobin derivatives, is very recalcitrant to the entry of antibiotics given by conventional parenteral means.

Browne and Stoller (1970), in a combined experimental and clinical study, have used the agent noxythiolin in the treatment of faecal peritonitis. Their experimental studies, using rats, mice, and guinea-pigs suffering from *E. coli* peritonitis, indicated the dramatic improvement in mortality gained by exhibiting this agent, and also the remarkable lack of toxicity. Clinically their study was confined to faecal peritonitis complicating perforated lesions of the large bowel, and they emphasized the very high mortality from this condition as described in the literature. Goligher and Smiddy (1957) reported a mortality of 70 per cent, whilst Dawson, Menon, and Roxburgh (1965) recorded a figure of 77 per cent. Browne and Stoller (1970) reported a series of 23 patients with faecal peritonitis treated by conventional measures but in addition irrigation was carried out with proflavine solution at operation, and the abdomen was then closed leaving behind 2·5–5 g. of noxythiolin in 100 ml. of sterile water, but without any postoperative infusion. Their results are very encouraging with a mortality of only 3 out of 23 patients, and 2 of these deaths were due to pulmonary embolism. From the table of their cases it does not appear as though a left-sided colonic resection was carried out with end-to-end anastomosis for either perforated carcinoma or diverticulitis of the descending colon or sigmoid.

Noxythiolin is not an antibiotic. Chemically it is oxymethylene methyl-thiourea, and although its beneficial effect is not fully understood it is thought possible that it decomposes with the liberation of small quantities of formaldehyde as follows:—

$$CH_3 \cdot NH \cdot CS \cdot NH \cdot CH_2OH \longrightarrow CH_3 \cdot NH \cdot CS \cdot NH_2 + HCHO.$$

As Browne and Stoller (1970) emphasize, noxythiolin seems to be an antibacterial agent effective *in vitro* against all micro-organisms, including those that are completely resistant to other antibacterial agents (Horsfield, 1967). This argues that one of the greatest advantages that noxythiolin has over any antibiotic in the peritoneal cavity is that resistant organisms will not develop. That the action of noxythiolin is not specifically antiseptic is suggested by the interesting work of Wright and McAllister (1967), who gave lethal doses of pure endotoxin to mice and found that noxythiolin had a highly significant protective effect. One other effect has recently been discovered by Jamieson (1970), who found that HeLa cells grown in tissue culture in the presence of 0·025 per cent noxythiolin suffered severe cytotoxic changes. This correlated with the finding of Garrett (1969) that intravesical instillations of noxythiolin were a helpful adjunct in the treatment of bladder neoplasms submitted to radiotherapy. If noxythiolin were found to be cytotoxic to malignant cells in the peritoneum it would be a very useful agent, particularly in the prevention of seedlings from colonic tumours. Conventional measures taken to prevent peritoneal seeding by malignant cells are rather unsatisfactory, particularly as agents such as mercury salts and the mustards are highly toxic and might well delay wound healing.

The present series of 9 cases indicates a variety of causes of peritonitis (*Table I*). Noxythiolin solution has been used in large quantities (up to 1·5 litres at the time of operation), washing out the peritoneal cavity until the returning fluid was quite clear. The concentration has been 5 g. of noxythiolin to 500 ml. of normal saline. As Jamieson (1970) points out, the effective bacteriostatic concentration lies between 0·075 and 0·125 per cent, so that the concentration employed here should be perfectly effective, and furthermore the dose of intraperitoneal noxythiolin delivered at laparotomy has been fortified by a continuous intraperitoneal infusion for up to 72 hours postoperatively. An interesting corollary of this has been to send the tip of the infusing tube for culture, and in only 2 cases was any significant infection present, which, by extrapolation, must mean that the adjoining peritoneal cavity was sterile.

The most impressive finding in the present cases has been the remarkable lack of toxicity shown by the patients in the postoperative phase. On only 1 patient (*Case* 5) was there any significant difficulty with the postoperative 'toxicity'.

Study of the laparotomy wound has also been most instructive. In only 2 patients (*Cases* 5 and 9) was there any significant evidence of wound infection. Both these wounds when cultured grew *E. coli* organisms. The other wounds in the series healed with quite conspicuous rapidity and lack of complications. Although a series of 9 cases with a wound infection rate of 22 per cent is not really a statistically significant sample it is suggestive. All 9 patients by the nature of their intra-abdominal pathology were very much at risk as regards wound infection, and these findings are very much at variance with those of Bird, Bunch, Croft, Hoffman, Humphreys, Rhind, Rosenberg, Whittaker, Wilkinson, and Hall (1971), who employed noxythiolin in a series of appendicectomy wounds and found that no benefit accrued from its use. Two criticisms can be cited against their paper: first, they do not appear to have done any bacteriological studies on the wounds under observation; and secondly, they used noxythiolin powder instilled directly into the wound. Noxythiolin powder has a relatively low molecular weight and therefore as it is water soluble must have a relatively high osmotic activity, tending to absorb water into the wound cavity and possibly to accentuate the formation of haematomas. Furthermore, if one assumes that noxythiolin breaks down with the liberation of formaldehyde this will *a fortiori* potentiate the osmotic activity of the solution locally in the wound cavity and leads to possibly damaging concentrations of formaldehyde in the wound. It is suggested that it would be rather more instructive to carry out a clinical trial of abdominal wounds using a more physiological concentration of noxythiolin in saline solution and it is hoped to do this in the near future. In this context it is interesting to record that in none of these cases was any brownish discoloration found around the wound, in contrast to the findings of Bird and others (1971).

The final point of discussion arises from doing emergency left-sided resections of the large bowel (5 in this series) with end-to-end anastomosis rather than the classic three-stage procedure in cases of perforated lesions of large bowel. Roxburgh, Dawson, and Yeo (1968) have presented a series of patients with perforated diverticulitis, and point out that the results obtained from immediate resection are very much superior to those of simple transverse colostomy and drainage of the perforated area, this latter procedure doing nothing for the basic pathology except diverting the faecal stream; furthermore, elderly people will not tolerate repeated operative interventions. The conclusion that immediate resection is the procedure of choice in the treatment of large-bowel pathology is borne out by Madden (1967), who over a 16-year period compared the results of treating perforated lesions of the large bowel by primary resection against staged procedures. The mortality-rate in patients treated by the former method was 8 per cent, and by the latter 35 per cent. In the context of this paper it is interesting to note that Madden recommended the instillation of 300 ml. of a penicillin solution (50,000 U. per mn.) at the time of operation.

In conclusion it is suggested that in the light of Browne and Stoller's (1970) paper on the use of noxythiolin at the time of operation, and the series of McKenna and others (1970) using very large quantities of irrigating fluid containing kanamycin and penicillin postoperatively, the best solution may well be to use noxythiolin at the time of operation in large quantities and to perfuse the peritoneal cavity postoperatively with the same agent via a strategically situated irrigating catheter. The advantages of noxythiolin are its lack of toxicity and the fact that, as far as is known, bacteria are not capable of producing noxythiolin-resistant mutants. Finally, the exciting work of Jamieson (1970) suggesting that noxythiolin has carcinostatic properties would make it ideal for use in intra-abdominal malignancies where the mustard compounds and mercury salts are not without real hazard.

In conclusion, it is emphasized that the dose régime used here is purely empirical, and it may well be that larger volumes and more prolonged perfusion times are feasible.

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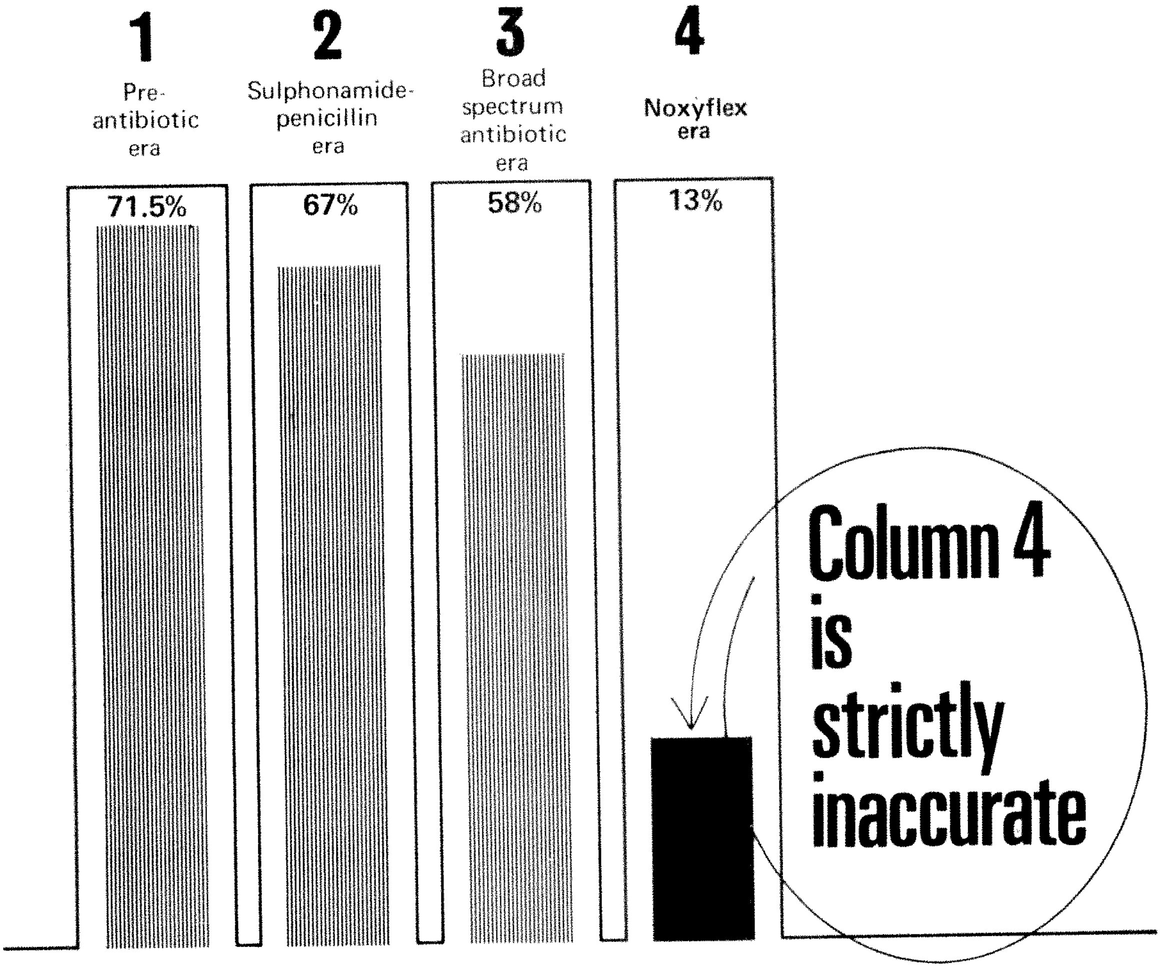
The graph below compares mortality rates due to faecal peritonitis, era by era.
It is not pedantically accurate because its sources differ. But the point is fairly made.



Column 4 is strictly inaccurate

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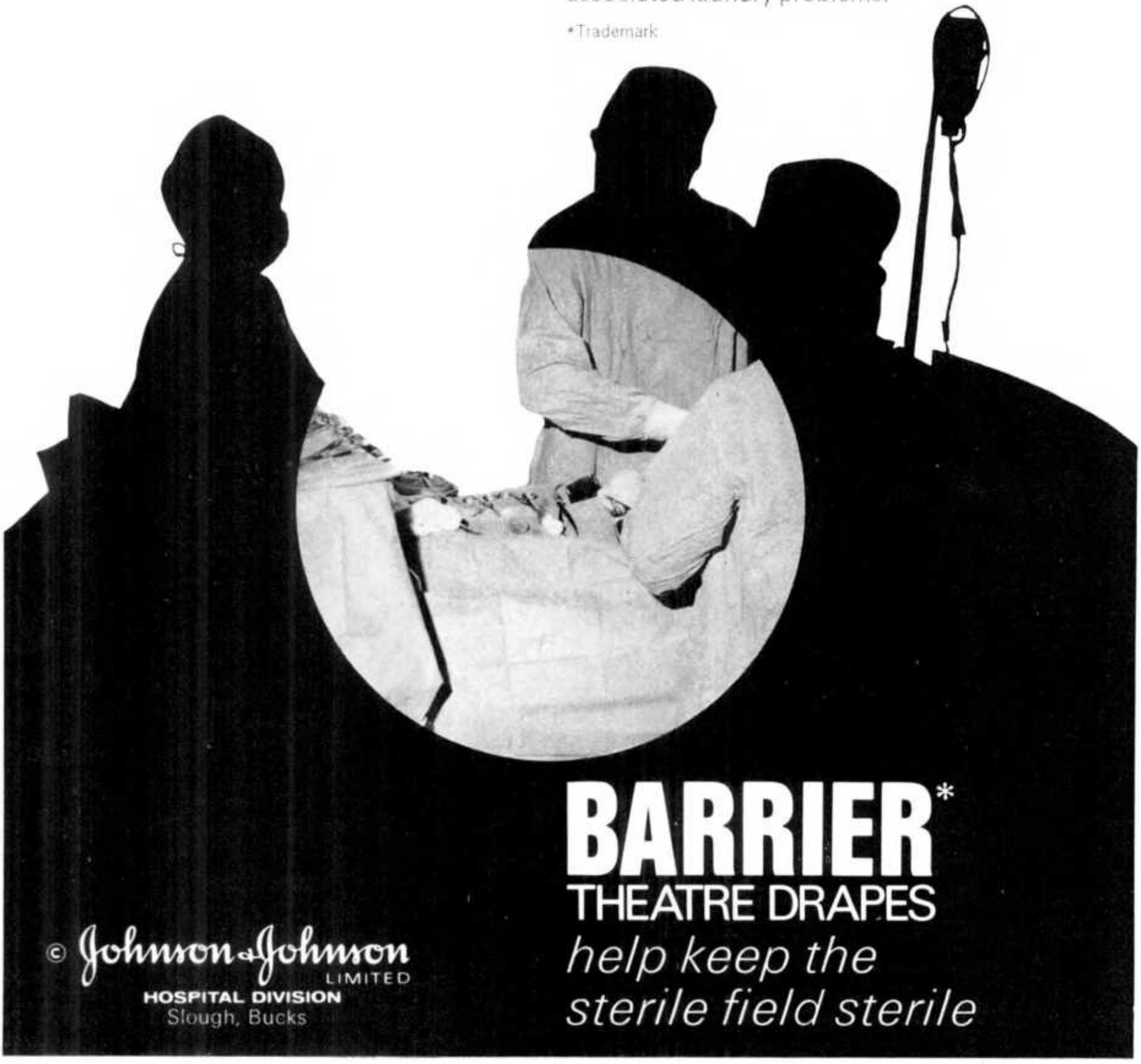

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SPONTANEOUS RUPTURE OF THE OESOPHAGUS

AVOIDANCE OF POSTOPERATIVE MORBIDITY

BY M. R. B. KEIGHLEY,* R. W. GIRDWOOD, M. I. IONESCU, AND G. H. WOOLER
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SUMMARY

Twelve cases of 'spontaneous rupture' of the oesophagus occurring over a period of 20 years (1951–71) are reviewed. The principal clinical and radiological features are described and the factors concerned in the pathogenesis of this condition are discussed. Although the mortality rate in this study was low (8 per cent) the incidence of severe postoperative complications was considerable, occurring in 10 of the 11 operative survivors. The importance of early diagnosis and adequate surgical treatment in the avoidance of this high morbidity is stressed.

SPONTANEOUS perforation of the oesophagus is no longer rarely documented in the literature and early clinical recognition is becoming increasingly common (Barrett, 1946; Mackler, 1952; Sealey, 1963). Although survival from the event without surgical treatment was extremely rare (Anderson, 1952) the results of direct suture of the torn oesophagus have indicated that this previously lethal condition can now be successfully treated (Barrett, 1947).

Despite comprehensive accounts of the clinical and radiological features (Christofordis and Nelson, 1957; Toghill, MacGuire, and Raut, 1968), spontaneous perforation still carries an alarming morbidity and mortality (Tuttle and Barrett, 1963).

This report re-evaluates the importance of early diagnosis and adequate operative repair not only to reduce the mortality of spontaneous rupture but also to avoid the considerable morbidity associated with a prolonged convalescence in those who survive.

CLINICAL MATERIAL

The records of all the patients admitted to the Thoracic Surgical Department of the General Infirmary at Leeds with spontaneous rupture of the oesophagus during the 20-year period between 1951 and 1971 were studied. The presenting clinical and radiological features were recorded and the factors concerned in the aetiology, mortality, and morbidity were analysed.

A diagnosis of spontaneous rupture of the oesophagus was made in 14 patients. Two of these occurred after lung resection for carcinoma, and although the site and appearances of the perforation in these cases were similar to those of the remaining 12 patients the question of operative damage to the oesophagus could not be excluded. For this reason these 2 cases were discarded from the present analysis and are described elsewhere. The remaining 12 subjects provide the basis of this report.

Incidence, Age, and Sex Distribution.—The annual incidence showed a slow decline from 1951 to 1971. This was largely the result of a steady fall in the admission of non-cardiac cases to the present unit and the frequent management of spontaneous rupture entirely by general surgical units. The records department of this hospital confirmed this trend, particularly over the last 5 years of this review.

The majority of these patients were men (75 per cent) and the average age was 57 years (range, 45–75 years).

Table I.—CLINICAL FEATURES OF 12 CASES OF 'SPONTANEOUS RUPTURE' OF THE OESOPHAGUS

Feature	*No. of Cases*
Predisposing factors	
Vomiting	12
Suppressed vomit	7
Alcohol	5
Large meal	5
Associated oesophageal pathology	
Hiatus hernia	2
+ Oesophagitis	1
Post-cricoid web	1
Mallory–Weiss tear	1
Symptoms	
Sudden chest pain and dyspnoea	11
Abdominal pain	7
Phrenic nerve irritation	4
Signs	
Pneumothorax or effusion	8
Abdominal signs	8
Surgical emphysema	7
Cyanosis	5
Radiographic features	
Hydropneumothorax	8
Effusion only	3
Mediastinal emphysema	3
Pneumoperitoneum	1

Presenting Features.—With only 1 exception all the patients presented with severe chest pain and dyspnoea. Physical examination revealed air or fluid in the affected hemithorax in 8 patients, and 5 patients were also cyanosed on admission. In addition to these features 7 patients complained of severe abdominal pain with clinical signs of upper abdominal peritonitis, and 4 patients had a history of phrenic nerve irritation with shoulder-tip pain. Surgical emphysema of the neck was present in 58 per cent (*Table I*).

There was only 1 case in whom a chest radiograph did not confirm the presence of air or fluid in the affected pleural cavity. Mediastinal emphysema was seen in 3 patients, and only 1 patient had radiographic evidence of air in the peritoneal cavity (*Table I, Fig.* 1).

Diagnosis.—A gastrografin swallow performed in 8 patients was without exception both diagnostic of oesophageal perforation and provided evidence of the site and extent of the leakage. The results of oesophagoscopy as a diagnostic measure were less reliable, with evidence of rupture in only 4 of the 6 patients in whom preoperative oesophagoscopy was performed.

The time lapse between perforation and diagnosis was analysed. The patients fell into four groups: 25 per cent presented within 6 hours of perforation, 25 per cent between 6 and 24 hours, a further 25 per cent between the first and second days, and the remainder (25 per cent) after 48 hours. In the latter group the diagnosis was in fact made between the fifth and twelfth days after perforation (*Fig.* 2).

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A high incidence (50 per cent) of diagnostic error occurred. Three patients were taken to the operating theatre with a diagnosis of perforated peptic ulcer; in 2 of these cases an ulcer was found at laparotomy and a gastrectomy was performed before they were referred to the thoracic department. Two cases were admitted under their physicians with a suspected myocardial infarction, and another patient was treated for 3 days for a spontaneous pneumothorax. Pulmonary embolus and pneumonia were also considered in the initial diagnosis of 2 other cases.

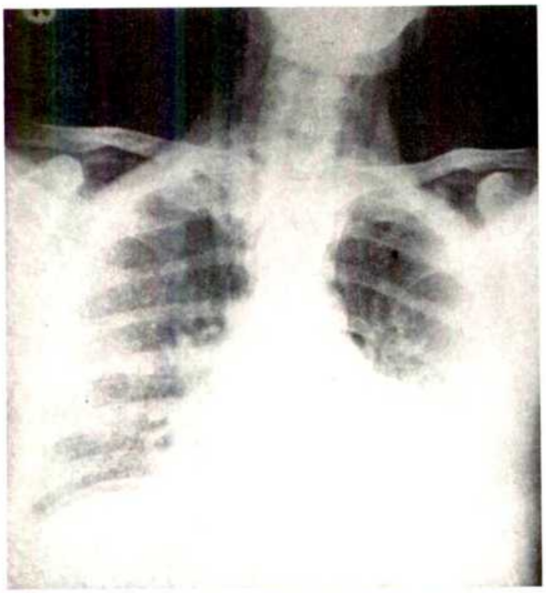

FIG. 1.—Anteroposterior chest radiograph demonstrating surgical emphysema of the neck, a pneumoperitoneum, and fluid in the affected hemithorax.

Table II.—OPERATIVE FINDINGS IN 12 CASES OF 'SPONTANEOUS RUPTURE' OF THE OESOPHAGUS

Finding	*No. of Cases*
Site of rupture	
Lower third	11
Middle third	1
Average length of tear	
Muscle, 4 cm.	(12)
Mucosal tear, 5·75 cm.	(7)
Direction of tear longitudinal	(10)
Side of rupture	
Left	11
Right	1
Extent of rupture	
Into pleura	11
Confined to mediastinum	1
Soiling of peritoneum	1

The figures in parentheses refer to the total number of cases where a record was made of the operative findings in question.

Operation Findings.—The site of rupture was recorded within the lower third of the oesophagus in all except 1 patient. In this case a longitudinal tear was identified at the level of the left main bronchus associated with a large mediastinal abscess. It was interesting to note that a long history of oesophagitis was recorded in this patient. Additional involvement of the cardia by spontaneous rupture occurred in 2 cases in whom a concomitant hiatus hernia was also demonstrated.

The operative records describe the tear as being longitudinal in direction, posterolateral in position, and predominantly on the left side (*Table II*). The length of the rupture measured an average of 4 cm. In 7 patients in whom the extent of the mucosal tear was also recorded it was found to be consistently longer, with an average length of nearly 6 cm.

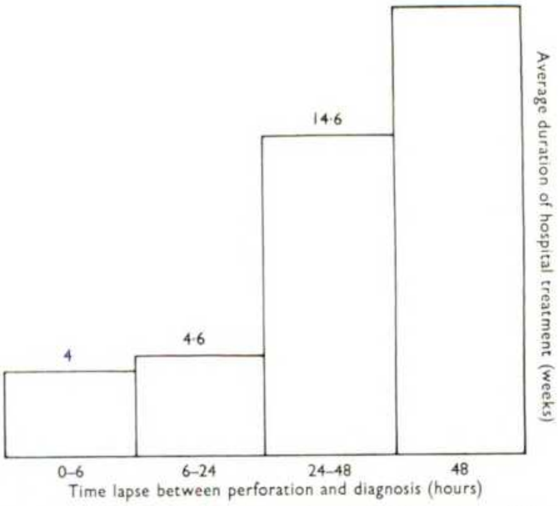

FIG. 2.—The relationship between the time of diagnosis and the morbidity.

Table III.—RESULTS OF TREATMENT IN 12 CASES OF 'SPONTANEOUS RUPTURE' OF THE OESOPHAGUS

Result			*No. of Cases*
Mortality			1
Morbidity from early complications			10
Empyema	7		
Oesophagopleural fistula	4		
Leaking suture line	3	Defined by contrast radiology	
Early stricture	3		
Subphrenic abscess	2		
Persistent sinus	1		
Renal failure (dialysis)	1		
Mediastinal abscess	1		
Morbidity from late complications			2
Longstanding stricture	1		
Chronic osteomyelitis	1		
Reoperation for complications			6
Rib resection/decortication	5		
Secondary anastomosis	3		
Jejunostomy	3		
Drainage of subphrenic space	1		

Treatment and Results.—Direct suture of the perforation was undertaken in every case despite a late diagnosis at over 5 days in 3 patients. Jejunostomy was also undertaken as a primary or secondary procedure in 5 patients. There was only 1 death in this series (an incidence of 8 per cent); this occurred following a delay in diagnosis in a patient referred to us 7 days after the onset of chest pain. He was admitted moribund with a tension pyopneumothorax. Despite immediate decompression and attempted resuture he died 24 hours after operation.

The incidence of postoperative complications as seen in *Table III* was considerable, occurring in 10 of the 11 survivors. These complications were largely the result of further leakage from the site of perforation, resulting in the formation of empyemata, oesophagopleural fistulae, a mediastinal abscess, and a persistent sinus in the wound. Evidence of leakage or stricture formation at the suture line was shown on postoperative contrast radiology in half of the cases. Subphrenic abscess formation was also demonstrated in 2 patients, suggesting leakage into the peritoneal cavity either before or after repair of the rupture.

These complications were attended by prolonged hospital stay, ranging from 2 to 22 weeks after operation, and in 3 patients the length of hospital stay exceeded 3 months. *Fig.* 2 shows a close relationship between the time the diagnosis was made after the perforation and the duration of hospitalization owing to postoperative complications.

Secondary surgical treatment for postoperative complications was undertaken in 50 per cent of the cases and in many of them more than one procedure was required (*Table III*).

Late complications occurring a year after the onset of perforation were recorded in only 2 cases. One patient developed chronic osteomyelitis in the vertebral bodies of D.V.5 and 6 following a long-standing empyema. The second case developed a stricture in the lower third of the oesophagus which persisted and required regular dilatations; this patient had had a previously normal oesophagus.

DISCUSSION

The principal clinical and radiological features in 12 cases of spontaneous rupture of the oesophagus have been outlined. These findings have emphasized the importance of early accurate diagnosis and immediate treatment in the avoidance of a high incidence of postoperative complications.

Most cases of spontaneous rupture occurred following forceful vomiting and particularly after attempts had been made to suppress this desire by contraction of the cricopharyngeus, thus converting the flaccid oesophagus into a high-pressure chamber (Moynihan, 1954). Post-emetic dehiscence, which includes all the cases described in the present study, has been renamed 'primary pressure rupture' and the term 'spontaneous rupture' is reserved for those occurring at rest or during sleep (Heroy, 1952; Clark and Tankel, 1964). 'Secondary pressure rupture' might be an apt description of those cases occurring after epilepsy (Klein and Grossman, 1943), asthma (Raffle, 1958), and parturition (Kennard, 1950). Abbott, Mansour, Logan, Hatcher, and Symbas (1970) have recently emphasized the importance of neurological disorders in the aetiology of this condition.

The lower third of the oesophagus is certainly the commonest site of perforation both in our own experience and in other reports (Nealon, Templeton, Cuddy, and Gibbon, 1961). Experimental pressure studies have consistently found this to be the weakest point of the oesophagus (Mackenzie, 1884; Bodi, Fanger, and Forsythe, 1954). This is considered to be a result of the distribution of smooth muscle, in which the longitudinal fibres taper out at the squamo-columnar junction and where the number and size of oblique fibres are also reduced (von Mollendorf, 1927).

Spontaneous rupture is primarily a muscular defect, the mucosa offering considerable resistance to pressure before perforation occurs (Mackenzie, 1884). Our own findings have shown, however, that when perforation has occurred the mucosa splits in such a way as to exceed the extent of the tear occurring in the muscular layer.

It is interesting that the left side should be involved more frequently than the right. This has been attributed to the support afforded by adjacent structures such as the aorta and liver (*Lancet*, 1963). Spontaneous perforation is not confined to the lower third of the oesophagus, however, and there are an increasing number of reports in which perforation has been recorded in the middle third and the cervical region (Russell, 1953; Ross, 1961; Hamilton, 1967).

The association of combined oesophageal pathology and spontaneous rupture deserves further discussion, particularly in those patients with concomitant hiatus hernia (3 in our series). It has been shown elsewhere that the pressure within the stomach during normal vomiting is considerably greater than that in the oesophagus (Atkinson, Bottrill, Edwards, Mitchell, Peet, and Williams, 1961). When vomiting is suppressed, however, contraction of the cricopharyngeus causes an enormous increase in the intraluminal oesophageal pressure. It is argued, therefore, that an incompetent hiatus is a predisposing factor in spontaneous rupture, particularly during normal vomiting, by allowing a high pressure to occur within the oesophagus even without involvement of the cricopharyngeal sphincter. It is interesting to note that evidence of suppressed vomiting was lacking in every patient with a hiatus hernia in this review, but was present in all but 2 of the remaining patients.

The patient in whom a post-cricoid web was found on preoperative oesophagoscopy also had no history of an attempt to avoid vomiting. It is conceivable that upper oesophageal obstruction may predispose to a high intraluminal pressure below the site of obstruction during normal vomiting, thereby resulting in oesophageal dehiscence.

The syndrome of haematemesis following repeated vomiting (Mallory and Weiss, 1929) which was recorded in 1 of our patients has been thought to be associated with spontaneous rupture (Small and Ellis, 1958). Recent evidence, however, suggests that the Mallory–Weiss syndrome is primarily a mucosal tear in the cardia following gastric distension and elevation of the oesophagogastric junction into the chest through a lax hiatus (Hodges, 1965). The pathogenesis of spontaneous rupture is quite different and is the result of a tear occurring in the muscular fibres of the oesophagus and must be regarded as an entirely different entity (Holmes, 1966).

The clinical and radiological diagnosis of spontaneous rupture has been described elsewhere (Barrett, 1946; Samson, 1951; Mackler, 1952; Marston and Valk, 1959; Sealey, 1963) and the principal findings in this study have already been stressed. Although this event is now a well-established cause of sudden abdominal pain or acute respiratory distress the early diagnosis of spontaneous rupture remains a relatively rare event. Errors of diagnosis were commonly the result of failing to obtain a chest radiograph in patients presenting with acute abdominal signs and being unaware of the value of a Gastrografin swallow in the early diagnosis. The importance of radiology by defining air within the mediastinum on a penetrated film and the use of contrast radiology in the diagnosis have been adequately stressed (Christoforidis and Nelson, 1957; Naclerio, 1957; Kerr, 1962; Toghill and others, 1968).

Prior to the first successful repair (Barrett, 1947) spontaneous rupture was almost uniformly fatal (Barrett, 1946). Although early primary repair has become the standard surgical practice the mortality-rate following this procedure continues to be considerable (Sealey, 1963; Abbott and others, 1970). The results of the present review are encouraging and should be attributed to prompt intercostal drainage, adequate débridement of the mediastinum, and an early feeding jejunostomy in all the patients presenting after 48 hours. On the other hand, the morbidity in terms of postoperative complications was alarming, occurring in 10 of the 11 survivors.

Complications largely occurred from leakage at the site of the sutured oesophagus. It is conceivable that inadequate repair may be responsible for the high morbidity following primary suture, particularly if careful examination of the extent of the mucosal tear is not undertaken at operation. Adequate repair of the perforation may thereby prevent secondary leakage from this site. Two of our patients developed a subphrenic abscess following spontaneous rupture. One must assume that this event could have been avoided if a Gastrografin swallow had been used to define the extent of the leakage.

It is well known that more damage occurs to the mediastinum and peri-oesophageal tissues following spontaneous rupture as compared with instrumental perforation. This is probably the result of autolysis from gastric contents entering the mediastinum under high pressure. The mortality and morbidity following spontaneous rupture have been attributed to this phenomenon (Tuttle and Barrett, 1963). For this reason recent authors have advocated alternative methods of operative treatment, particularly in those patients presenting 24 hours after perforation. These have included onlay gastric patch repair (Thal and Hatafuku, 1964) and T-tube drainage (Abbott and others, 1970). We feel that the emphasis should be placed not on new methods but on early diagnosis and immediate and adequate primary suture.

It appears that the greatest hazard of spontaneous rupture lies not only in a high mortality but in the incidence of severe and debilitating postoperative complications. This is associated with a considerable morbidity in terms of the length of hospital stay. It is concluded that the only means of reducing this alarming morbidity lies in the increasing awareness of this condition and the use of contrast radiology to define the site and extent of the perforation. The importance of adequate and early direct suture of the full extent of the mucosal tear in preventing further leakage cannot be overstressed.

CONCLUSIONS

1. Spontaneous rupture of the oesophagus carries a high morbidity in those who survive surgical treatment.
2. The incidence of postoperative complications would be considerably reduced if early diagnosis was established. The use of immediate contrast radiology in all patients with sudden chest pain and abdominal signs after forceful vomiting is advised, so that the site and extent of oesophageal rupture may be defined.
3. Adequate repair of the perforation by examining the extent of the mucosal dehiscence may prevent secondary leakage from the site.

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SHORT NOTES OF RARE OR OBSCURE CASES

A CASE OF PRIMARY LIVER TUMOUR ASSOCIATED WITH PORPHYRIA

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SUMMARY

A case is described of primary liver carcinoma in a patient with a 10-year history of porphyria. Death resulted from occlusion of the pulmonary artery by tumour embolus.

PORPHYRIA has been described secondary to liver tumours (Hamminga, 1951; Tio, Leisjne, Jarrett, and Rimington, 1957), but in the case presented here the porphyria preceded the recognition of a primary liver carcinoma by 10 years. No similar example has been found in a survey of the literature.

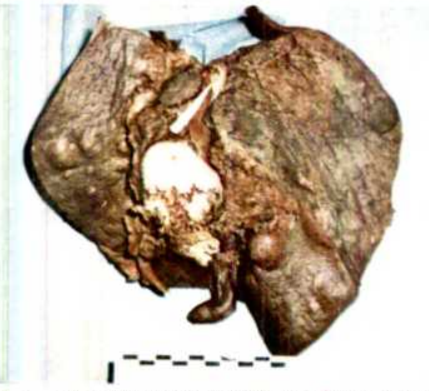

FIG. 1.—Liver; tumour has invaded the inferior vena cava.

CASE REPORT

The patient, a 52-year-old glasswork engineer, was seen in the Rupert Hallam Department of Dermatology, Hallamshire Hospital, Sheffield, in July, 1960, with a blistering eruption of the hands and face. This was initially thought to be a light-sensitivity reaction aggravated by heat from the furnaces at his place of work and was accordingly treated with oral chloroquine sulphate and topical steroids. Closer questioning 1 week later revealed that he had been drinking up to 8 pints of beer daily since his youth in the Merchant Navy and that for 3 years he had suffered intermittent attacks of 'haematuria'. He had no other urinary complaints and specifically denied any alimentary or neurological symptoms. Apart from the skin eruption and dark urine the physical examination was normal and in particular there was no hepatomegaly. The urine, which was dark brown in colour and fluorescent under Wood's light, repeatedly contained an excess of porphyrins but no blood. The serum bilirubin, thymol turbidity and floculation tests, and serum alkaline phosphatase were all normal. The bromsulphthalein test had to be abandoned when the patient collapsed on injecting the dye. A diagnosis of porphyria was made and the oral chloroquine, which is known to aggravate existing porphyria, was stopped. No specific therapy was offered but the patient was advised to reduce his alcohol intake. Unfortunately he repeatedly failed to attend and was lost to review.

In July, 1970, the patient was admitted to the Northern General Hospital, Sheffield, with a 3-day history of severe pain in the right loin. He had lost 19 kg. in weight in the preceding 7 months and complained of general malaise and anorexia for 3 weeks. A marked weakening of the voice was noted and it was difficult to converse with him. On examination the patient was noticed to be jaundiced and had scattered spider naevi over the face and trunk. The abdomen was grossly enlarged and a nodular liver was palpable, reaching to four fingers below the costal margin. No other abdominal masses were felt and there was no ascites. The blood electrolytes were normal although the blood-urea was 84 mg. per 100 ml. Serum amylase was normal. The liver-function tests were as follows: bilirubin, direct positive, 4·6 mg. per 100 ml.; alkaline phosphatase, 20·1 K.A. units; zinc turbidity, 9 U.; total proteins, 6·79; electrophoresis, small increase in alpha II globulins and gamma-globulins; serum glutamic oxaloacetic transaminase, 74 I.U. per litre; serum glutamic pyruvic transaminase, 31 I.U. per litre. Urinary porphyrins on a single test were not raised.

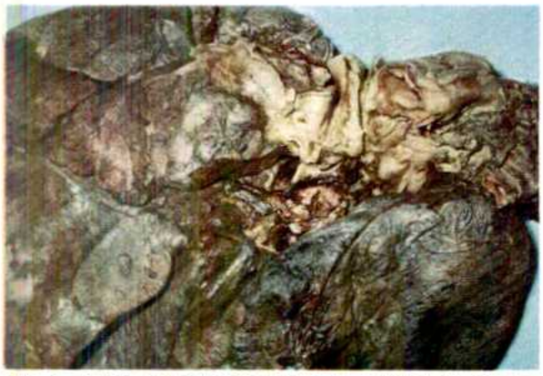

FIG. 2.—Lung; the pulmonary artery is occluded by tumour embolus.

A diagnosis of carcinomatosis with multiple liver secondaries was made. The patient's condition rapidly deteriorated with signs of bronchopneumonia and he died 3 days later.

The salient post-mortem findings were as follows: The peritoneal cavity contained some blood-stained fluid. The liver was massively enlarged and infiltrated with tumour (*Fig.* 1). This appeared to be secondary tumour but no primary was identified. The tumour had spread into the inferior vena cava. A mass of necrotic glands was present in the porta hepatis. The spleen was of normal size and the gall-bladder contained two pigment mulberry stones but no tumour. The lungs were grossly oedematous and congested and blood-stained fluid was present in the trachea and main stem bronchi. The pulmonary artery was occluded by tumour embolus (*Fig.* 2).

The liver histology showed extensive infiltration by discrete nodules of primary hepatic carcinoma which were walled off in many areas by fibrous tissue and showing characteristic polymorphic and malignant cells with attempts at columnar and rosette formation (*Fig.* 3). There was no evidence of liver cirrhosis.

DISCUSSION

The porphyrias can best be divided into two main types: hepatic and erythropoietic, depending on the main site of formation of the abnormal porphyrins and their precursor (Goldberg, 1968) (*Table I*).

Table I.—TYPES OF PORPHYRIA

- Hepatic porphyria
  - Acute intermittent
  - Variegate (mixed)
  - Cutaneous hepatic
    - Hereditary
    - Acquired
  - Hereditary coproporphyria
- Erythropoietic porphyria
  - Erythropoietic protoporphyria
  - Congenital

Hepatic porphyria may present in one of two ways. The acute intermittent type is transmitted as a Mendelian dominant character, manifesting itself by unexplained abdominal pains, paresis, or psychiatric states. The cutaneous type presents as a photosensitivity disease, often with evidence of hepatic insufficiency. The diagnosis is made by finding abnormal porphyrins in the urine or faeces.

Alcohol and drugs, such as chloroquine, barbiturates, sulphonamides, and oestrogens, are known to provoke acute attacks, as may the withdrawal of protein and carbohydrates from the diet. In Turkey cases of porphyria due to fungicide intoxication have been described (Cam, 1959).

Hamminga (1951) reported a case of porphyria with liver metastases from an intestinal tumour, and Tio and others (1957) described the case of a woman who developed photosensitivity associated with marked porphyrin excretion in old age. She had a benign liver tumour, the removal of which cured her clinical symptoms. Church (1971) had a case of porphyria in which a liver tumour was shown on liver scan.

In the present case it cannot be proved that the primary liver carcinoma was responsible for the porphyria as the opportunity was not taken to study the biochemical nature of the tumour tissue. Nevertheless, the association of hepatic porphyria and liver tumour now seems real, and it is suggested that serial liver scans be performed in all patients with hepatic porphyria in order to detect such tumours at an early stage.

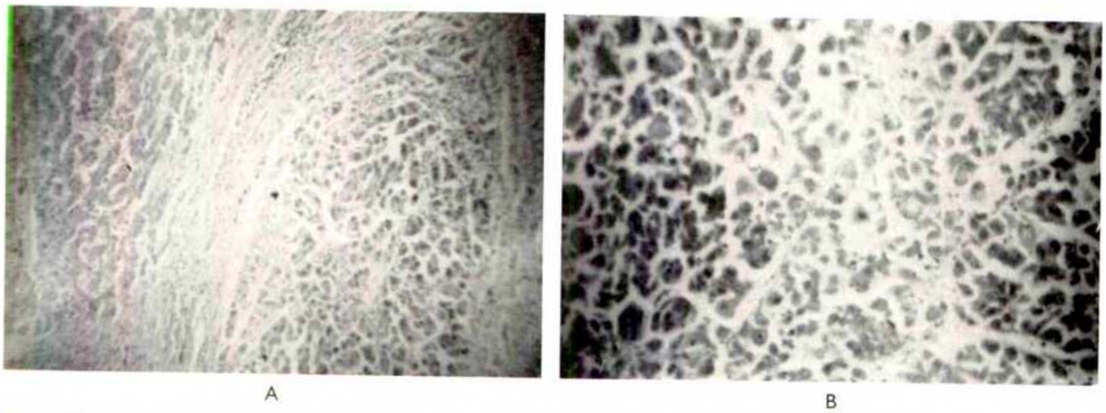

FIG. 3.—Photomicrographs of the liver: A, low-power view; B, high-power view, showing characteristic polymorphic malignant cells with attempts at columnar and rosette formation.

Tumour embolus large enough to block the pulmonary artery is uncommon, but it is now recognized that right atrial myxoma and choriocarcinoma cells may present with recurrent pulmonary emboli, eventually producing pulmonary hypertension (Oakley, 1970).

When the pulmonary artery is totally occluded by tumour the usual primary sources are sarcoma, or renal or hepatic carcinoma which have directly invaded the inferior vena cava. In these instances death results from acute cor pulmonale.

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PEDUNCULATED TERATOMA OF RECTUM INFESTED WITH BILHARZIASIS

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SUMMARY

A teratoma presenting as a pedunculated rectal polyp is reported. The teratoma was infested with *Bilharzia* ova.

TERATOMAS of the rectum are rare. Most of the reported cases have been solid or cystic dermoids. In the case reported here representatives of all three germinal layers were present and thus it warrants the name 'teratoma'. The teratoma was infested with *Bilharzia* ova, and this is believed to be the first report of such an association.

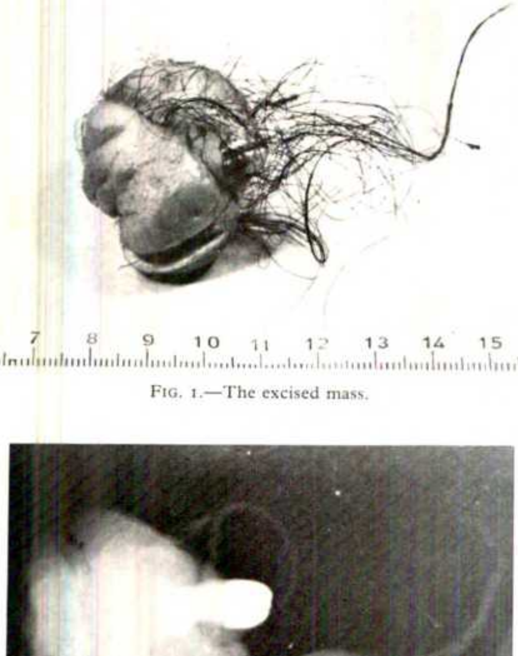

FIG. 1.—The excised mass.

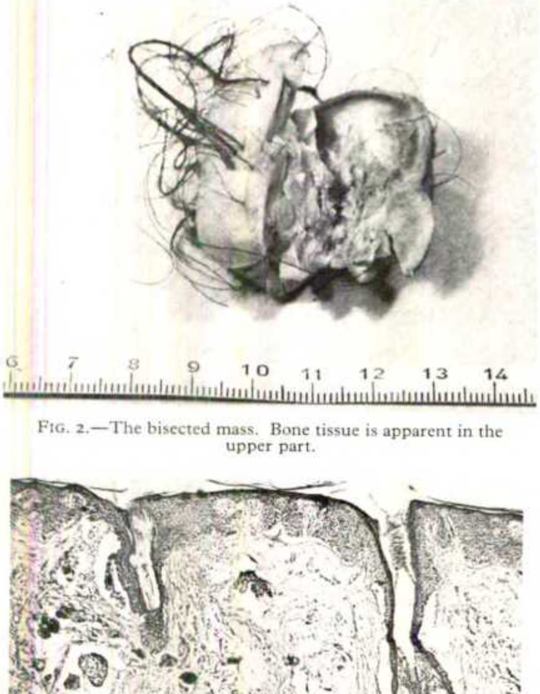

FIG. 2.—The bisected mass. Bone tissue is apparent in the upper part.

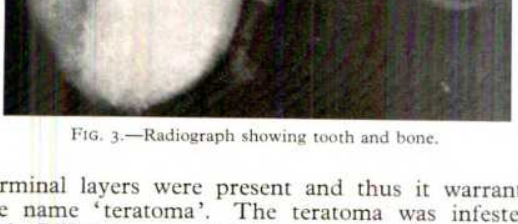

FIG. 3.—Radiograph showing tooth and bone.

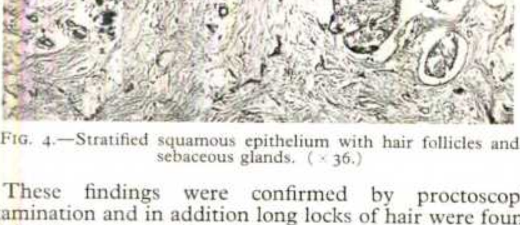

FIG. 4.—Stratified squamous epithelium with hair follicles and sebaceous glands. (× 36.)

CASE REPORT

An 8-year-old girl presented complaining of bleeding per rectum of 2 days' duration. No mass protruded per rectum during defaecation. The girl had been treated 2 years before for intestinal bilharziasis. The patient looked healthy and had no recent history of trauma.

On rectal examination a tooth was palpated. The immediate impression was that this might have been swallowed. The tooth was found to be stuck to a smooth mass lying free in the lumen of the lower rectum, being attached to the anterior wall in the middle line by a slender stalk.

These findings were confirmed by proctoscopic examination and in addition long locks of hair were found arising from the surface of the mass.

Under general anaesthesia and through a proctoscope the pedicle was transfixed and the mass excised.

The mass measured 4 × 3 cm. (*Fig.* 1) with a tooth definitely stuck to its substance and with a mass of hair growing over the whole surface. There was a small superficial ulcer on the surface which may have accounted for the bleeding that the patient had had on admission. Otherwise, the surface was smooth and the consistency was firm.

On bisection of the mass yellowish tissue was found, interspersed in places by hard whitish tissue (*Fig.* 2), which was later proved to be bone. The mass was completely solid with no cystic spaces.

Radiographic examination showed a tooth arising from an area of bone, simulating a tooth arising from part of a mandible (*Fig.* 3).

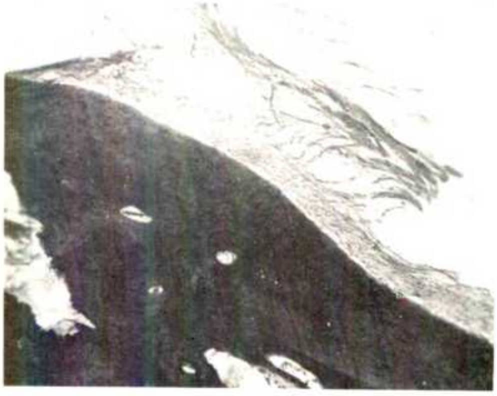

FIG. 5.—Bone and smooth muscle. (× 45.)

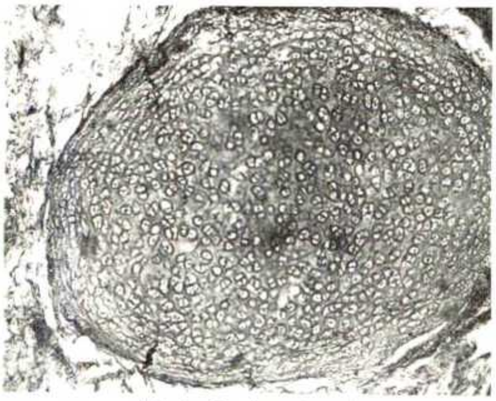

FIG. 6.—Cartilage. (× 45.)

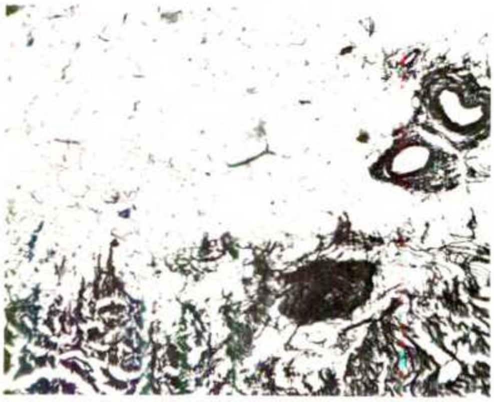

FIG. 7.—Adipose tissue, smooth muscle, and blood-vessels. (× 45.)

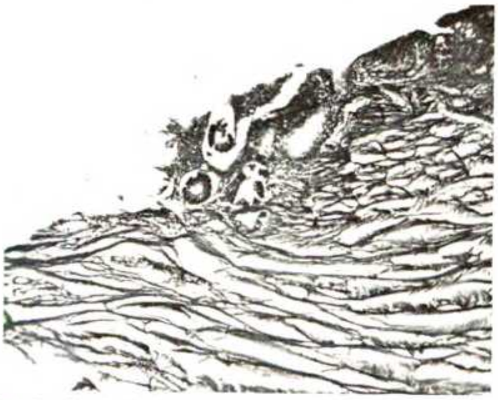

FIG. 8.—Glands lined by columnar epithelium with basal nuclei. (× 45.)

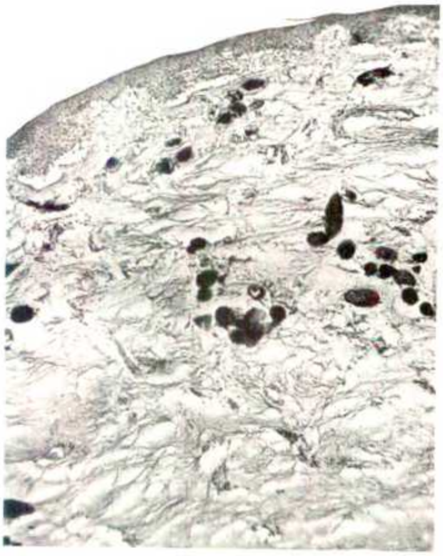

FIG. 9.—*Bilharzia* ova under the cutaneous covering. (× 50.)

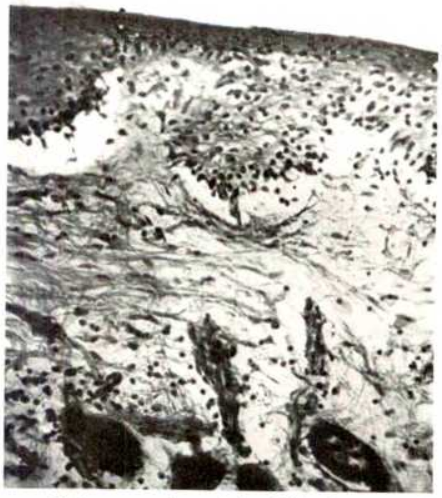

FIG. 10.—High-power view of the *Bilharzia* ova under the cutaneous covering. (× 174.)

HISTOLOGY.—Sections showed a conglomeration of tissues. The surface was covered with stratified squamous epithelium with hair follicles and sebaceous glands (*Fig.* 4). The substance of the mass included bone (*Fig.* 5), a circular area of cartilage (*Fig.* 6), adipose tissue, and smooth muscle (*Fig.* 7). There were also a few glands lined by columnar mucus-secreting epithelium with basal nuclei, simulating intestinal or biliary-duct epithelium (*Fig.* 8).

The most interesting feature on microscopy was the presence of *Bilharzia* ova amongst the tissues (*Figs.* 9, 10). The ova were mostly concentrated under the skin covering.

DISCUSSION

Teratomas have been reported in different positions in the body. These sites include the sacrococcyx, the mediastinum, the ovaries, the testis, the liver (Kiryabwire and Mugerwa, 1967), the stomach (Paul, Cooray, and Wickremasinghe, 1962), and the Fallopian tube (Gray and Hitchock, 1969).

Willis (1953) defines a teratoma as 'a true tumour or neoplasm composed of multiple tissues of kinds foreign to the part in which it occurs'.

A convenient classification of teratoid tumours is that made by Hedblom (1937), who separated these tumours into epidermoids, dermoids, and teratomas. The epidermoids are cysts containing only derivatives of ectoderm. The dermoids contain tissues of mesodermal as well as of ectodermal origin. The teratomas are solid tumours which contain derivatives of ectoderm and mesoderm as well as entoderm. The case of the pedunculated rectal dermoid reported by Nigam (1947) contained representatives of ectoderm and mesoderm, viz., skin, hair, bone, and fibromuscular tissue, but not entodermal structures and so was rightly called 'dermoid'. In the case reported here the ectoderm was represented by skin, hair, sebaceous glands, and a tooth. The mesoderm was represented by bone, cartilage, fat, and smooth muscle. The entoderm included mucous glands lined by columnar epithelium, and thus the tumour is a true teratoma.

The most popular theory about the mode of origin of teratomas was elaborated by Willis (1951), who suggested that teratomas arise from foci of totipotential cells which escape the influence of the primary organizer during embryonic development. He suggested that the disturbance occurs in the area of the primitive streak and the head process, because a large number of teratomas occur in the median and paramedian regions of the body; hence the occurrence of the present teratoma strictly in the middle line of the anterior rectal wall.

Teratomas are definitely more common in females. Gross, Clatworthy, and Meeker (1951) reported 40 cases, 32 of which were in females, and it was suggested that the female ovary differentiates later than the male testis, making females more susceptible to developmental abnormalities and accounting for the higher incidence of teratomas in females.

The presence of *Bilharzia* ova in the present teratoma can be explained if we remember that the patient had had bilharziasis earlier in her life, and that the veins into which the *Bilharzia* worms would migrate to deposit their ova in the rectal wall are the same veins which drain the teratoma.

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JOINT RUPTURE IN REITER'S DISEASE

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SUMMARY

A case of knee-joint rupture in Reiter's disease, in which a posterior communicating cyst was excised, is reported. The mechanisms of joint rupture and the differentiation of the clinical signs from those of deep venous thrombosis in the calf are discussed. The relevant literature has been reviewed.

SPONTANEOUS joint rupture is an occasional complication of joint disease and occurs most frequently in association with inflammatory joint disease, particularly rheumatoid arthritis (Dixon and Grant, 1964; Good, 1964; Jayson, Swannell, Kirk, and Dixon, 1969). Rupture occurs most commonly at the knee-joint. An acute polyarthritis with effusions, commonly involving the knee-joints, occurs in Reiter's disease, but rupture of a joint has only been reported once (Weese and McCarty, 1969). We report a second case of knee-joint rupture in Reiter's disease in which excision of a communicating posterior cyst was carried out.

CASE REPORT

An 18-year-old unmarried man with no previous history of joint disease was admitted to hospital in

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November, 1968, with a 2-week history of general malaise, accompanied by pain and swelling of the knees, the right ankle, and the second and third metacarpophalangeal joints of the left hand. He also had pain in the lower back. At the onset of his illness he had developed dysuria without a urethral discharge, and later an erythematous ulcerated lesion appeared on the roof of his mouth. He had not had conjunctivitis or skin lesions. He admitted to a casual sexual contact 4 weeks prior to admission. There was no family history of joint disease.

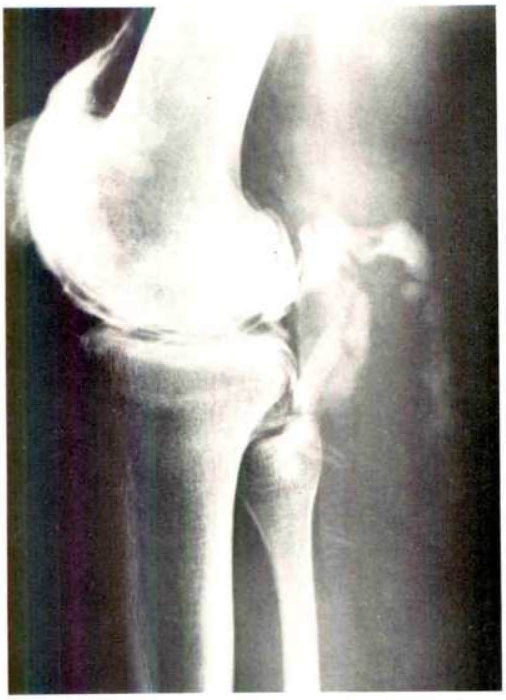

FIG. 1.—Arthrogram of the right knee showing the posterior cyst and the extravasation of dye from the upper part of the cyst.

On examination there was swelling, tenderness, and limited movement of both knees, the right ankle, and the second and third metacarpophalangeal joints of the left hand. There was no tenderness of the sacro-iliac joints.

Investigations revealed the following: haemoglobin concentration, 13·8 g. per 100 ml.; E.S.R. (Westergren), 95 mm. in 1 hour; total leucocyte count, 10,900 per c.mm. with a normal differential count; serum uric acid, 2·8 mg. per 100 ml. Serological tests for gonorrhoea, syphilis, brucellosis, and the rheumatoid factor were negative. Cultures of mid-stream urine, blood, and joint fluid were sterile. Direct examination of the synovial fluid showed the presence of many polymorphs but no 'Reiter's cells' (Pekin, Malinin, and Zvaifler, 1967). Direct examination of the urine showed the presence of many pus cells. Radiographs of the involved joints were unremarkable.

The patient was treated with soluble aspirin (4 g. per day), bed-rest, and immobilization of the legs and left hand in plaster-of-Paris splints. The knees were aspirated and injected with hydrocortisone acetate (50 mg.). He gradually improved and was discharged symptom-free 6 weeks later, at which time his haemoglobin concentration was 13·5 g. per 100 ml. and his E.S.R. 67 mm. in 1 hour. He was able to discontinue the salicylate therapy and was symptom-free for over a year until June, 1970, when he began to be troubled by pain and swelling of the third and the fourth right metatarsophalangeal joints and small effusions were noted in his knees. His haemoglobin concentration was 16·2 g. per 100 ml. and his E.S.R. 22 mm. in 1 hour. Despite an intra-articular injection of hydrocortisone acetate (50 mg.) the right knee continued to be swollen but without pain, stiffness, or limitation of movement.

In early September, 1970, the patient noticed a fullness at the back of his right knee which prevented full extension. Three days later while at work he stumbled, forcibly straightening the right knee. He immediately developed severe pain in the calf which became progressively tender, swollen, and red, and he noticed a simultaneous reduction in the size of the knee-joint effusion. He had no other symptoms and was admitted to hospital a day later.

On examination the right knee was swollen and tender and the range of movement was 10–115°. There was a tender cyst, 4 cm. in diameter, in the popliteal fossa. The circumference of the calf was increased by 4 cm. and was warm and tender. Homan's sign was positive but there was no engorgement of the superficial veins. Peripheral pulses were normal. There was a little tenderness of several of the metatarsophalangeal and the left sacro-iliac joints. Rupture of the right knee-joint was confirmed by arthrography (*Fig.* 1).

At this time the haemoglobin concentration was 14·1 g. per 100 ml., the E.S.R. was 65 mm. in 1 hour, and the total leucocyte count was 8400 per c.mm. with a normal differential count. The tests for gonorrhoea and rheumatoid factor were negative on both serum and synovial fluid. Culture of the synovial fluid was sterile. Examination of the synovial fluid again showed many polymorphs but no 'Reiter's cells'. Radiographs showed the presence of early erosive changes in several metatarsophalangeal and both sacro-iliac joints.

The patient was treated with soluble aspirin (4 g. per day), bed-rest, and splintage of the right leg. The right knee was aspirated and injected with hydrocortisone acetate (50 mg.). The acute symptoms settled rapidly but because of the continued presence of an enlarged posterior cyst which prevented full extension of the joint, excision was undertaken on the seventh hospital day. The cyst was found to lie between the heads of the gastrocnemius muscle with a communication to the posterior knee-joint. The communication was closed without the use of a fascial flap. It was confirmed, as suggested by the arthrogram, that rupture had taken place from the cyst. Pathological examination of the cyst showed it to be lined by synovial tissue. The appearances of this tissue and of a portion of synovial tissue removed from the posterior compartment of the joint were consistent with a diagnosis of Reiter's disease (Kulka, 1962).

The patient made an uneventful recovery. At the present time he has no symptoms or signs in the right knee and the range of movement is 0–130° with no extension lag. His foot symptoms have been improved by the provision of suitable in-soles for his shoes. His haemoglobin concentration is 14·9 g. per 100 ml. and his E.S.R. 17 mm. in 1 hour.

DISCUSSION

The diagnosis of Reiter's disease in the present case is based upon the history, the pattern of the arthritis, and the urinary-tract findings. The patient also had typical lesions on the roof of the mouth. Weinberger and Bauer (1955) thought that the diagnosis of Reiter's disease should be restricted to cases in which the triad of arthritis, conjunctivitis, and urethritis is present. However, ocular symptoms may be minimal or absent (Hancock and Mason, 1965). A small number of patients appear to have unremitting disease and the annual risk of subsequent attacks of Reiter's disease, which remains constant over many years, is about 15 per cent (Csonka, 1960). It is amongst this group of patients with continuing or recurrent disease that sacro-iliac joint involvement is most common. Sacro-iliitis may occur in up to 40 per cent of cases and the subsequent differentiation of Reiter's disease from ankylosing spondylitis may be difficult (Good, 1962; Hancock and Mason, 1965; Sairanen, Paronen and Mahonen, 1969).

Most reports of joint rupture have been in patients with rheumatoid arthritis but it has been recorded in association with osteo-arthrosis (Tait, Bach, and Dixon, 1965). The knee-joint is most commonly involved but rupture has been reported in the wrist (Jayson and others, 1969) and in the elbow (Goode, 1968). Rupture of the knee-joint is generally associated with the presence of a cyst in the popliteal space, and indeed, as in the present case, the rupture usually takes place from this cyst. These cysts are typically enlargements of the normal gastrocnemio-semimembranous bursae (Baker's cysts; Baker, 1877), but they may occur in other situations as in the case reported here (Perri, Rodnan, and Mankin, 1968). Jayson and Dixon (1970c) have demonstrated that there is a valvular connexion between the joint space and the posterior cyst at the knee and that this only allows the movement of fluid from the joint to the cyst. Very high joint pressures may be generated in patients with inflammatory joint disease with effusion and this will be transmitted to the cyst (Jayson and Dixon, 1970b). Indeed, because of the valvular mechanism the pressure in the cyst may be higher than that in the knee. The possibility of rupture is increased in inflammatory joint disease since there is an increase in joint elastance (Jayson and Dixon, 1970a). Knee-joint rupture is usually accompanied by the sudden onset of pain in the calf and many patients notice that there has been a reduction in the size of the joint effusion. The physical findings in the calf resemble those of a deep venous thrombosis (Good, 1964; Hench, Reid, and Reames, 1965). However, if the possibility of joint rupture is considered a correct diagnosis will usually be made, since there is often evidence of joint disease and a posterior cyst and there is rarely engorgement of the superficial veins as occurs with deep venous thrombosis. Arthrography is the most useful investigation (Tait and others, 1965; Perri and others, 1968) and demonstrates the posterior cyst and the extravasation of fluid beneath the deep fascia and its dispersion amongst the muscle bundles. Some fluid may pass into the superficial fascia (Tait and others, 1965), as in the present case. With this type of arthrography 15–20 ml. of a water-soluble radio-opaque dye are injected into the anterior knee-joint, a firm supporting bandage is applied, and the patient is briefly exercised (1–2 minutes) before radiographs are taken.

Although there has been only 1 previous report of joint rupture, which also occurred in the knee-joint, in Reiter's disease (Weese and McCarty, 1969), thrombophlebitis of the leg veins has been reported as a complication (Csonka, 1966; Engleman and Weber, 1968). These reports did not exclude the possibility that the symptoms and signs were due to joint rupture.

Immediate management consists of rest and aspiration of the knee-joint. Local support of the calf and the intra-articular injection of corticosteroids may be helpful. Although the symptoms can be controlled by such means, in the presence of continuing inflammatory joint disease a recurrence would seem likely. Experience in rheumatoid arthritis suggests that excision of the posterior cyst with closure of the defect in the posterior capsule of the joint, together with anterior synovectomy of the knee-joint in some cases, offers a more definitive form of management (Geens, Clayton, Leidholt, Smyth, and Bartholomew, 1969). In the case reported here the joint symptoms settled but the persistence of an enlarged posterior cyst which prevented full extension of the knee-joint led us to undertake surgical excision of the cyst. Grahame, Ramsey, and Scott (1970) have reported the beneficial effect on both the joint synovitis and the posterior cyst of the intra-articular injection of radioactive colloidal gold. This, or the injection of other isotopes, may offer an alternative to surgical treatment.

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CENTRAL RUPTURE OF THE LIVER WITH MASSIVE LIVER-CELL NECROSIS

A CASE REPORT AND REVIEW OF THE LITERATURE

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SUMMARY

A case of massive central rupture of the liver in which the patient became jaundiced is described. Autopsy revealed, in addition to the intrahepatic haematoma, large areas of infarction in the liver, some of which had become infected and had given rise to septic embolization to various organs. There was deranged liver function which is ascribed to the structural changes found in the liver. The occurrence of hepatocellular jaundice with this type of liver injury has not, to our knowledge, been previously recorded. It is suggested that immediate investigation and treatment are essential if the patient is to survive.

CENTRAL rupture of the liver following blunt trauma to the abdomen is an unusual injury. The case reported here is distinguished further by the development of severe liver dysfunction, a complication that we have been unable to find recorded in the literature.

CASE REPORT

A 69-year-old woman, who had previously been in good health, walked into the Casualty Department of University College Hospital, Kingston, Jamaica, on 19 Jan., 1969, half an hour after the car which she had been driving had overturned following a 'blow-out' of a front tyre. She had not lost consciousness and she remembered the steering wheel striking her chest.

Examination revealed no abnormality except for slight bruising and tenderness over the right costal margin. Over the next 3 hours her blood-pressure changed from 140/90 to 110/60 mm. Hg and the pulse-rate increased from 80 to 96 per minute. She vomited once. The tenderness in the right hypochondrium increased and bowel-sounds, which had been normal, disappeared. However, there were no signs of free fluid in the peritoneal cavity and abdominal paracentesis was negative. A chest radiograph was normal and the haemoglobin was 8·7 per 100 ml. A diagnosis of ruptured liver was made and a laparotomy was performed 5 hours after the accident.

Through an upper midline incision the peritoneal cavity was found to contain a little blood-stained fluid. The liver was slightly enlarged, had rounded edges, and was notably tense, but its surface was smooth and not bruised and its capsule was perfectly intact. There was some bruising of the stomach and a small tear in the mesentery of the terminal ileum was oversewn. The other abdominal organs were normal. The abdomen was closed without drainage, there being troublesome oozing from the wound edges at this time. The patient had received 500 ml. of normal saline, 500 ml. of Dextraven, and 1 litre of blood intravenously.

The following day the patient continued to ooze from her wound. Investigations showed that the haemoglobin was 9·3 g. per 100 ml.; white blood count, 17,800 per c.mm.; platelet count, 135,000 per c.mm.; whole-blood clotting time, 5 minutes; prothrombin time, 16 seconds; partial thromboplastin time, 58 seconds; and plasma-fibrinogen, 600 mg. per 100 ml.

On the second postoperative day gastric aspiration was discontinued and it was noticed that the patient was jaundiced. The jaundice increased rapidly and on the third day the following investigations were performed (the results were only obtained a few days later): serum bilirubin, 12·0 mg. per 100 ml. (direct 6·6 mg. per 100 ml.); serum glutamic oxaloacetic transaminase, 648 U. per 100 ml.; alkaline phosphatase, 22 K.A. units; thymol flocculation, negative; serum electrolytes: Na, 138 mEq./l.; K, 4·1 mEq./l.; Cl, 101 mEq./l.; and HCO$_3$, 17 mEq./l.; blood-urea, 58 mg. per 100 ml.; Hb, 8·9 g. per 100 ml.; white blood count, 11,900 per c.mm. The urine output was 600–800 ml. per 24 hours and the urine contained bilirubin and urobilinogen.

On the fifth postoperative day the patient's temperature rose to 38·3° C. and the pulse-rate increased to 100/120 per minute. She was digitalized and a chest radiograph showed some opacification at the base of the right lung. The serum bilirubin was now 10·0 mg. per 100 ml. (direct 6·5 mg. per 100 ml.); serum glutamic oxaloacetic transaminase, 422 U. per 100 ml.; serum glutamic pyruvate transaminase, 572 U. per 100 ml.; alkaline phosphatase, 20 K.A. units; and blood-urea, 92 mg. per 100 ml. That evening her condition became worse and she complained of feeling cold and sweaty. Her temperature was 38·9° C., the pulse-rate was 160 per minute, and the blood-pressure was 120/70 mm. Hg. An electrocardiogram showed a sinus tachycardia and a central venous line a pressure of 1–2 cm. of saline. She was transfused with saline but her condition continued to deteriorate. She became confused, and whilst a nasogastric tube was being passed, she aspirated vomit and died.

At autopsy the immediate cause of death was aspiration of vomit. The liver weighed 1600 g., was tense, and showed a large, subcapsular haematoma on the diaphragmatic surface of the right lobe (*Fig.* 1). The capsule was intact. The cut surface revealed a massive central rupture extending throughout the right lobe with small tears in the left lobe, the destroyed parenchyma being replaced by fresh blood-clot (*Fig.* 2). There were, in addition, large, irregular, yellowish areas of infarction throughout both lobes (*Fig.* 3). The extrahepatic biliary system and blood-vessels were normal.

Microscopically, liver cells adjacent to the haematoma were necrotic with some areas showing incipient organization with fibroblastic cells. The centres of many of the infarcted areas had undergone suppuration and cystic change and Gram-negative organisms were demonstrated in some of these lesions. Cells more remote from the haemorrhage and necrosis showed mild fatty change only. Similar septic infarctions with, in some cases, abscess formation with clumps of bacteria were found in the myocardium of the left ventricle and intraventricular septum and in the subpleural regions of both lungs. There was acute fibrinous pleurisy over the right lung and some of the lung sections showed small blood-vessels filled with Gram-negative organisms. The adrenal cortex showed focal areas of haemorrhagic necrosis. The kidneys were slightly swollen and pale and the cut surface of the left kidney revealed a wedge-shaped cortical septic infarction. Microscopically there was also evidence of early tubular necrosis.

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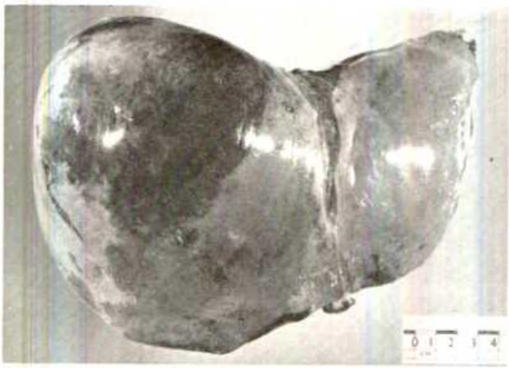

FIG. 1.—Upper surface of the right lobe of the liver showing the subcapsular haematoma. (The capsular tear seen in the extreme left of the picture is an artefact produced during manipulation at autopsy.)

DISCUSSION

With the rising number of motor-vehicle accidents blunt trauma to the abdomen is increasing, and Fitzgerald, Crawford, and DeBakey (1960) state that in their experience the liver is the most commonly involved organ in such injuries. Although many large series of liver injuries have been published (Sparkmann and Fogelman, 1954; Madding, 1955; Hellstrom, 1961; Crosthwait, Allen, Murga, Beall, and DeBakey, 1962; Hanna, Bell, and Cochran, 1965; McClelland and Shires, 1965) central rupture of the organ is very rare as in most cases the liver capsule is torn. Robertson and Graham (1933) collected 5 patients, including 2 of their own, and a further case was added later by Robertson (1937). Since then a few cases have been reported and these have had various clinical and pathological presentations—delayed rupture of a slowly expanding intrahepatic haematoma (Richardson, Gumbert, and Gale, 1967), extensive necrosis of the right lobe of the liver (Foster and Chandler, 1967), acute renal failure following a central haematoma compressing the inferior vena cava (Vasko and Scott, 1966), and a case which was diagnosed a year after injury (Shapiro, McBride and Luna, 1967).

Jaundice may occur after central rupture of the liver (Sandblom, 1948) and was considered to be due to haemorrhage into the biliary system (haemobilia) with subsequent obstruction to bile outflow. In a review of 52 published reports of haemobilia by Steichen and Sheiner (1966), they note that 13 of the patients had a central liver rupture. Since haemobilia was not present in our patient it seems reasonable to assume that the jaundice resulted from resorption of bile from the haematoma cavity and/or from the massive liver-cell necrosis. The necrosis was perhaps caused directly by the trauma, or by pressure on the liver cells or the blood-vessels supplying them by the expanding haematoma.

The rise in transaminase levels probably reflected the degree of liver damage (Wroblewski and LaDue, 1956), and although Martin (1947) stated that trauma involving up to 50 per cent of the liver in dogs did not impair the conventional liver-function tests, Hellstrom (1966) found a significant increase in serum-transaminase activity in these animals which was roughly proportional to the extent of the liver injury.

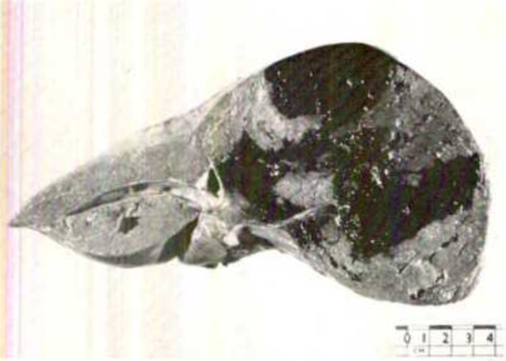

FIG. 2.—Cut surface of the liver showing massive central haemorrhage into the right lobe with subcapsular extension. Small tears (arrow) are seen in the left lobe.

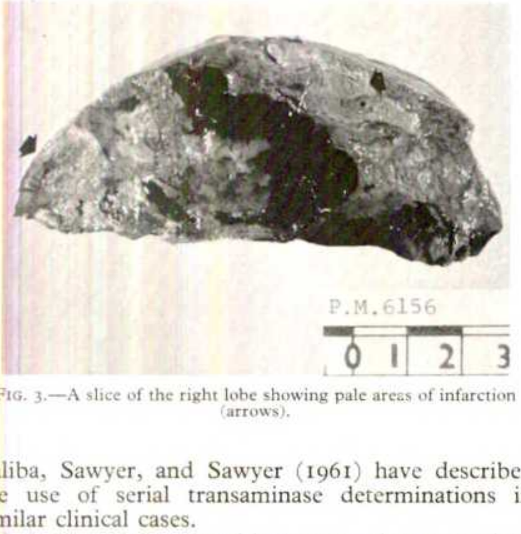

FIG. 3.—A slice of the right lobe showing pale areas of infarction (arrows).

Saliba, Sawyer, and Sawyer (1961) have described the use of serial transaminase determinations in similar clinical cases.

Infection of the central haematoma is a recognized complication (Sandblom, 1948) and it is believed that the infecting organisms are derived from the bloodstream. In our patient it was the infarcted areas and not the haematoma that had become septic. There was no obvious primary source of infection but the organisms may have been derived from the bowel. It would appear that the septic emboli to the heart, lungs, and left kidney came from these infected areas in the liver. Other forms of emboli that have been described following liver trauma such as fat emboli (Grant and Reeve, 1951) and liver tissue itself (Steiner, 1957; Johnston, 1959) were not demonstrated in this patient.

Suspicion that this type of injury has occurred should be alerted by the combination of the appropriate clinical history and the findings at operation of a tense liver with rounded edges. The present case illustrates how short the postoperative period may be and thus early investigation and further treatment are essential. The central haematoma is a space-occupying lesion and can be demonstrated by a variety of means; selective hepatic arteriography seems to have been the most successful (Boijsen, Judkins, and Simay, 1966; Hermann and Hoerr, 1967), with operative cholangiography (Spencer, Menguy, and Eiseman, 1963; Whelan and Gillespie, 1965) and hepatic scintiscanning (Graff, 1963; Burdine and Hill, 1967) being useful in some cases.

When faced with this sort of problem at operation the initial line of attack should probably be to evacuate the haematoma and, after thorough débridement of the cavity, to attempt to suture the liver as would be done for the more common 'straightforward' liver tears.

Curative operation in the present case would have been difficult because of the extent of the liver injury, but as massive liver resections are now an accepted form of treatment for extensive liver trauma (Byrd and McAfee, 1961; Poulos, 1963; Judd and Moore, 1966; Foster and Chandler, 1967) right lobectomy may have offered the only chance of saving this patient.

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MALAKOPLAKIA OF THE COLON

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SUMMARY

A case of malakoplakia of the colon in a young man who presented with symptoms and signs suggestive of ulcerative colitis is reported. It is suggested that a careful search for Michaelis-Guttmann bodies in all chronic inflammatory lesions may reveal a much higher incidence of malakoplakia.

MALAKOPLAKIA (soft plaque) is an extremely rare non-neoplastic lesion of uncertain origin. For many years it was believed to be limited to the urinary bladder where it produces scattered, smooth, rounded, yellowish swellings surrounded by a zone of hyperaemia in the trigone and base of the bladder. Later, however, similar lesions affecting other parts of the urinary system and also the genital tract have been reported, and more recently there have been reports of malakoplakia affecting the gastro-intestinal tract. In the present paper a case of colonic malakoplakia which presented a difficult diagnostic problem is reported.

CASE REPORT

The patient, a 29-year-old farmer, presented to his medical practitioner in July, 1969, complaining of pain in the left upper quadrant of his abdomen associated with troublesome flatulence. These symptoms persisted and by September, 1969, the pain had become much more severe and radiated to his back. At that time he had also noticed that his stools were soft, offensive, and sometimes mixed with blood, but they did not float and were dark in colour. He had lost his appetite and had had repeated attacks of nausea and vomiting. Later the stools had become more watery, contained blood and mucus, and his general condition had deteriorated considerably. Sigmoidoscopy revealed oedematous friable mucosa and a biopsy of the mucosa showed ulceration suggestive of ulcerative colitis; no parasites were found. An indefinite mass was also detected in the left upper quadrant of the abdomen and barium-enema studies suggested ulcerative colitis. The patient was treated with oral cortisone, prednisolone enemata, and sulphasalazine. His general condition improved and the diarrhoea became less troublesome. The mass in the left upper quadrant persisted. A second barium enema revealed the presence of a fistula between the descending colon and a loop of small bowel. A diagnosis of Crohn's disease was entertained but the treatment was not changed. The mass seemed to diminish in size and by October, 1969, he was much improved and was sent home.

Six weeks later the patient returned in a very poor condition with evidence of anaemia and toxaemia and with a swinging temperature up to 38·4° C. The diarrhoea was no longer troublesome but the abdominal mass was larger and very tender. Two weeks later, on 19 Dec., 1969, laparotomy was performed elsewhere and a large, irregular, fixed mass was found in the region of the splenic flexure involving both the large and small bowels. The rest of the bowel was normal except for some thickening of the caecum. A loop of small bowel, which included the enterocolic fistula, was detached from the mass and about 6 cm. were resected. The opening in the large bowel was sutured and the area was drained. Transverse colostomy was performed. Biopsies taken at the time of the operation were sent to the Department of Pathology of the University of Cape Town, where a diagnosis of malakoplakia was made.

On 25 Feb., 1970, the patient was admitted to Groote Schuur Hospital. He was obviously toxic with a swinging pyrexia of up to 39° C., a white cell count of 13,300, and a haemoglobin level of 7·5 g. per cent. The mass in the left upper quadrant was easily palpable and about 12 × 8 cm. in size. The patient was treated with several antibiotics including ampicillin and cephalothin, while sulphasalazine was continued. His general condition appeared to improve, but he developed an abscess over the left greater trochanter which had to be drained. The temperature continued to swing and the mass persisted. A further barium enema revealed an obstructing lesion of the descending colon with leakage into the paracolic region.

On 14 April, 1970, laparotomy was performed. A large mass was found in the left loin involving the greater portion of the descending colon, which was resected together with the upper part of the sigmoid colon and the left half of the transverse colon up to the colostomy.

The report of the pathologists was as follows:—

'Specimen consists of a colon measuring 35 cm. in length. Roughly half-way along its length is a hard mass which is closely adherent to the bowel wall; it measures 6·0 cm. in diameter. Its outer surface is congested and roughened, whilst the cut surface is grey with irregularly branching, linear, yellow areas, which project above the cut surface.

'The opened bowel shows some narrowing at the site of the mass with mild dilatation of the proximal segment (9·0 cm. in circumference) compared to the distal segment, which measures 6·0 cm. in circumference.

'The mucosal surface is grossly abnormal with a loss of haustrations except for small segments near the lines of excision.

'The mucosa in most of the specimen is yellowish-tan in colour and thickened. This thickening is accentuated in focal areas giving rise to nodules and pseudo-polypi, which project from the surface.

'Sections into the wall of the intestine show the thickened, yellowish mucosa to be well delineated from the normal-appearing muscularis. Section through the mass shows it to be intimately related to the bowel wall. The subserosal tissues cannot be discerned from this mass but the muscularis has retained its normal appearance except for an area where it is traversed by a diverticulum. Section along the part of one of the diverticula shows it to extend into the "tumour" mass for a distance of 2·5 cm. (*Fig.* 1.)

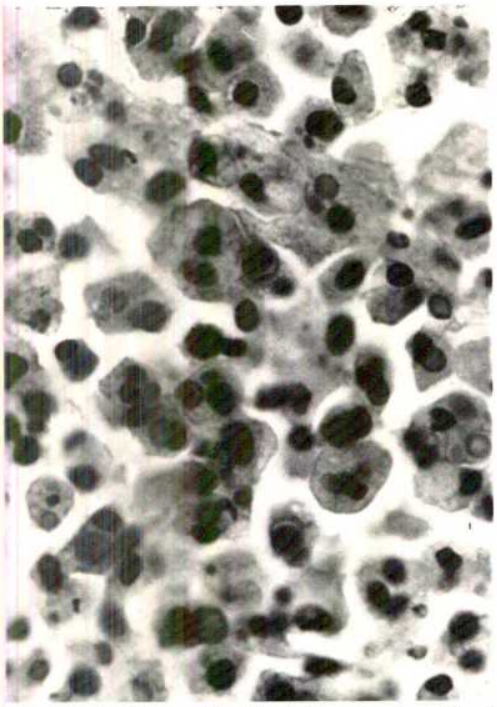

FIG. 1.—Section showing cells with calcified spherules (Michaelis-Guttmann bodies), some of which are laminated.

'The histological features are uniform throughout the bowel wall, the differences being merely quantitative in type. In the smaller, yellow nodules, sheets of macrophages are present in the submucosa, with sparing of the mucosa, muscularis mucosa, muscularis, and serosa. In the polypoidal lesion aggregates of these cells are once again seen, except that extension into the mucosa with consequent ulceration are present. The muscularis and serosa are uninvolved except where diverticuli have penetrated the muscularis; here the macrophages have extended into the serosa and presumably resulted in the formation of a large mass.

'The mass is composed of sheets of histiocytes with very little intervening stroma or other inflammatory cells. In areas, foreign body-type giant cells are present. At the periphery of the mass, the cells have become elongated and spindle shaped. All of these varieties of cells contain intracytoplasmic PAS-positive granules and many contain calcified spherules (Michaelis–Guttmann bodies), some of which are laminated. No bacteria could be demonstrated.'

The patient's postoperative course was satisfactory but on the ninth postoperative day he became distended and vomited and examination revealed signs of peritonitis. His abdomen was therefore re-explored and 3 m. of twisted and strangulated small bowel had to be resected. The subsequent course was rather stormy, but he gradually improved and was discharged from hospital on the twenty-seventh postoperative day.

On 29 Aug., 1970, the patient was readmitted for assessment. He was in excellent general health and had gained 22·5 kg. in weight. An excretory urogram showed some narrowing of the left ureter but good function of the left kidney. On 4 Sept. continuity of the colon was restored, and at surgery no pathology could be found, apart from an area of thickened peritoneum in the left paracolic gutter. Biopsy revealed areas of fibrosis and haemosiderin deposits, but no evidence of malakoplakia. He recovered rapidly and was discharged on the thirteenth postoperative day having normal bowel function. When last seen in December, 1970, he was in excellent health and sigmoidoscopy failed to reveal any evidence of ulceration or mucosal abnormality.

DISCUSSION

In 1902 Michaelis and Guttmann gave an account of a lesion of the bladder which had the characteristic features of malakoplakia. It was, however, left to Von Hanseman to suggest the descriptive term in 1903. He noted that the predominant cells in the plaques were histiocytes with many of these cells containing large inclusions, which have been called Michaelis-Guttmann bodies, but could not find a specific aetiological factor. Thereafter, there were sporadic reports of lesions invoving the bladder and less commonly the upper urinary tract (Melicow, 1957). In 1958, Haukohl and Chinchinian reported involvement of the testis, and further cases have been described by Blackwell and Finlay-Jones (1959) and Brown and Smith (1967). In 1965 Goldman reported a case with the typical lesion in the prostate.

A case of malakoplakia of the colon was reported by Turner and Lattes in 1963 and another by the same authors in 1965. Involvement of the colon has also been reported by González-Angulo, Corral, and García-Torres (1965) and Finlay-Jones, Blackwell, and Papademetriou (1968). In 1967 Yunis, Estevez, Pinzon, and Moran described a case of malakoplakia involving the bladder, colon, and stomach, and in 1970 Blackshear reported the lesion in an appendix.

From most of the reports it would appear that the condition tends to be self-limiting and there have been reports of spontaneous regression (Cristol and Broders, 1946; Boonstra and Bates, 1950). Deaths from complications have been reported by Scott and Scott (1958), Turner and Lattes (1963), and Goldman (1965). Females have been affected more often than males in a ratio of 4·5 to 1.

Although malakoplakia has been recognized for more than 70 years and the pathology has been well described, the aetiology is still in doubt. Early investigations suggested that the lesions were variants of tuberculosis, sarcoid, or a non-specific granuloma. This hypothesis gained some support from later reports of favourable clinical responses to long-term administration of drugs effective against mycobacteriae.

Turner and Lattes (1965) concluded on the basis of histochemical studies that the characteristic Michaelis-Guttmann bodies in 'malakoplakia cells' are of glycolipid composition 'compatible with capsular polysaccharide, lipopolysaccharide, or endotoxin of micro-organisms'. *Escherichia coli* has often been cultured from the lesions and therefore proposed as an aetiological agent. Yunis and others (1967) suggested that these bodies consisted of a neutral glycoprotein with a central core of acid mucopolysaccharide, possibly of bacterial capsular origin. Around this core are deposits of glycolipids, calcium, and iron. They also observed transitions from small cytoplasmic granules within 'malakoplakia cells' to typical Michaelis-Guttmann bodies.

Electron microscopic studies by McKiel, Eisenstein, and McDonald (1962) revealed that the Michaelis-Guttmann bodies are often laminated, sometimes with a peripheral dark zone and a central pale area. At the periphery, long, thin, needle-like crystals, measuring 200–600 Å in length, have been observed. The authors suggested that this crystalline form may be due to appatite and that malakoplakia is an inflammatory state with histiocytic phagocytosis of fatty acids and/or polysaccharides with subsequent calcification uninfluenced by either fungi or virus.

Finlay-Jones and others (1968) reported their electron microscopic observations and suggested that the Michaelis-Guttmann bodies develop from large lipid-containing cytoplasmic phagosomes which undergo calcification.

No doubt meticulous search for Michaelis-Guttmann bodies in all chronic inflammatory lesions, especially those associated with *E. coli* infections, will reveal a much greater incidence of malakoplakia than has been appreciated up to the present time.

Acknowledgements.—We gratefully acknowledge permission to publish this case from the Medical Superintendent of Groote Schuur Hospital, Dr. Burger, and we would also thank Dr. Comfort of East London, who did the first operation and referred the case to us.

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REVIEWS AND NOTICES OF BOOKS

The Detective-Physician. The Life and Work of Sir William Willcox, K.C.I.E., C.B., C.M.G., M.D., F.R.C.P. By PHILLIP H. A. WILLCOX, M.A., M.D., F.R.C.P. Pp. 332+xiv. 1970. London: William Heinemann Medical Books Limited. £3·50.

THIS is an excellent account of the life of a very distinguished physician who was most probably the last physician to practise both in medicine and as an analyst to the Home Office.

It is often difficult for a son to write the life history of his father, but Dr. Philip Willcox has performed his task in an interesting and lucid manner. There can be no doubt that Sir William's clinical records, kept as they were in a meticulous manner, were a great help and formed a sound basis for his biography.

The medical profession and the lay public alike are always interested in the mystery of murder especially if this entails extensive investigation.

Sir William Willcox enjoyed a very busy and varied life and this book which describes his activities is divided into five parts.

Part 1 concerns his early years and education and his training at St. Mary's Hospital with Sir Alexander Fleming and Sir Bernard Spilsbury. In 1910, while he was Consulting Physician and Senior Analyst to the Home Office, Willcox was concerned in the Hilldrop Crescent mystery in which Crippen was convicted and hanged. He resented being referred to as 'the man who hanged Crippen'.

Part 2 covers the period between 1912 and 1915. Willcox was very busy during this time as a scientific witness; he was also employed in wartime research dealing with gases which might be used in modern warfare. It was during this period that he had to deal with the 'Brides in the Bath' case.

Part 3 is devoted to Willcox's career as Consulting Physician to the Army. He served in the Dardanelles, Baghdad, Northern Persia, and India, and returned home in 1919.

Part 4 covers the years from 1919 to 1935, and reveals Willcox's great interest in teaching clinical medicine at St. Mary's Hospital and also his researches into new drugs, poisons, and rheumatic diseases.

Part 5, dealing with the final phase of his active life, details his many activities, including being Master of the Society of Apothecaries in 1935–6. He was cofounder of the Empire Rheumatism Campaign. Willcox died of a stroke in 1941 while still in active practice.

Medical historians will welcome this book, for in it Willcox is revealed as a medical seer and as a consistent searcher after justice both in his professional life and in the Courts of Law.

Blood Volume and Extracellular Fluid Volume. Second edition. By SOLOMON N. ALBERT, B.A., M.D., D.A., F.F.A. R.C.S., F.A.C.A., Maryland. 9×6 in. Pp. 295+xxxvii. Illustrated. 1971. Springfield, Illinois: Charles C. Thomas. $16.75.

THE second edition of this practical and useful monograph has been extensively revised and new illustrations and clinical cases have been added.

The surgeon of today has to undertake extensive operations for cancer, and on badly damaged patients, the results of road accidents. It is therefore important that there should be a practical evaluation of blood-loss so that proper replacement can be given.

This book gives all the answers; the author, a practical anaesthetist and a dedicated physiologist, reviews the basic principles of technique for measuring blood-volume and extracellular fluid volume. There can be no doubt that this book will interest the modern surgeon, the anaesthetist, and the physiologist.

There is an extensive bibliography at the end of this book, as well as some useful figures showing the normal blood-volume values in millilitres in both men and women.

Regionale Anästhesie mit dem Langzeitanästhetikum Bupivacain. By HANS NOLTE and JUSTUS MEYER, Munden. 9×6 in. Pp. 121+vii. Illustrated. 1971. Stuttgart: Georg Thieme Verlag. DM.22·80.

A SYMPOSIUM was organized in Bad Oeynhausen, Western Germany, dedicated exclusively to the recently developed local anaesthetic bupivacain (Marcain or Carbostesin).

The first conclusion of this symposium was that local anaesthesia still maintains its place regardless of the tendency to perform all kinds of minor operations under general anaesthesia.

Bupivacain surpasses most of the current local anaesthetics by its long-lasting effect; for instance, conduction anaesthesia lasting for approximately 5 hours is impressive.

Obstetricians reported their results of paracervical, peridural, and caudal anaesthesia during deliveries, but warned against bradycardia and acidosis of the newborn.

Although almost any kind of abdominal operation can be performed under peridural anaesthesia with bupivacain, its special use in general surgery is in postoperative pain suppression, administering intercostal or peridural blockade, if necessary for 1–3 days, by means of a peridural catheter. Dr. J. Crul, who is a Dutch professor in anaesthesiology, showed how in peripheral arterial diseases peridural anaesthesia with bupivacain suppresses pain and enables one to perform angiographies and operations on the diseased vessels by the same anaesthetic manipulation.

Head Injuries. Proceedings of an International Symposium held in Edinburgh and Madrid 2nd to 10th April, 1970. 10×7 in. Pp. 342+xvi. Illustrated. 1971. Edinburgh: Churchill Livingstone. £6.

THIS large volume contains the papers read at an International Symposium held in Edinburgh and Madrid in April, 1970.

The volume is divided into eleven sections. Sections 1–6 contain the papers read at Edinburgh, while Sections 7–11 were delivered in Madrid.

Section 1 is concerned with the prevention of head injury both in children and adults.

Section 2 deals with care at the roadside and the prevention of second accidents.

Section 3 is devoted to the organization of head-injury services.

In Section 4 craniofacial injuries come under review.

Section 5 is concerned with the long-term complications and the care of head injuries.

Section 6 deals with rehabilitation and resettlement, and Section 7 is devoted to the organization of head-injury care in the hospital.

Section 8 deals with the emergency care of head and multiple injuries, while Section 9 is concerned with the pathophysiological basis for the management of head injuries.

Section 10 deals with the diagnosis and treatment of head injuries, and lastly, Section 11 concentrates on the results of neurosurgical care of head injuries.

This is a very comprehensive symposium on head injuries and every facet of the ever-increasing problem comes under review.

An excellent reference volume on a very important subject.

Recent Advances in Cancer and Radiotherapeutics. Edited by KEITH E. HALNAN, M.A., M.D., M.R.C.P., F.F.R., Director, Glasgow Institute of Radiotherapeutics. 9¾ × 6 in. Pp. 412. Illustrated. 1972. Edinburgh: Churchill Livingstone. £6.

CANCER is a common disease and anything new in its treatment is of real interest to the medical profession, particularly surgeons.

This book, with its thirteen contributors, covers the whole field of cancer therapy in a very practical way. All the contributors are experts in their own particular field. The editor has brought together active workers in related fields to survey selected topics in a critical way.

Robert McWhirter gives an analysis of the treatment of breast cancer, and this is of importance when doctors are asking if radical mastectomy is really necessary in the treatment of this condition.

I. D. H. Todd reviews the present position of cancer chemotherapy, while M. L. N. Willoughby gives an excellent account of the management of childhood leukaemia.

Peter Clifford reviews the present position in regard to Burkitt's lymphoma; he writes with conviction, for he has treated many cases at the Kenyatta Hospital in Nairobi.

The later chapters in this book cover progress in chemotherapy, surgery, immunology, radiobiology, and radiotherapeutics.

This is a book which will appeal to all clinicians, but especially to surgeons and radiotherapists. Surgical registrars and tutors will find this book invaluable.

Diagnostische und therapeutische Fortschritte in der Krebschirurgie. By F. LINDER, Heidelberg, G. OTT, Bonn, and H. RUDOLPH, Heidelberg. 9 × 6 in. Pp. 260 + xvi. 1971. Berlin: Springer Verlag. DM.68.

ON the occasion of the eightieth birthday of Professor K. H. Bauer, one of the greatest living surgeons, his pupils and staff gave a series of lectures dealing with the present situation in cancrology.

Although the world is waiting for spectacular discoveries some advances in diagnosis and therapy are evident. Recent developments in angiography and endoscopy are definite achievements in the diagnostic field. Incontestable progress has been made in the therapy of Wilms's tumours, where the combined attack by operation, radiation, and chemotherapy (actinomycin D) has proved to be a success.

Radioactive gold implantation in the hypophysis is popular with the specialists of Professor Bauer's medical institution in Heidelberg University, though in other centres this method finds fewer followers.

This book gives an up-to-date account of recent developments in cancrology.

Surgery of Rheumatoid Arthritis. Edited by RICHARD L. CRUESS, M.D., Montreal, and NELSON S. MITCHELL, M.D., C.M., Montreal. 10 × 7 in. Pp. 211 + x. Illustrated. 1971. Oxford: Blackwell Scientific Publications. £9·75.

THIS interesting volume is the outcome of a course of lectures entitled 'The Surgical Management of Rheumatoid Arthritis', which was given under the sponsorship of the Postgraduate Board of the Royal Victoria Hospital and McGill University in Montreal in May, 1970.

The thirty-two contributors cover the whole surgical field of rheumatoid arthritis in a most comprehensive way. The emphasis is on prevention of deformities.

Many operations are currently available, and sufficient numbers of patients have been followed to permit an analysis of the results of surgery which can offer the basis for a sound surgical approach.

The many and varied surgical techniques are well described and illustrated. A dynamic brace for finger-joint reconstruction in arthritis is discussed.

This book will make a strong appeal, not only to orthopaedic surgeons, but also to plastic surgeons and rheumatologists.

Manual of Preoperative and Postoperative Care. Second edition. Edited by JOHN M. KINNEY, M.D., New York, RICHARD H. EGDAHL, M.D., Mass., and GEORGE D. ZUIDEMA, M.D., Baltimore. 9 × 6 in. Pp. 644 + xiv. Illustrated. 1971. London: W. B. Saunders Co. Ltd. £4·70.

THE second edition of this up-to-date and very practical volume is the work of over thirty contributors, who come from various surgical centres in the United States and Canada.

Every aspect of pre- and postoperative care has been carefully covered. References to standard books and important articles are to be found at the end of the various chapters. This volume is divided into two main parts.

Part 1 is concerned with general principles, such as wound healing, fluid and electrolyte therapy, blood transfusion, cardiac failure, shock, and transplantation.

Part 2 deals with the surgical care of organs and systems. This second part should prove to be of real value to surgeons as all the articles are written by practising surgeons with mature clinical experience.

The chapters dealing with multiple injuries and the care of the burned patient are outstanding.

A useful book for the modern surgeon at a very moderate price.

Contemporary Burn Management. Edited by HIRAM C. POLK, jun., M.D., Louisville, and H. HARLAN STONE, M.D., Atlanta. 9¼ × 6 in. Pp. 444 + xx. Illustrated. 1971. Edinburgh: Churchill Livingstone. £9·50.

THIS is a useful and informative book devoted to an important subject, considering that patients with burns occupy more than 10,000 hospital beds each year in America and some 7000 die as the result of the burn injury.

This book is divided into six parts. Treatment of shock associated with burns is discussed in Part 1, including crystalloid resuscitation, the Brooke formula, and fluid therapy with Dextran. Professor A. W. Wilkinson contributes an important chapter on limited-volume therapy with colloid.

Part 2 is concerned with respiratory injury, and tracheal intubation is discussed.

Part 3 deals with early wound care and the various methods of treating burns are discussed in some detail.

Immunological problems are considered in Part 4, and streptococcal, staphylococcal, Gram-negative bacteria, and fungal infections are analysed in Part 5. In Part 6 an excellent summary is given, in which techniques of wound closure, grafting, and splinting come under review.

This is a very useful reference volume giving an up-to-date account of the treatment of burns in both America and Great Britain.

It will prove of real value to both surgeons and surgical residents as a practical guide to treating patients with thermal injury. An excellent production.

Chest Injuries. By Roshan Lall Gupta, M.S., F.R.C.S. (Edin.), F.R.C.S. (Eng.), F.A.C.S., F.R.S.M. (London), Meerut, India. 8½ × 5½ in. Pp. 215 + v, with 34 illustrations. 1972. Meerut: Saritee Pvakashun. No price given.

In India as in other parts of the world chest injuries are common in both children and adults. Professor Gupta with his large clinical experience of chest injuries in both England and India has written a very practical book on these conditions. He is to be congratulated on the way in which this monograph has been printed in India on good-quality paper with well-produced illustrations.

This book should prove of real use to students and practitioners in India who want to know more about chest injuries.

Stapedectomy. By Harold F. Schuknecht, M.D., Boston. 11 × 8½ in. Pp. 119 + vii. Illustrated. 1971. Edinburgh: Churchill Livingstone. £10·50.

Today stapedectomy is a common operation and it is essential that medical men should know what the operation can achieve. Dr. Schuknecht has performed this operation on over 6000 patients and he presents his methods and results in this monograph. The clinical features of otosclerosis are examined, and the criteria for the selection of patients who will benefit from stapedectomy are discussed. The intricate operation of stapedectomy is described and illustrated in considerable detail. Special attention is given to the selection of the prosthesis used in this operation. Complications which may occur following this operation are also described.

The histopathological studies carried out by the author are interesting and convincing, and the illustrations are excellent.

This book is a valuable addition to surgical literature.

Septic Shock in Man. Edited by S. G. Hersky, M.D., Bronx, Louis R. M. Del Guercio, M.D., Bronx, and Rita McConn, Ph.D., Bronx. 9¼ × 6¼ in. Pp. 313 + xxi. Illustrated. 1971. Edinburgh: Churchill Livingstone. £4·75.

Shock is a very common condition and septic shock is associated with a very high mortality rate.

This book with its many contributors from America and Canada covers every facet of this important problem.

It is divided into eight parts. Part 1 is concerned with the background patterns in septic shock. Part 2 deals with the respiratory aspects, including pulmonary mechanics and respiratory measurement in acutely ill patients. Part 3 is devoted to oxygen transport and utilization, including oxygen uptake in septic shock. In Part 4 the metabolic aspects come under review, while in Parts 5 and 6 the cardiocirculatory aspects are examined in detail, including the use of corticosteroids in the treatment of septic shock. Part 7 deals with special problems including those of fluids in burns. Part 8 contains a very careful summary of the whole problem.

By compiling the collective experience of a diverse group of medical investigators in shock units the editors have attempted to stimulate further inquiry into this very lethal condition.

This book will have a wide appeal to all medical men, but especially to surgeons, anaesthetists, and physiologists.

The Thyroid. A Fundamental and Clinical Text. Third edition. Edited by Sidney C. Werner, M.D., D.Sc. (Med.), New York, and Sidney H. Ingbar, M.D., Boston. 10 × 7 in. Pp. 914 + xxvii, with 276 illustrations. 1971. London: Harper & Row. £14.

The third edition of this enormous work has a new co-editor and an almost completely new group of contributors. It is pleasing to note that some British contributors have been included in this edition.

The general format of the work has been preserved, but the text has been expanded.

The work is comprehensive and every facet of thyroid anatomy, physiology, pharmacology, and pathology has been well covered.

Full discussion is given to the various thyroid states, and Selwyn Taylor's article on the aetiology and pathogenesis of non-toxic sporadic goitre is excellent.

The illustrations, especially the photomicrographs, are quite a feature of the book.

There can be little doubt that this volume will become the standard work of reference on the thyroid gland and its diseases.

A Practice of Anaesthesia. Third edition. Edited by W. D. Wylie, M.A., M.B. (Cantab.), F.R.C.P., F.F.A. R.C.S., Hon. F.F.A., R.C.S.J., London, and H. C. Churchill-Davidson, M.A., M.D. (Cantab.), F.F.A. R.C.S. London. 9 × 6 in. Pp. 1549 + xviii. Illustrated. 1972. London: Lloyd-Luke (Medical Books) Ltd. £12.

The third edition of this comprehensive work on anaesthesia has been completely revised and brought up to date. It is the effort of the anaesthetists of St. Thomas's Hospital, as all the eight associate editors and the eight contributors are from that hospital.

Anaesthesia is a large branch of medicine today and it includes physics, chemistry, pharmacology, physiology, and electronics in its make-up. In this new edition some important chapters have been introduced, such as anaesthesia for dental surgery, special care units, and modern pharmacological principles as applied to this specialty.

Although this is a multi-author work the style of the book has remained unchanged and the text is still lucid and factual.

This is by far the best work on anaesthesia in the English language; it is completely up to date and as a work of reference it could not be bettered.

Chirurgische Differential-Diagnostik. Edited by Karl Vossschulte, Klinikstr., and Ludwig Zukschwerdt, Hamburg. 10½ × 7 in. Pp. 859 + xii. Illustrated. 1972. Stuttgart: George Thieme Verlag. DM.188.

This is a new textbook on the differential diagnosis in surgical conditions. Twenty-eight contributors have helped to cover the vast field from cutaneous lesions to the acute abdomen. While many subjects are discussed in detail, neonatal obstructions are dismissed in less than half a page. The book contains many lists and tables and a large number of excellently produced illustrations. On the other hand, it is strictly limited to diagnosis and does not discuss pathology or mention treatment.

It is difficult to decide for what type of reader this book has been written. It contains too much information for the medical student but, on the other hand, the practising surgeon would wish to know something about the pathology and treatment when referring to a textbook about the differential diagnosis.

In its final section this book has a long list of the normal values of many pathological investigations and this final chapter was certainly the most helpful to the reviewer.

The Anatomical Basis of Medical Practice. By R. Frederick Becker, Ph.D., James W. Wilson, Ph.D., M.D., and John A. Gehweiler, M.D. 11 × 8¼ in. Pp. 907 + xv. Illustrated. 1971. Edinburgh: Churchill Livingstone. £11.

The title of this large work might be altered to 'Living Anatomy', for the authors have certainly proved that anatomy is indeed alive. The modern medical student requires a book such as this, in which embryology, surface markings, and radiology play such an enormous part.

The authors have wisely stressed the anatomical relationships which are important in clinical medicine and surgery.

The embryology as presented depicts the many and varied congenital defects which may occur not only in the thorax and abdomen but also in the neck and brain.

The radiological anatomy is illustrated with excellent skiagrams showing the course and distribution of arteries by means of angiograms. The surface markings are depicted on living models and they are excellent.

The illustrations are quite a feature of this large volume and the line drawings have the distinct advantage in that they are mostly original.

One only wishes that such a book as this was available when one was a student in the dissecting room.

This book is alive and will be popular with students, nurses, and practitioners everywhere.

Anatomy, Regional and Applied. Fifth edition. By R. J. Last, M.B., B.S. (Adel.), F.R.C.S., Los Angeles. 9½ × 6½ in. Pp. 925 + xvi. Illustrated. 1972. Edinburgh: Churchill Livingstone. £8.

This book was born of popular demand in 1954 and since that date five new editions, besides several reprintings, have appeared. These figures show the approval of students throughout the world.

In the recent edition the new (P.N.A.) nomenclature is used throughout the text. There are 32 new illustrations, which are all original and excellent. This book retains its place as the best production on regional and applied anatomy that has so far been published.

Praxis der Schockbehandlung. Edited by Theodor Ott Lindenschmidt, Hamburg, Erich Rugheimer, Erlangen, and Hans Willenegger, Liestal. 9 × 6 in. Pp. 211 + ix. Illustrated. 1971. Stuttgart: Georg Thieme Verlag. DM.26·80.

This volume consists of the papers of a meeting held in 1970 involving surgeons, anaesthetists, and those responsible for blood-transfusion services. The book contains seventeen papers on various aspects of shock, dealing with aetiology, assessment, and treatment. The administrative problems of a blood-transfusion service have not been neglected and the majority of the papers presented are practical rather than theoretical. The discussion is presented in full. This volume should be of interest especially to those concerned with blood-transfusion services and most papers contain extensive lists of references. It is unfortunate that the papers do not have summaries, but there is a good index.

An Atlas of Diseases of the Eye. Second edition. By E. S. Perkins, M.D., Ph.D., F.R.C.S., Institute of Ophthalmology, University of London, and Peter Hansell, M.R.C.P., Hon. F.R.P.S., F.B.P.A., Westminster Medical School, London. 10 × 7¾ in. . Pp. 86 + xi. Illustrated. 1971. Edinburgh: Churchill Livingstone. £6.

The second edition of this atlas has been considerably expanded to include sections on glaucoma and anomalies of ocular movement. Several new drawings have been added and the atlas is the best so far produced with coloured drawings. The various pictures depicting the fundus of the eye are superb.

The student and practitioner will find this atlas an admirable book for ready reference.

Surgical Departments in Hospitals. The Surgeon's View. Edited by D. M. Douglas, M.B.E., M.B., Ch.M., M.S. (Minn.), F.R.C.S., F.R.C.S. (Edin.), Dundee. 8½ × 5½ in. Pp. 134 + ix. Illustrated. 1972. London: The Butterworth Group. £2·50.

This is a useful book, for it contains the views of Scottish surgeons from Aberdeen, Glasgow, Edinburgh, Falkirk, and Dundee. The problems of hospital construction with regard to out-patient departments and the lay-out of operating-theatre units and intensive care units are discussed in some detail. The important question of resuscitation facilities receives due consideration.

Some of the most interesting features of this book are the discussions on teaching and research facilities in various hospital centres.

This book will prove a useful reference volume when any new hospital projects are put forward by the Ministry; it should ensure that surgeons in the future will have some knowledge of hospital organization in Scotland.

Symposium on the Hand, Vol. 3. Edited by Lester M. Cramer, D.M.D., M.D., F.A.C.S., Philadelphia, and Robert A. Chase, M.D., F.A.C.S., Palo Alto. 11 × 8½ in. Pp. 287 + ix. Illustrated. 1971. London: Henry Kimpton. £16·10.

This volume contains the proceedings of the Symposium of the Educational Foundation of the American Society of Plastic and Reconstructive Surgeons held at Stanford University in March, 1970. The papers contain the clinical and operative experiences of twenty-six leading hand surgeons of the world.

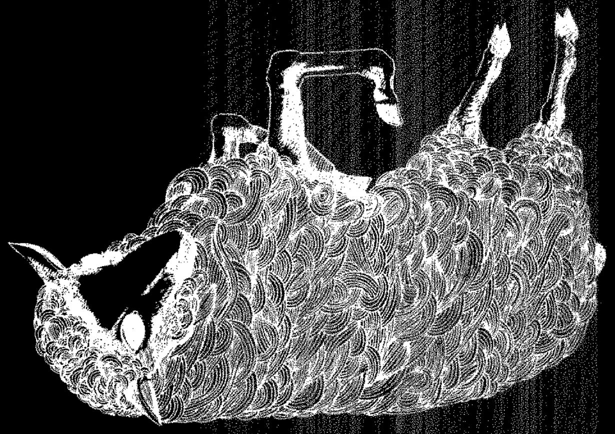
Many and varied facets of the injured hand are described in this volume, but the outstanding article is by Paul Brand on the rehabilitation of the hand in leprosy.

Another interesting paper is by L. Gómez Correa of Mexico City on hand replantation; it reveals that under suitable circumstances such a procedure is possible.

As one would expect, the treatment and reconstruction of the burned hand and fingers receive due notice. Such subjects as the painful hand, treatment of Dupuytren's contracture, assessment of peripheral nerve injuries, and the Boutonnière deformity are all considered and discussed at length.

Hand clinics are becoming common place today in our teaching hospitals and there can be no doubt that they have played an important part in lessening the bad deformities of the hand which were common a few decades ago.

This book will be a *must* to all hand and plastic surgeons.



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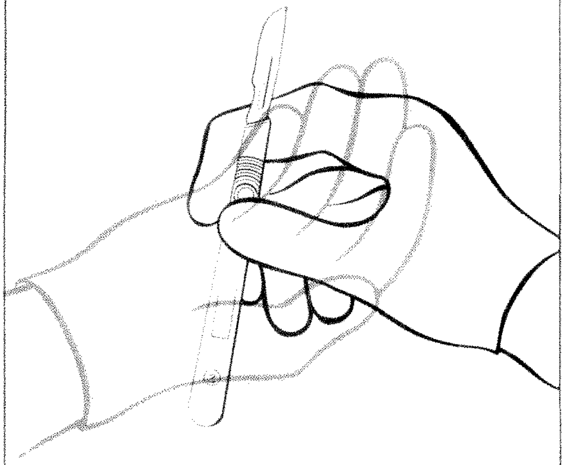

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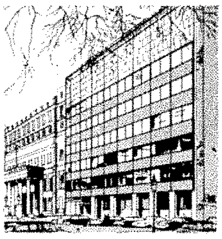

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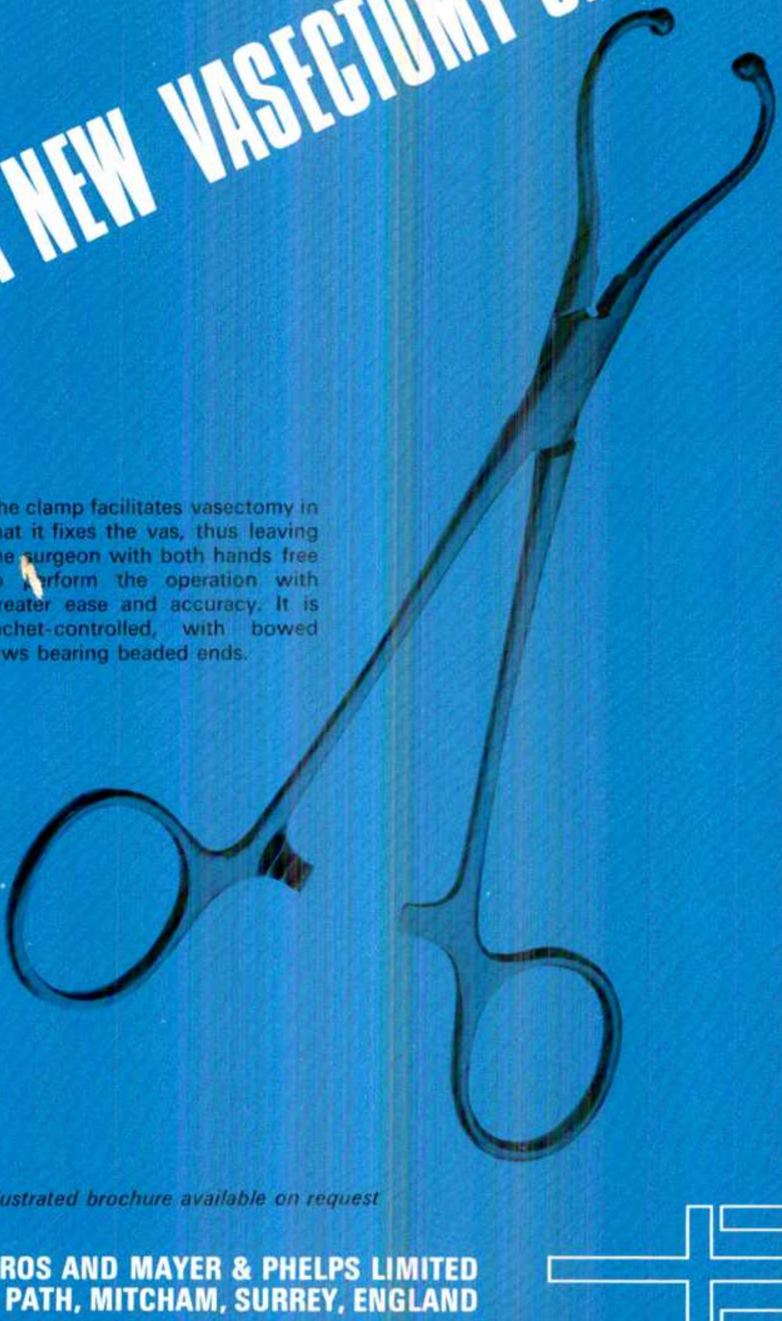

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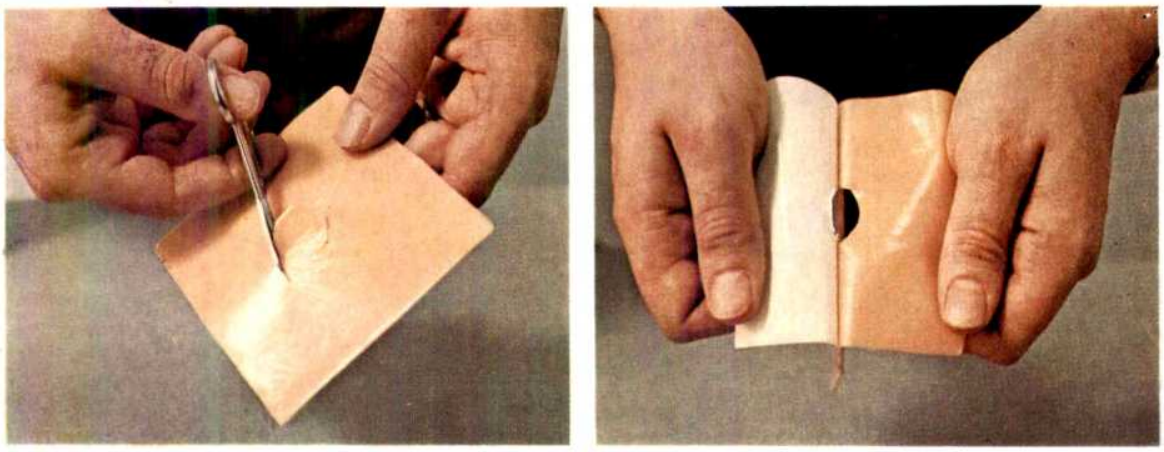

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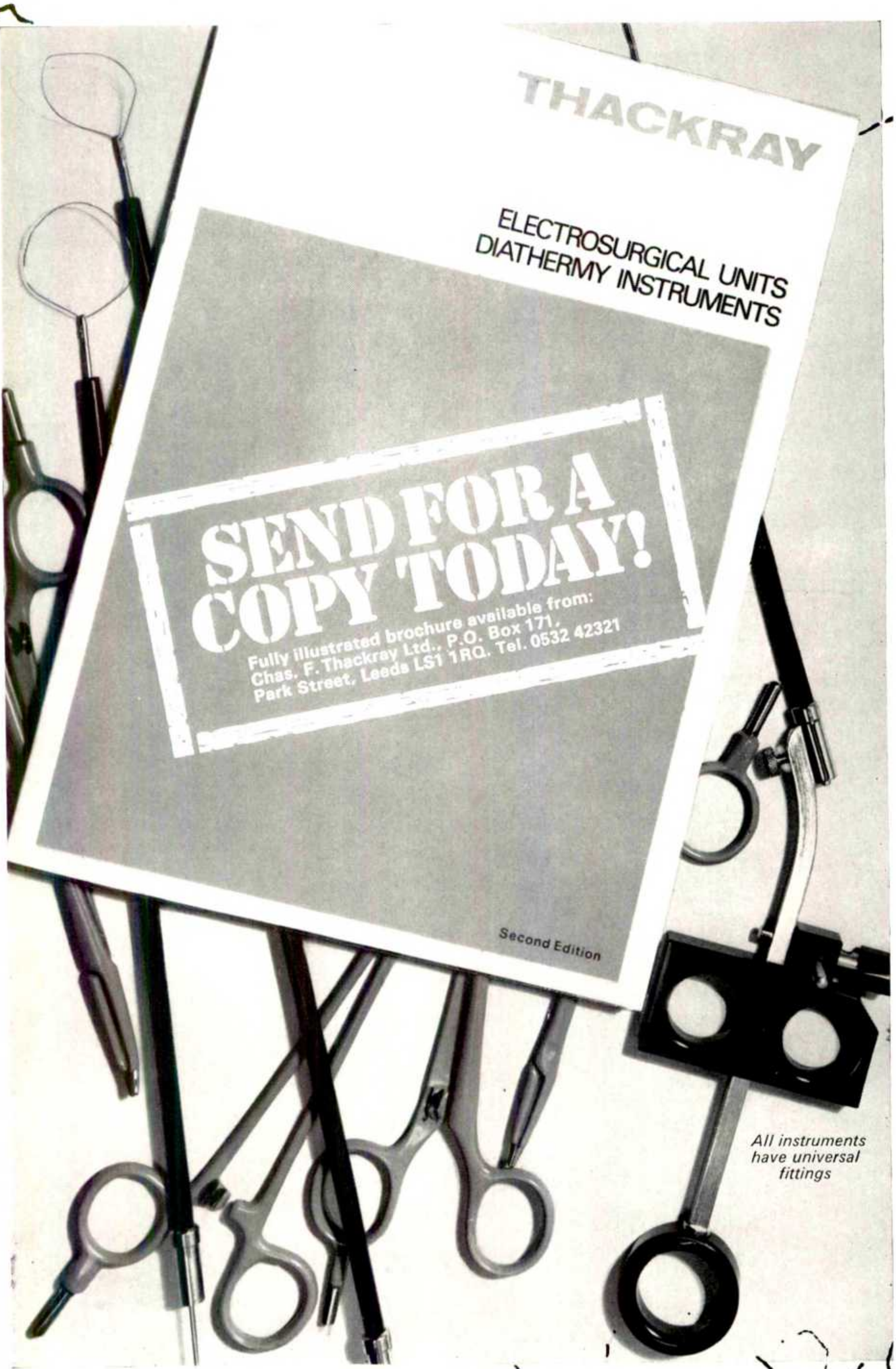

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CONTENTS

PAGE

ORIGINAL PAPERS

DIETARY FAT, DYSPEPSIA, DIARRHOEA, AND DIABETES - - - - - - *Peter Childs* 669

THE ORIGIN OF PHLEBOLITHS - - - - - - - - - - *Philip Shemilt* 695

FEMORO-FEMORAL CROSS-OVER GRAFTS - - - - - *R. Baker and E. J. C. Parker* 701

AXILLARY-FEMORAL BY-PASS GRAFTS IN THE TREATMENT OF AORTO-ILIAC OCCLUSIVE DISEASE *A. V. Pollock* 704

NEUROLOGICAL COMPLICATIONS OF RUPTURED ABDOMINAL AORTIC ANEURYSM *P. M. Bolton and L. H. Blumgart* 707

CRYOSURGERY IN THE TREATMENT OF HEAD AND NECK NEOPLASIA - - *H. B. Holden and P. McKelvie* 709

VENOUS STASIS AND DEEP-VEIN THROMBOSIS *A. N. Nicolaides, V. V. Kakkar, E. S. Field, and P. Fish* 713

ANATOMY OF THE EXTERNAL ANAL SPHINCTER - - - *Changyul Oh and Allan E. Kark* 717

LONG-TERM REVIEW OF FUNCTION FOLLOWING PULL-THROUGH OPERATIONS OF THE RECTUM *R. C. Bennett, E. S. R. Hughes, and A. M. Cuthbertson* 723

THE FATE AND FUNCTION OF THE THYROID REMNANT - - - *H. B. Young and N. Macleod* 726

EVALUATION OF BREAST TUMOUR SEX CHROMATIN (BARR BODY) AS AN INDEX OF SURVIVAL AND RESPONSE TO PITUITARY ABLATION - - - - - - - - - - *Michael Perry* 731

AMPUTATION NEUROMA OF THE GREAT AURICULAR NERVE AFTER PAROTIDECTOMY - *Michael Hobsley* 735

SHORT NOTES OF RARE OR OBSCURE CASES

ANTEROPOSITION OF THE PORTAL VEIN AND SPONTANEOUS PASSAGE OF GALL-STONES *Wilfred Brook and Michael Gardner* 737

MESENTERIC NEUROFIBROMATOSIS IN CHILDHOOD - - - *S. Cywes and Margaret J. Mayell* 739

CHRONIC SCHISTOSOMAL APPENDICITIS - - - - - *J. C. Voigt and M. M. Gregory* 743

FOREIGN-BODY PERFORATION OF A JEJUNAL DIVERTICULUM - - - - - *Malcolm Fidler* 744

NICKEL SENSITIVITY TO SURGICAL SKIN CLIPS - - - - - *Laurence F. Tinckler* 745

REVIEWS AND NOTICES OF BOOKS

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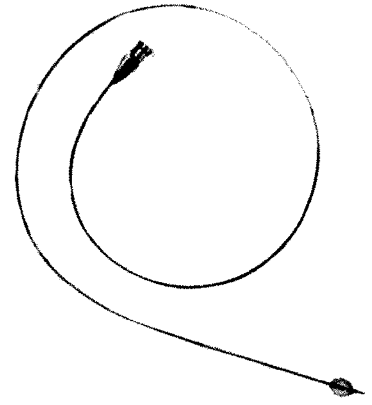

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	62	*Occlusion*
	12	*Arterial*
	82	*Dilation*
	91	*Double Lumen Balloon (Short Tip)*
	92	*Double Lumen Balloon (Whistle Tip)*
	22	*Irrigation*
	41	*Biliary Balloon Probe (Short Tip)*
	42	*Biliary Balloon Probe (Guide Tip)*
	A	*Revision Number*
	080	*Length in Centimeters*
	6F	*French Size of Catheter Body*

Edwards Model No.	*Max. Liq. Cap. (cc.)*	*Max. Air Cap. (cc.)*	*Balloon Diam. At Max. Liq. Cap. (mm)*
FOGARTY VENOUS THROMBECTOMY CATHETER			
32-080-6F	1.5	3	12
32-080-8F	2.25	4.5	14
32-080-8/10F*	4.5	8	19
FOGARTY OCCLUSION CATHETER			
62-080-8/14F*	10	20	28
FOGARTY ARTERIAL EMBOLECTOMY CATHETER			
12C-080-3F	0.2	0.6	
12C-080-4F	0.75	1.7	
12C-080-5F	1.5	3.0	
12C-080-6F	2.0	4.5	
12C-080-7F	2.5	5.0	
FOGARTY DILATION CATHETER			
82-080-5F	1.5	3.0	

*Size of uninflated balloon

Edwards Model No.	*Max. Liq. Cap. (cc.)*	*Max. Air Cap. (cc.)*	*Balloon Diam. At Max. Liq. Cap. (mm)*
EDWARDS DOUBLE LUMEN BALLOON CATHETER			
91A-060-5F (Short Tip)	1.25	2.0	11
91A-060-6F (Short Tip)	1.75	3.0	13
92-060-5F (Whistle Tip)	1.25	2.0	11
92-060-6F (Whistle Tip)	1.75	3.0	13
FOGARTY IRRIGATION CATHETER			
22C-023-10F (Venous)			
22C-080-4F (Arterial)			
22C-080-6F (Arterial)			
FOGARTY BILIARY BALLOON PROBE			
41-023-5F (Short Tip)	0.4	.8	9
41-023-6F (Short Tip)	1.25	2.5	13
42-023-5F (Guide Tip)	0.4	.8	9
42-023-6F (Guide Tip)	1.25	2.5	13

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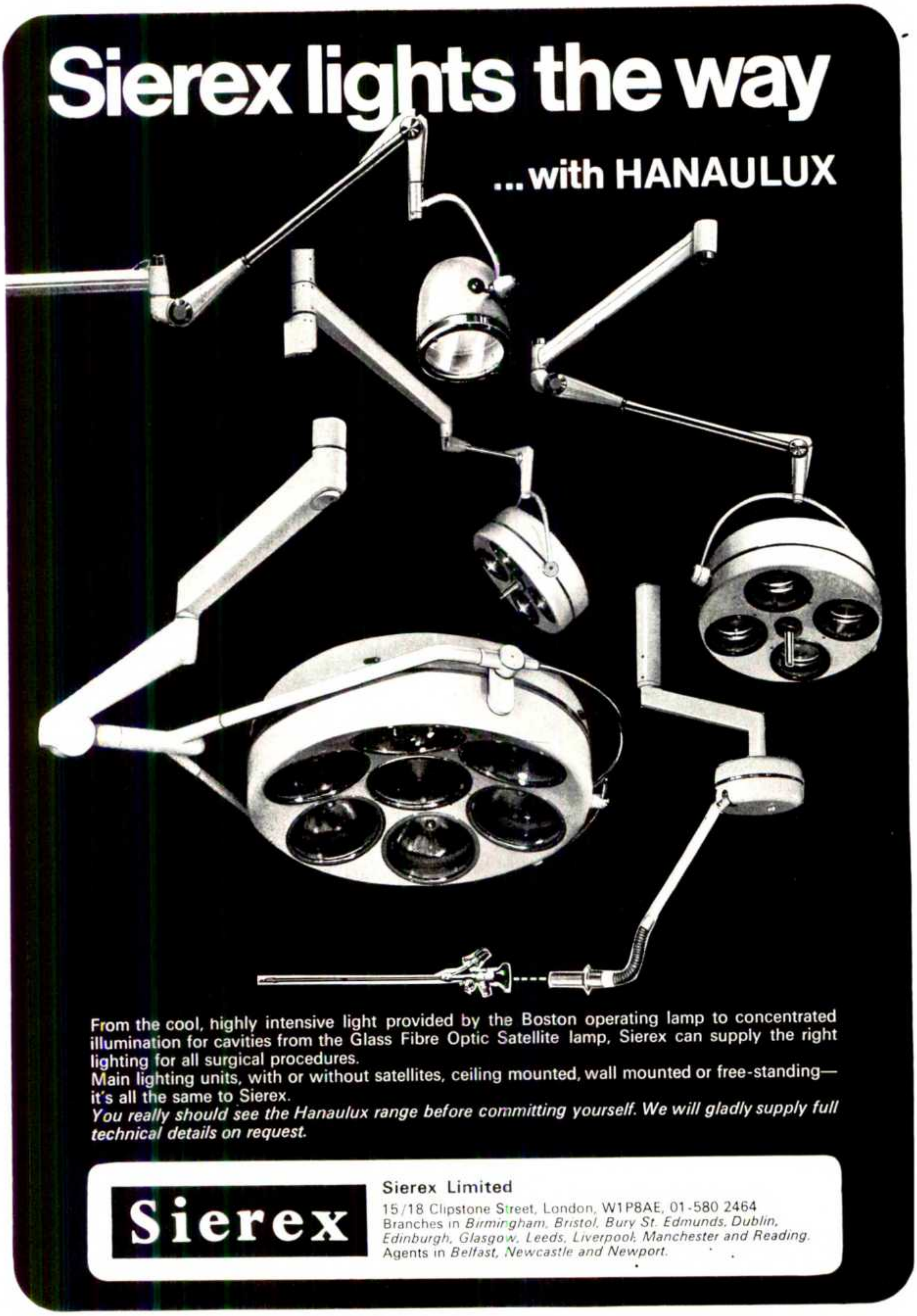

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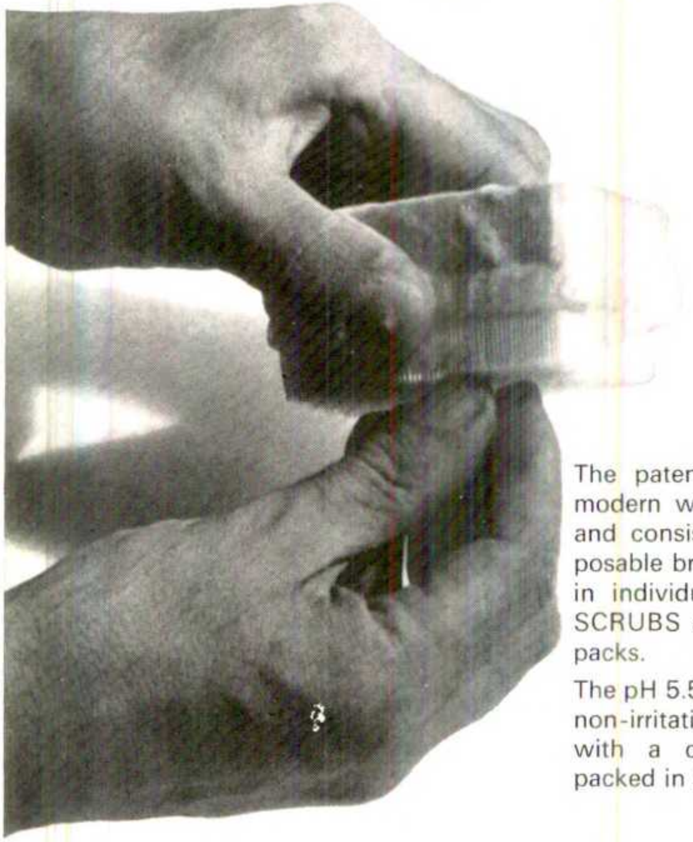

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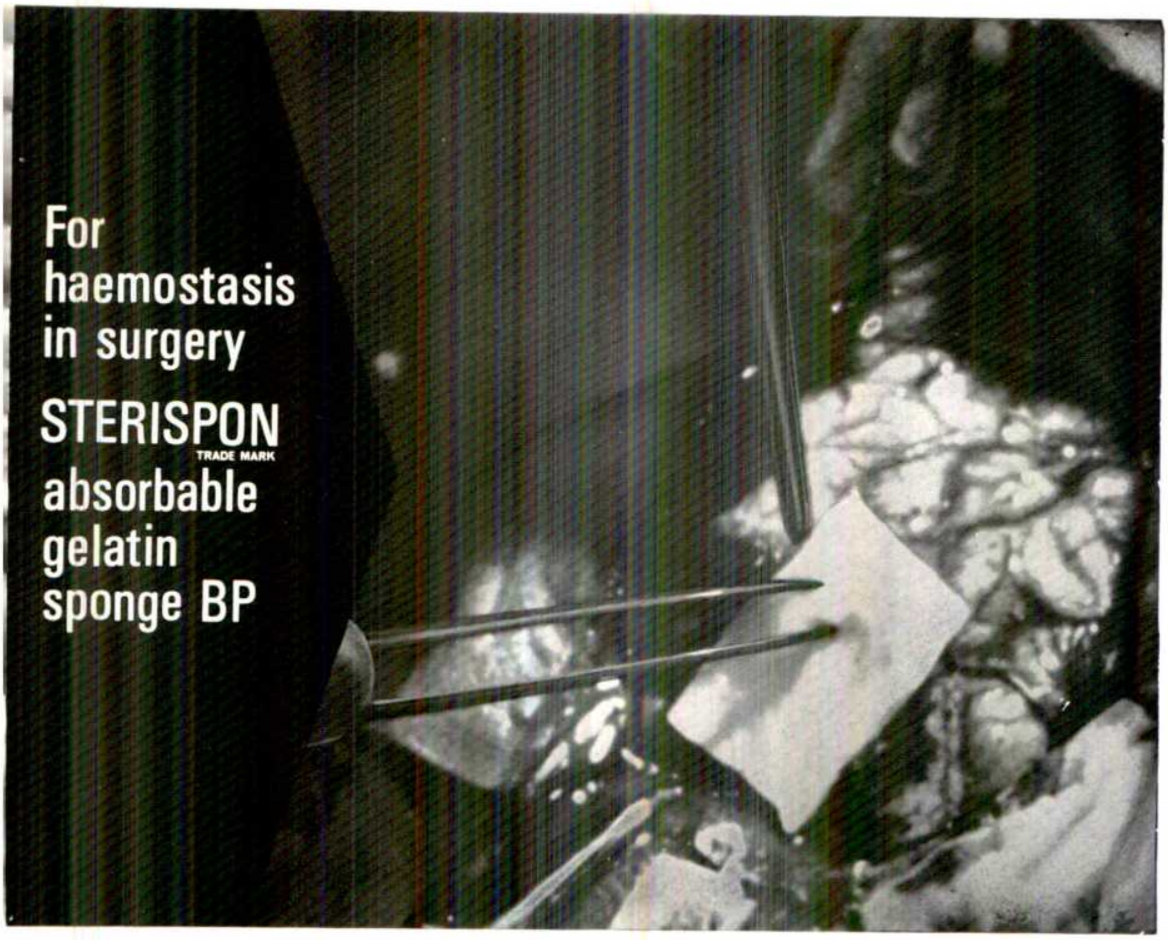

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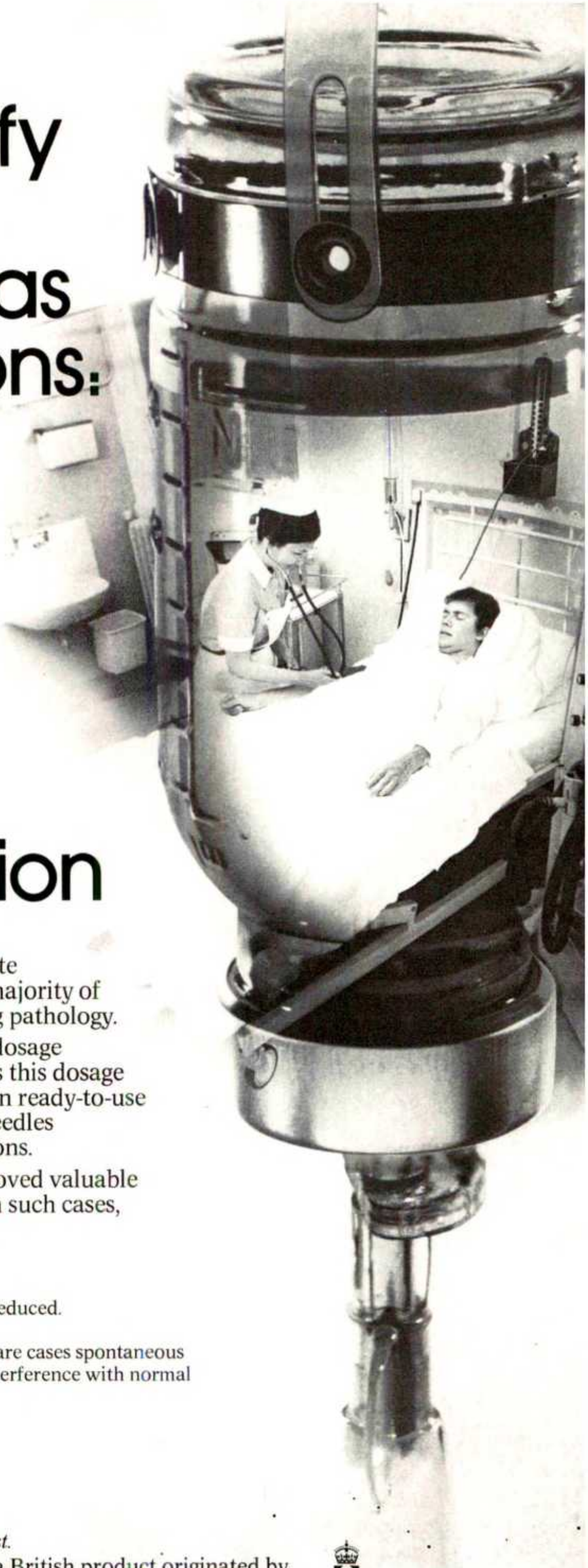

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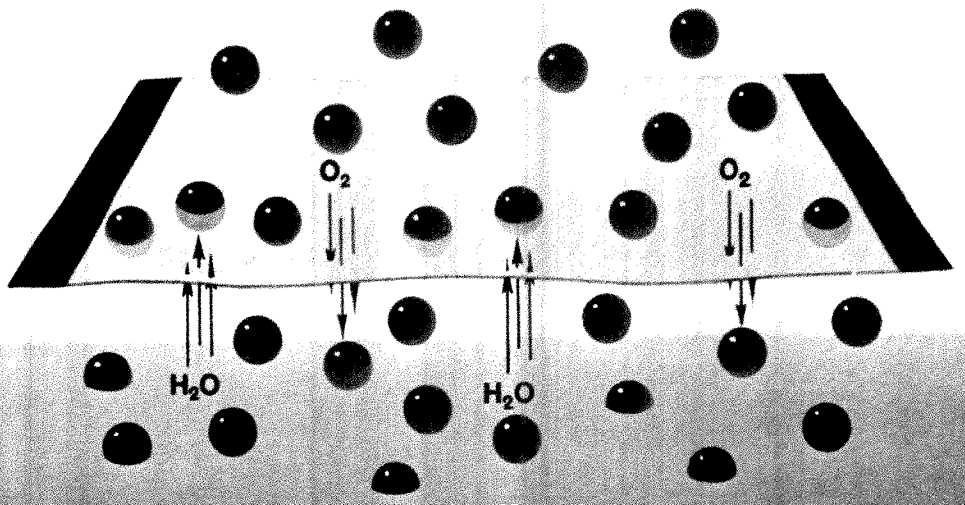

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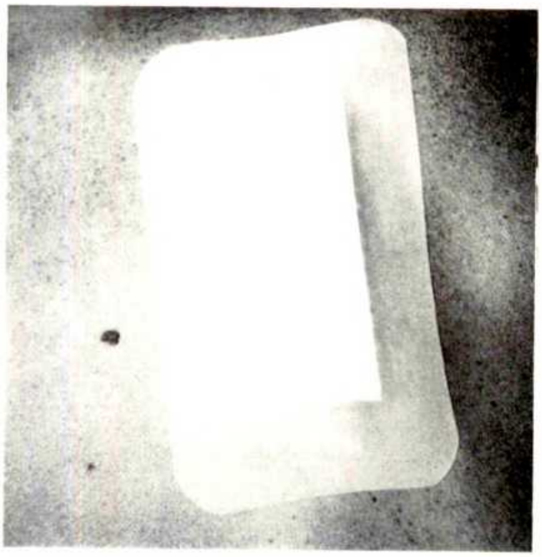

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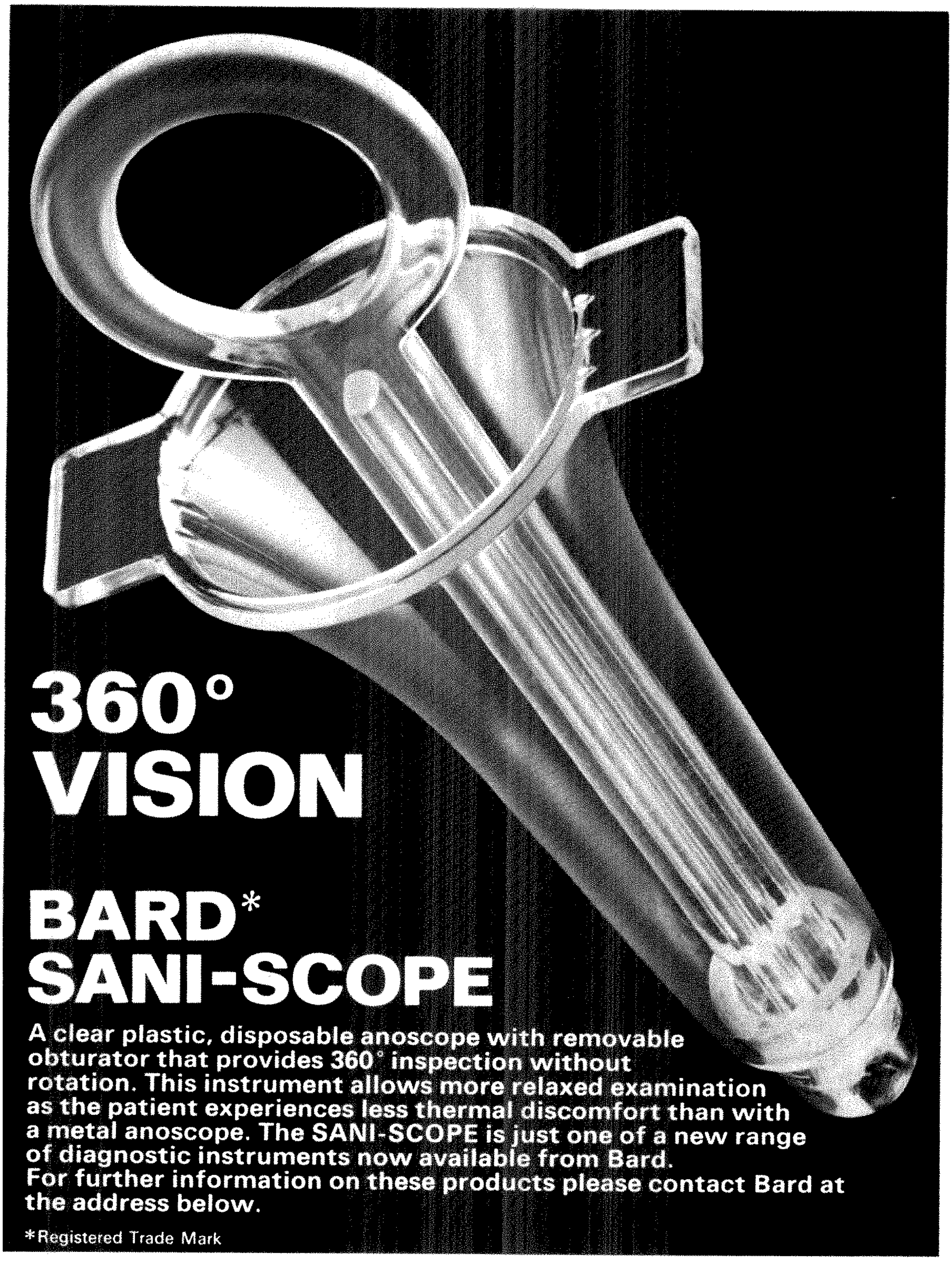

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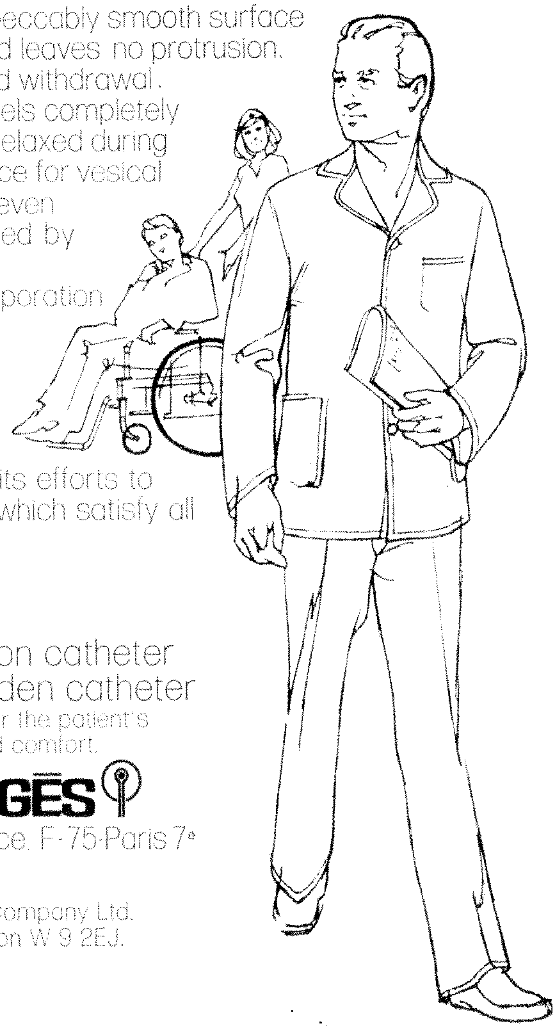

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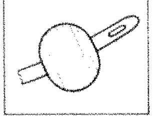

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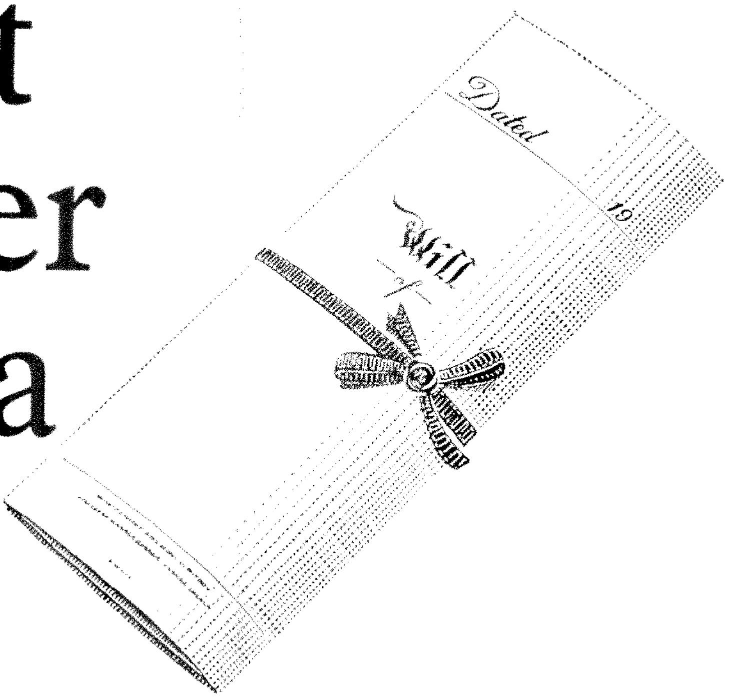

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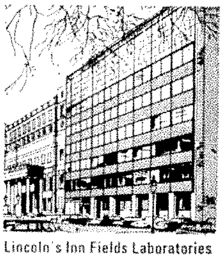

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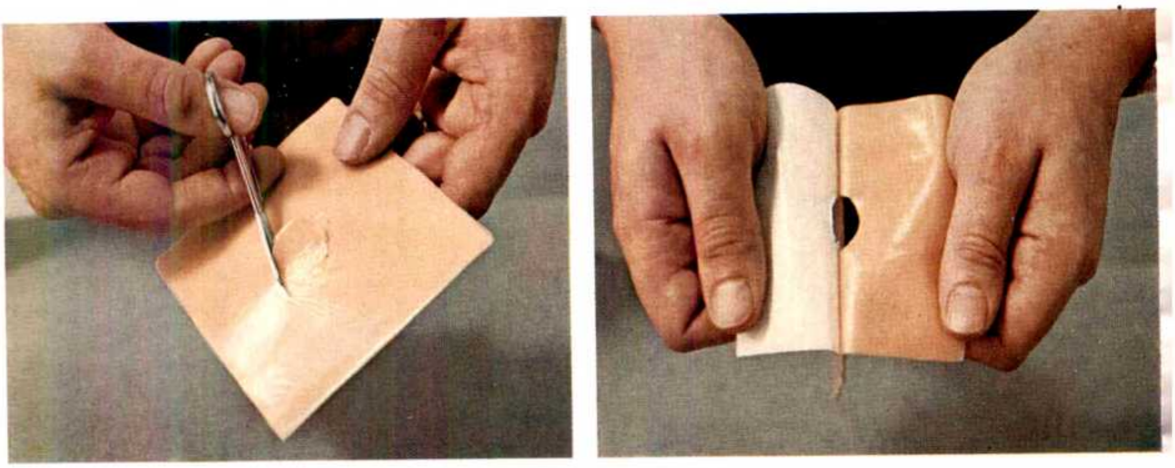

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Vol. 59 SEPTEMBER, 1972 No. 9

ORIGINAL PAPERS

DIETARY FAT, DYSPEPSIA, DIARRHOEA, AND DIABETES*

By PETER CHILDS

CONSULTANT SURGEON, PLYMOUTH GENERAL HOSPITAL, PLYMOUTH, DEVON

SUMMARY

This paper postulates that fat intolerance is a widespread metabolic disorder characterized by impairment of glucose tolerance caused by excess dietary fat intake, and cured in most cases by the fat-free diet as defined in this paper.

Fat intolerance may present as flatulent dyspepsia, surgical disease or disorder in the biliary tract, peptic ulceration, diarrhoea associated with spasm or diverticular disease of the colon or colitis, or as maturity-onset diabetes mellitus; one, two, or more of these syndromes may occur at the same or different times in the same patient. The dietary fat intake and the effect of the fat-free diet in each of these syndromes have been investigated, and the findings and their implications are discussed.

Treatment of disease and disorder in the biliary tract by sphincterotomy of the sphincter of Oddi in a series of 57 cases and of duodenal ulcer by pyloroplasty alone in 50 cases is reported. The results of treatment of duodenal ulcer by pyloroplasty alone in a series of 38 cases are compared with those after vagotomy and pyloroplasty in a similar series of 38 cases. Cure of peptic ulceration by pyloroplasty alone is reported, and vagotomy is considered to be unnecessary. The normal pylorus is defined, and the naked-eye appearances of the pylorus observed during 87 cholecystectomies are reported. The significance of these observations and of radiological abnormalities seen in routine barium-meal examinations of cases of disease or disorder in the biliary tract is discussed. Evidence is presented that the function of and pathological changes in the sphincter of Oddi and the pylorus are affected by the dietary fat intake and determine the absence or presence of abnormality in the biliary tract or of peptic ulceration respectively.

The clinical syndromes of fat-intolerant diarrhoea and its association with spasm of the colon, colitis, and diverticulitis, and of abdominal pain due to fat intolerance seen in a series of 17 children, are described as clinical entities.

The effect of the fat-free diet on glucose tolerance has been investigated in a series of 65 patients, and the significance of the increased tolerance observed has been assessed statistically. Four hundred and thirty-three glucose-tolerance tests have been performed to assess the change in glucose tolerance in 134 patients who had been on the fat-free diet for periods of 3 months to 2 years as treatment for dyspepsia due to disease or disorder of the biliary tract, peptic ulceration, diarrhoea associated with spasm of the colon, diverticulitis or colitis, obesity, and migraine. Among these patients were 23 who also suffered from diabetes mellitus. Cure of maturity-onset diabetes mellitus by the fat-free diet is reported, and evidence is produced to show that it is an acquired abnormality of the metabolism caused by excess dietary fat intake.

THE opportunity to study the natural history of dyspepsia and related conditions in the same patients over the past 20 years has produced evidence that dietary fat intake, dyspepsia, diarrhoea, and diabetes are closely interrelated. This paper presents the evidence and hypotheses which follow from this fact.

1. THE FAT-FREE DIET

The fat-free diet (F.F.D.) has been an essential part of the treatment (*Table I*). It was developed entirely from the experiences of patients, the foods and drinks forbidden being those which had caused symptoms or precipitated 'attacks' affecting the digestive system or the bowel. The diet has been called fat-free so that patients understood the purpose and avoided taking fat in any form that they could identify. It is not free of all fat; there is fat in lean meat, poultry, fish, bread, vegetables, and other foods. Patients must adhere strictly to the instructions; the total fat intake has to be decreased drastically, and vegetable fat cannot be added instead of animal fat.

---

* This paper embodies the substance of a lecture delivered to the Plymouth Medical Society in Plymouth, Devon, on 10 Dec., 1971.

Table I.—THE FAT-FREE DIET

You must NOT eat or drink any of the following, *or anything containing them*:

Butter
Cheese
Cream
Ordinary or Channel Island MILK

Margarine
YOLK of EGG
Salad cream or mayonnaise

Kipper, mackerel, or any fatty or 'oily' fish

Lard
Pork
Bacon
Ham
Sausage

Mutton
Liver
Suet

Pastry
Cake
Biscuits:
- sweet
- half-sweet
- Cornish wafer

Chocolate
Toffee

NEVER FRY   DO NOT use   Vegetable oil or fat
'edible' fat
olive oil

Look at list of 'contents' of every tin or packet: if they include fat, vegetable oil, or 'edible' fat—DO NOT USE

You CAN eat or drink the following:

FAT-FREE (or skimmed) MILK. *Beware*: NOT Low fat or MILK-FAT-FREE MILK

Alcohol
Cereals
Porridge

Bread, white or brown, fresh or toasted

Sugar
Boiled sweets

Jam
Honey
Marmalade

'Milk' puddings } made with fat-free milk
Junket }

WHITE of EGG

Custard made with egg-free powder and fat-free milk   Meringue

Biscuits: cracker or water

Potatoes: 'Boiled' 'Jacket', or mashed with fat-free milk: NOT   Roast, fried or chipped, or mashed or treated with butter

Lean beef
Lean lamb
Lean tongue

Lean breast and leg of poultry

White fish—boiled, grilled (no fat), or cooked in wine

Marmite
Bovril
Oxo

Fat-free soups
FRUIT: fresh or stewed

Mint sauce
Tomato ketchup
Fat-free pickles

YOU NEED NEVER BE HUNGRY:
YOU CAN EAT *FAT-FREE FOOD* whenever you feel the need

I have observed a large number of patients on this diet for many years; it has not deprived them of essential fatty acids. Davidson and Passmore (1969) pointed out that nature intended that human beings should obtain their requirements of vitamin D by irradiation of their skin. Fat-free milk provides calcium. Vitamin A is present in heart, kidney, halibut, and carotene in many fruits and vegetables. I have found no evidence that the F.F.D. is deficient, but any diet can be deficient if an inadequate quantity or variety is taken, and when necessary, for example, if a patient is aged and house-bound, appropriate supplements can be given. At all times, however, the need to keep the total fat intake at a minimum must be remembered.

I have estimated the change in the daily intake of fat and carbohydrate of patients who have adhered to the F.F.D.; the figures are approximate and are minimal values. The average daily decrease in dietary fat intake in 133 patients was at least 950 calories; the greater part of this was derived from cows' milk (53 per cent) and the pig (33 per cent (*Table II*). The daily intake of carbohydrate in 9 patients before and the change in carbohydrat intake after they started to take the F.F.D. ar shown in *Figs.* 1 and 2.

Table II.—AVERAGE DAILY DECREASE IN DIETARY FAT INTAKE IN 133 PATIENTS ON THE F.F.D.

FAT-CONTAINING FOODSTUFF NOT ALLOWED IN F.F.D.	DECREASE IN DIETARY FAT INTAKE (MINIMAL) (cal. per day)	PERCENTAGE TOTAL DECREASE IN DAILY DIETARY FAT (approx.	
Butter	265	28	53 per cent from cows' milk
Cheese	60	6	
Cream	45	5	
Milk (except fat-free milk)	135	14	
Margarine	85	9	
Eggs (yolk)	45	5	
Pork	60	6	33 per cent from the pig
Ham	25	3	
Sausages	40	4	
Bacon	90	9	
Lard	100	11	
Total	950	100	

II. DYSPEPSIA

A. Flatulent Dyspepsia.—Flatulent dyspepsia the commonest syndrome of indigestion, is characterized by a 'blown' or 'full feeling' in the epigastrium, discomfort not amounting to pain associated with belching, and 'acidity' or 'heartburn' These symptoms may be accompanied by attacks o nausea and vomiting of 'froth', mucus, and recently eaten food. Flatulent dyspepsia is due to fat intolerance; the symptoms are caused by eating too much fat and are cured by the F.F.D. Antacids are not necessary when a patient adheres to the F.F.D.

Flatulent dyspepsia may be the only complaint, or it may present as a 'back-cloth' to attacks of pain with or without jaundice, due to disease or disorder in the biliary tract; or in association with peptic ulceration, or radiological evidence of hiatus hernia or disease or disorder of the large bowel; or accompanying other conditions in which the dietary fat intake may or may not be recognized or significant.

B. The Biliary Tract.—

1. *The Evidence.*—The symptoms of flatulent dyspepsia are significant and are often identified as associated with dietary fat intake in 70 per cent of patients who suffer from disease or disorder of the biliary tract. Pain with or without jaundice and physical signs direct attention to the biliary tract.

In 1960 I reviewed 1699 'dyspeptic' patients seen and treated in the preceding 10 years. A clinical diagnosis of disease or disorder of the biliary tract was made in 721, and was confirmed by a cholecystogram or at operation in 379. However, the cholecystogram was normal in 342 cases in which the history and physical signs were identical with those in proved cases, i.e., typical 'biliary tract' pain, jaundice in some cases, and a palpable tender gall-bladder or guarding of muscles and tenderness in the right subcostal region. One hundred and seventy-eight of 532 'dyspeptic' patients seen during 1969–71 were proved to have gall-stones, while a cholecystogram showed no abnormality in 170 with identical symptoms and signs.

Patients suffering from disease or disorder of the biliary tract can, therefore, be grouped as follows:—

a. Those with proved gall-stones or a non-functioning gall-bladder.

b. Those in whom a cholecystogram, often repeatedly, is negative.

c. Those who have already undergone cholecystectomy.

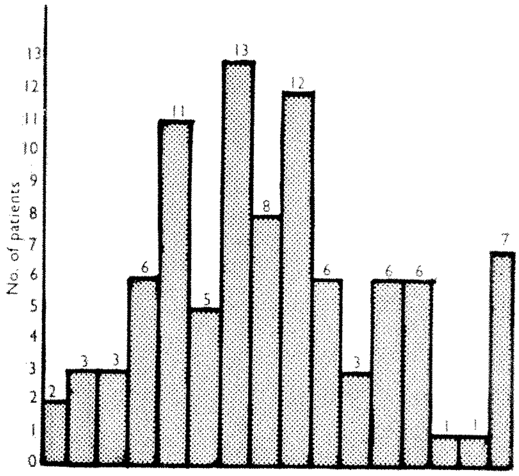

FIG. 1.—Daily carbohydrate intake in 93 patients before starting the F.F.D.

Table III.—RELATION OF DIETARY FAT INTAKE TO SYMPTOMS IN PATIENTS WITH PROVED GALL-STONES

Fat Intake and Symptoms		*No. of Cases*
On strictly F.F.D.		17
Symptom-free	11	
Suffered attacks of pain	6	
Not strictly on F.F.D.		22
Symptoms related to fat intake (2 had become pregnant)	22	
No longer dieting because they were symptom-free		11
Requiring urgent admission	4	
Symptom-free to present date	7	
Total No. of patients questioned		50

The results of inquiries in respect of dietary fat intake in each of these groups are given below.

a. Dietary fat intake in patients known to have gall-stones or a non-functioning gall-bladder.—Fifty patients who had been on the waiting list for cholecystectomy for more than 1 year who were known to have stones in or non-function of the gall-bladder had been instructed to adhere to the F.F.D. Only 6 patients who had adhered to the F.F.D. suffered from any symptoms; in 3 of these a distended mucocele of the gall-bladder was the cause of some discomfort. The F.F.D. cured all the symptoms in the remaining cases; there was only recurrence of symptoms when fat was taken (*Table III*). With few exceptions the F.F.D. cured symptoms in the patients who were suffering from gall-stones in or non-function of the gall-bladder. The exceptions have been: (i) when distension of a mucocele caused symptoms; (ii) a group of cases, to be considered in detail later, in which there was stenosis or hypertrophy of the sphincter of Oddi.

The series of patients on the waiting list did not include those for whom urgent or emergency admission was necessary. Those suffering from acute infection in the gall-bladder or common bile-duct or from persistent jaundice were not cured of symptoms by the F.F.D.; only 45 of 379 (12 per cent) cases with proved gall-stones required urgent or emergency operation.

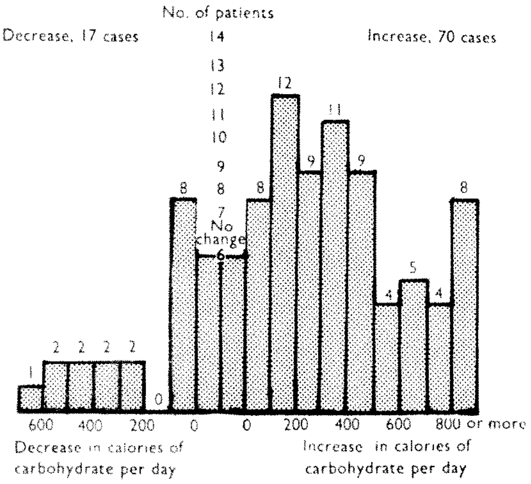

FIG. 2.—Change in carbohydrate intake on the F.F.D. in 93 patients.

b. Dietary fat intake in patients whose cholecystogram was negative.—The F.F.D. cured all the symptoms in the majority of these cases. It was impossible to carry out a statistically significant follow-up, but many patients have been followed for many years and the results have been as follows:—

i. Many patients who adhered to the F.F.D. or even to a low-fat intake remained symptom-free and did not require further investigation or treatment.

ii. Some patients who were symptom-free on the F.F.D. assumed that they were 'cured' and reverted to their former feeding habits. A small number remained symptom-free, but the majority of those who resumed their previous dietary fat intake have been seen and investigated again. In some, gall-stones had formed or the gall-bladder had become non-functioning, and these patients have undergone cholecystectomy or are on the waiting list. In others the cholecystogram was still negative and the patients have again become symptom-free on the F.F.D.

iii. Fourteen out of 170 patients whose cholecystogram was negative despite typical symptoms and signs of disease or disorder in the biliary tract did not respond to the F.F.D. There was stenosis or hypertrophy of the sphincter of Oddi in these cases; they are considered in more detail later.

iv. A small number of patients have eventually developed and undergone operation for a duodenal ulcer. This significant finding is considered later.

c. Dietary fat intake after cholecystectomy.—Follow-up of 43 patients who had undergone cholecystectomy more than 8 years earlier revealed that only 4 did not restrict their dietary fat intake.

Cholecystectomy had not cured fat intolerance. Some patients suffered the same symptoms of disease or disorder of the biliary tract after the gall-bladder and its contained stones had been removed as before the operation, but restriction of dietary fat intake relieved symptoms in 36 cases. In 3 cases sphincterotomy of the sphincter of Oddi was necessary; in only 1 of these was a stone present in the common bile-duct (*Table IV*).

Table IV.—RESULTS OF CHOLECYSTECTOMY AFTER MORE THAN 8 YEARS

Results	*No. of Cases*		
No further surgery required			40
Symptom-free. No fat restriction		4	
Symptom-free if fat intake restricted		19	
Same symptoms as before operation if fat taken	5		
Symptoms bad enough to require F.F.D.		13	
Additional symptom—diarrhoea	4		
Symptoms as before, with jaundice but cured (5 year—F.U., 8 year—F.U.)		2	
Now diabetic		2	
Further operation required			3
Stone impacted in ampulla of Vater		1	
Sphincterotomy of sphincter of Oddi		2	
Total cholecystectomies performed 1959–62			43

d. Sphincterotomy of the sphincter of Oddi (*see* Appendix 1).—Sphincterotomy of the sphincter of Oddi was performed in 57 patients. In 23 there were the usual indications for exploring the common bile-duct: jaundice at the time of operation in 15, a stone palpable in the common bile-duct in 1, during cholecystectomy after acute pancreatitis in 1, and the common bile-duct found to be dilated at time of cholecystectomy in 6. The duct was explored in 3 patients because the gall-bladder did not empty for 3–5 days after a cholecystogram. In 30 patients who all suffered from symptoms of disease or disorder of the biliary tract, pain had not been cured by the F.F.D.; the cholecystogram was positive in 6 and negative in 14, while cholecystectomy had been performed previously in 10.

Obstruction at the lower end of the common bile-duct owing to stenosis or to hypertrophy of the sphincter of Oddi was present in all the cases on which sphincterotomy was performed. In no patient could a urethral sound (Clutton's) larger than 6/10 be passed through the sphincter; in the majority even this size would not pass until sphincterotomy had been commenced. In 14 of the patients in whom the F.F.D. had not cured pain no stone, infection, or other abnormality than obstruction at the sphincter was found in the common bile-duct; in 6 of these cases section of the gall-bladder showed hypertrophy of the muscle layer and hyperplasia of the Rokitansky-Aschoff sinuses to be the only abnormalities. Stone was present in the common bile-duct in 13 of the 57 patients and was associated with jaundice in 6. Infection was present in the common bile-duct in 18 cases and was associated with stone in 7, with jaundice in 10, and with both stone and jaundice in 4.

Follow-up of 38 cases more than 1 year after sphincterotomy showed that pain was cured and patients were symptom-free if they restricted their dietary fat intake or, in some cases, adhered to the F.F.D. Only 2 patients were taking fat freely; 1 of these was symptom-free, while the other suffered occasional symptoms. In 2 cases there had been minor episodes of ascending cholangitis with fever and jaundice. In 1 of these who was explored again the sphincter had not stenosed; a 16/20 urethral sound (Clutton's) passed easily but culture of the common bile-duct bile grew *Escherichia coli*.

2. *Discussion*.—

a. 'Biliary tract' pain.—Acute attacks of pain related to disease or disorder in the biliary tract are precipitated by a specific and excessive ingestion of fat, usually after a period of prolonged high dietary fat intake. The latter may itself cause pain of more gradual onset, but such a pain may be associated with a 'hormonal' episode such as menstruation or 'taking the Pill', or the first attack of 'biliary colic' may occur in relation to pregnancy, most commonly at 6 months or soon after delivery. 'Hormonal' episodes of pain occur when the dietary fat intake has been high for some time. The F.F.D. removes the stimulus which causes 'biliary tract' pain. As shown above, patients suffering from 'biliary tract' pain have been cured by the F.F.D. unless irreversible changes have occurred in the sphincter of Oddi. If flatulent dyspepsia has been present in these patients this too has been cured by the F.F.D.

Colic due to a gall-stone is relatively uncommon. Mobile stones in the gall-bladder cannot cause pain; most gall-bladders which contain stones communicate freely with the common bile-duct and there is no evidence that stones repeatedly become impacted and released. A gall-stone can impact in the cystic duct and the gall-bladder will initially undergo spasmodic contractions; once these have ceased the gall-bladder becomes 'non-functioning' and pain is then due to distension or consequent acute infection of the gall-bladder. A stone in the common bile-duct may cause pain when impacted at the lower end of the duct, but most stones move freely up and down the duct. Stones even when present in the gall-bladder or common bile-duct cannot cause pain in the majority of cases, nor is stimulation of pain by dietary fat and relief by the F.F.D. compatible with the theory that stones are the usual cause of biliary tract pain.

The occurrence of typical 'biliary colic' in so many cases in which the cholecystogram is negative has been stressed earlier. Cronin and Middleton (1963) similarly concluded that gall-stones or cholecystitis could not explain the symptoms in such patients. The F.F.D. cures the symptoms in most of these cases but if it does not sphincterotomy of the sphincter of Oddi does so. The same 'biliary tract' pain which occurs in the absence of the gall-bladder as was present before cholecystectomy is cured by the F.F.D. in most cases and by sphincterotomy of the sphincter of Oddi when the F.F.D. fails. Cattell, Colcock, and Pollack (1962) recognized that obstruction of the common bile-duct occurred at the sphincter of Oddi, either as the only demonstrable change in the entire biliary tract or complicating other conditions in the common bile-duct or gall-bladder. They found that sphincterotomy was necessary to cure symptoms in selected cases. They accepted that in long-standing cases chronic spasm could lead to fibrotic stenosis of the sphincter, but concluded that fibrosis was a more common cause of obstruction than spasm. They used intravenous cholangiography to diagnose obstruction. I have found that failure to cure symptoms by the F.F.D. is a certain indication of the need for sphincterotomy.

Ivy, Voegtlin, and Greengard (1933) showed that, provided the gall-bladder was concurrently excited to contract, 'gall-bladder pain' was experienced in a normal human subject when there was spastic obstruction of the intramural portion of the common bile-duct. Ivy (1947) found no evidence of sphincters in the biliary tract other than the sphincter of Oddi; the latter when in spasm could prevent evacuation of the gall-bladder. Bergh and Layne (1938) caused 'biliary colic' by distension of the bile-duct, and Bergh (1948) found that an irritable sphincter could result in hypertrophy of the sphincter muscle.

It is primarily the function of the sphincter of Oddi which determines whether normal or abnormal conditions exist in the biliary tract; the dietary fat intake plays a major part in determining whether the sphincter functions normally or not. In the early stages of disease or disorder of the biliary tract isolated episodes of spasm of the sphincter of Oddi 'triggered' by an excess of dietary fat intake result in an 'attack' of 'biliary tract' pain. Spasm is reversible and the F.F.D. prevents all symptoms. When hypertrophy or fibrosis of the sphincter has occurred owing to repeated episodes of acute spasm or to chronic 'subclinical spasm' caused by a prolonged high dietary fat intake, pain is not relieved by the F.F.D. and sphincterotomy is necessary. This hypothesis that spasm, hypertrophy, or fibrosis of the sphincter of Oddi causes obstruction at the lower end of the common bile-duct accounts for the incidence of infection and stone formation in the common bile-duct. It explains inadequate, incomplete, and sometimes little or no emptying of the gall-bladder, 'layering' of bile, stone formation, and infection in the gall-bladder. It is consistent with the clinical finding during an acute attack of 'biliary colic' of a tender, palpable, distended gall-bladder which is no longer palpable once the acute pain has ceased. Such cases, often incorrectly labelled 'acute cholecystitis', show no pyrexia or rise in the total or differential white blood count. If a cholecystogram is performed after the attack a normally functioning gall-bladder is shown; if stones are present in such a gall-bladder and cholecystectomy is performed the gall-bladder wall is found to be normal on section or may show hypertrophy of muscle and hyperplasia of Rokitansky-Aschoff sinuses as the only abnormalities. The latter, noted earlier in the series of sphincterotomies, must be the consequence of prolonged sphincter spasm, hypertrophy, or fibrosis which makes emptying of the gall-bladder more difficult.

The gall-bladder cannot empty during the acute phase of sphincter spasm. The dietary fat stimulus which caused the spasm may also increase the flow of liver bile, thereby increasing distension of the obstructed bile-duct and gall-bladder. If the flow of bile is great enough contraction of the gall-bladder, though it cannot empty the gall-bladder, may increase pressure in the common bile-duct sufficiently partially to overcome the spastic sphincter so that bile escapes into the duodenum, producing the copious bile vomit which sometimes occurs at the height of the pain.

The constant severe central epigastric pain which radiates outwards to the right and sometimes to the left subcostal regions through to the back and interscapular region must be caused by distension of the whole biliary duct system. Colicky pain spreading from the right hypochondrium must be due to contractions of the gall-bladder attempting to empty into an already distended and obstructed common bile-duct. It is impossible to say how much pain is due to the spastic sphincter itself.

b. Jaundice.—Approximately one-third of all the patients who suffered from gall-stones became jaundiced at some time (*Table V*). Jaundice occurred when the common bile-duct was filled with stones and debris or in association with cholangitis with or without stones in the common bile-duct, but it was seen most often after an 'attack' of 'biliary colic'. In some cases stone was present in a normal or non-functioning gall-bladder but there was no stone or infection in the common bile-duct itself. In other cases a cholecystogram performed after the jaundice had cleared was normal. In a small number of cases in which jaundice had persisted for longer than usual exploration of the common bile-duct revealed no abnormality apart from some hypertrophy of the sphincter of Oddi. In 1 case not even this abnormality was present.

Table V.—INCIDENCE OF JAUNDICE IN PATIENTS WITH PROVED GALL-STONES, 1950–9

Incidence of Jaundice	*No. of Cases*		
A. The whole series:			
Total No. with proved gall-stones			379
Not jaundiced, and no relevant history of jaundice		266	
Actually jaundiced when seen		36	
With history of associated 'biliary colic'	22		
Painless jaundice	13		
Associated with rigors	1		
Relevant history of jaundice, not jaundiced when seen		77	
Total No. jaundiced, or with relevant history of jaundice			113
B. Patients who had actually undergone operation:			
Total No. who had undergone operation			228
Jaundice present in, or relevant history of jaundice			74
C.B.D. explored in		30	
Stones found in C.B.D.	16		
No stones in C.B.D.	14		
Stones removed from C.B.D. at later operation		6	
C.B.D. explored at first operation	1		
C.B.D. not explored at first operation	5		
Total No. of cases in which stone found in C.B.D.			22
Jaundice present, or relevant history of jaundice in absence of stone in C.B.D.			52

The clinical presentation of the jaundice in these cases was always the same. A fat-containing meal had been eaten, and some hours later the patient experienced a severe attack of central epigastric pain which often radiated to the interscapular area and in some cases to the right and left subcostal regions. It was a constant pain, becoming more severe at times. In some patients there was also aching or severe pain under the right costal margin, and colicky pain radiated from the gall-bladder area. While the pain was severe some patients vomited a copious, watery, yellow or green, bitter fluid. The pain ceased as suddenly as it commenced and the patient apparently recovered completely. Twenty-four to 48 hours after the pain had ceased symptomless jaundice developed. There was darkening of urine only in some patients, the conjunctivae became icteric in others, while the jaundice sometimes involved the whole body. It was transient, persisting only for a day or two, or became widespread and remained for a week or longer, but it faded without any treatment other than the F.F.D.

This transient jaundice, so often called 'obstructive' and raising fears of a stone in the common bile-duct, could not be caused by extrahepatic obstruction. It occurred when there were no stones in the common bile-duct (*Table V, B*), and it was seen when there were no stones in the gall-bladder and the cholecystogram performed after the jaundice had cleared was normal. It was symptomless and painless, commencing only when the patient had recovered from the acute 'attack' and the pain; it developed after any spasm or potential obstruction had subsided completely, and at the height of the most severe pain there was often evidence in the form of copious 'bile' vomit that bile was escaping from the common bile-duct. No pyrexia or rise in the total or differential W.B.C. or other evidence of infection accompanied the jaundice. This jaundice like the pain was 'triggered' by a high dietary fat intake, and when the jaundice was recurrent some patients identified a particular food which precipitated it. Laboratory tests indicate that the jaundice is obstructive in type but that bile is present in the stools. It may be that back-pressure from the distended bile-ducts transmitted to the liver is responsible, but this can act only for the duration of pain and part of the cause of the distension must be continued formation of bile. It is possible that the fat which stimulates the pain may also cause the jaundice. As it is certain that the jaundice will clear operation is not performed while it is present and liver biopsy cannot be obtained.

The disturbed metabolism due to excess dietary fat intake (*see below*) may be the cause of jaundice.

C. Peptic Ulceration.—

1. *The Evidence.*—

a. Pyloroplasty alone as the surgical treatment of duodenal and gastric ulcer (*see* Appendix 2).—Capper (1967) showed that gastric ulcers healed after pyloroplasty because 'a wide, incompetent pylorus does not permit a narrow, forceful regurgitation' of duodenal contents into the stomach. I have since 1967 used pyloroplasty alone in the surgical treatment of peptic ulceration and related conditions because I concluded that if the duodenal contents could 'squirt' one way gastric contents could 'squirt' in the opposite direction.

Pyloroplasty alone was followed by healing of both duodenal and gastric ulcers (*Table VI*). Failure only occurred when the pyloroplasty did not remain widely open, and the ulcers healed after a second pyloroplasty; in only 1 case has a third pyloroplasty been necessary and this has proved successful. The causes of failure have been identified. In 1 case two layers of sutures had been inserted; the second layer inverted the first layer too much and the patient's stomach only emptied when she was lying on her right side. In 2 cases scar tissue formed as a duodenal ulcer healed and constricted the pyloroplasty. In the other cases which required a second operation serum-proofed silk sutures had caused excessive tissue reaction and constricted the lumen by massive fibrosis and adhesions.

Table VI.—RESULTS OF PYLOROPLASTY ALONE AS THE SURGICAL TREATMENT OF DUODENAL AND GASTRIC ULCER

REASON FOR OPERATION	NO. OF CASES	REQUIRED SECOND OPERATION	FOLLOWED UP FOR MORE THAN 1 YEAR	'CURED'	RECURRENT SYMPTOMS		ALSO REQUIRED OPERATION ON BILIARY TRACT
					Ulcer	Other	
Duodenal ulcer	50	7	38	34	1	3	7
Gastric ulcer	18	2	15	15	0	0	0
Prepyloric muscle hypertrophy	14	1	13	11	1	1	7
Total	82	10	66	60	2	4	14

Table VII.—RESULTS OF VAGOTOMY AND PYLOROPLASTY COMPARED WITH THOSE OF PYLOROPLASTY ALONE AS THE SURGICAL TREATMENT OF DUODENAL ULCER

TYPE OF OPERATION	NO. OF CASES FOLLOWED UP FOR MORE THAN 1 YEAR	NO. OF CASES 'CURED'	RECURRENT SYMPTOMS		EPISODIC DIARRHOEA
			Certainly due to Ulcer	Possibly due to Other Causes	
Vagotomy and pyloroplasty (operations performed 1964–7)	38	29	6	3	6
Pyloroplasty alone (operations performed 1968–70)	38	34 (4 cases required second operation)	1	3	0

Symptoms of recurrent ulceration have always developed within 3 months of the pyloroplasty in the cases which failed. I have used a single layer of Dexon to close the pyloroplasty in 30 cases during the past 18 months, and there has been no symptom of failure in any of these cases.

b. Comparison between vagotomy and pyloroplasty, and pyloroplasty alone as the surgical treatment of duodenal ulcer. The results of treatment of duodenal ulcer by pyloroplasty only in 38 cases followed for more than 1 year, and by vagotomy and pyloroplasty in 38 cases followed for more than 4 years have been compared (*Table VII*).

Over all, 34 of 38 patients on whom pyloroplasty only was performed and 29 of 38 patients who underwent vagotomy and pyloroplasty are certainly cured of ulcer. Four of the 'pyloroplasty only' series did require a second operation because of technical failure of their first operation. It is likely that the cause of failure in the 'vagotomy and pyloroplasty' series was due, as in the 'pyloroplasty only' series, to technical failure of the pyloroplasty. Within the past year I have operated on 2 failed cases of the 'vagotomy and pyloroplasty' series; in both, the first pyloroplasty which had been sutured with serum-proofed silk had become stenosed, and I have performed a new pyloroplasty using Dexon and a single layer of sutures. There is a significant difference between the two series in the incidence of episodic diarrhoea, which occurs only in those patients who have suffered a vagotomy. The evidence from my preliminary results is that vagotomy is not necessary to cure an ulcer and is detrimental to the patient.

Table VIII.—COMPARISON OF CASES TREATED BY VAGOTOMY AND PYLOROPLASTY AND THOSE TREATED BY PYLOROPLASTY ALONE FOR DUODENAL ULCER

TYPE OF OPERATION	TOTAL NO. OF CASES	SEX		HISTORY OF MELAENA AT HAEMATEMESIS	HISTORY OF PERFORATION	HISTORY OF FAT INTOLERANCE		ALSO REQUIRED OPERATION ON BILIARY TRACT			
		Male	Female			Before Operation	After Operation	Earlier	At Same Time	Later	Total
Vagotomy and pyloroplasty (operations performed 1964–7)	38	31	7	14	5	22	20	1	2	2	5*
Pyloroplasty alone (operations performed 1968–71)	50	37	13	16	3	26	No figure available. Low fat diet or F.F.D. routinely recommended	1	5	1	7†

* Cholecystectomy, 2 cases; cholecystostomy, 2 cases; sphincterotomy, 1 case.

† Cholecystectomy and sphincterotomy, 3 cases; cholecystostomy, 2 cases; sphincterotomy, 2 cases.

Table IX.—RESULTS OF VAGOTOMY AND PYLOROPLASTY FOR DUODENAL ULCER AFTER 4 OR MORE YEARS WITH REFERENCE TO FAT INTOLERANCE

Results	*No. of Cases*	
'Cured'		29
Symptom-free. No dietary restriction of any kind	9	
Symptom-free if avoids 'fats and fries'—less or	8	
more	5	
Symptom-free on low-fat diet	2	
Recurrent symptoms required treatment and cured by F.F.D.	3	
Required operation on the biliary tract	2	
'Not cured'		9
Undoubtedly recurrent ulceration	6	
Equivocal symptoms	3	
Total (operations performed 1964–7)		38

c. Fat intolerance in duodenal ulcer patients.—The patients in both series of duodenal ulcer cases who suffered from symptoms 'possibly due to other causes' were all fat intolerant (*Table VII*); they presented symptoms of flatulent dyspepsia, with pain of 'biliary tract' type in some cases. The clinical features in the two series are compared in *Table VIII*. It had been found to be wise or even essential to restrict the dietary fat intake after pyloroplasty for duodenal ulcer. Follow-up of patients who had undergone vagotomy and pyloroplasty for duodenal ulcer showed that a similar restriction had been found necessary (*Table IX*). The incidence of fat intolerance and disease or disorder of the biliary tract in patients suffering from duodenal ulcer is significant.

d. Observations on the normal pylorus and changes which occur in it.—From 1969 to 1971 I observed during 87 cholecystectomies the state of the oesophageal hiatus, prepyloric muscle, and pyloric aperture or ring. The normal pyloric aperture relaxed to a lumen of 2 cm. diameter; proximally the antrum and distally the duodenal cap relaxed to 3–4 cm. diameter; only at the level of the pyloric ring, at the pyloric aperture itself, was there any decrease in diameter of the lumen from the antrum to the duodenum; in the relaxed state there was no 'pyloric canal'. Palpation of the stomach wall in the prepyloric region in these cases revealed little or no increase in the thickness of the muscle layer compared with the pars media of the stomach (*Fig. 3*).

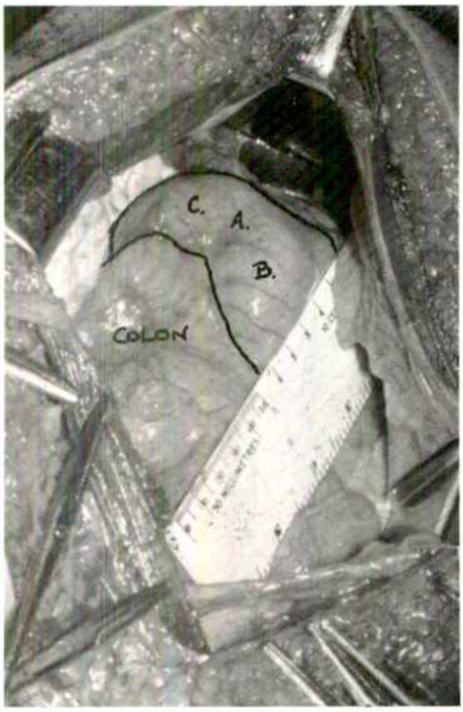

FIG. 3.—Normal pylorus in relaxed state. A, Slight constriction at relaxed pyloric ring, with 2-cm. diameter pyloric aperture. B, Immediate prepyloric region relaxed to 4 cm. and more, with no thickening of muscle in its wall. C, Relaxed duodenal cap.

There was no apparent enlargement of the oesophageal hiatus in 27 of the 87 cases, but only in 9 of these cases was there also relaxation of the pyloric ring to 2 cm. with no evidence of thickening of the prepyloric muscle. In 28 cases the pyloric ring relaxed to 2 cm. with no evidence of hypertrophy of the prepyloric muscle, but in 59 cases there was restriction of relaxation of the pyloric ring, and the greater the restriction the more marked was palpable thickening of the prepyloric muscle. All stages were found, from the normal pylorus, through increasing extent of restricted relaxation of the pyloric aperture and hypertrophy of the prepyloric muscle, to 2 cases with a duodenal ulcer crater present, gross narrowing of the pyloric ring, and marked prepyloric muscle hypertrophy with formation of a 'pyloric canal' just proximal to the ring (*Tables X, XI*).

Table X.—OBSERVATIONS OF PREPYLORIC MUSCLE HYPERTROPHY MADE DURING 87 CHOLECYSTECTOMIES (MID-1969 TO MID-1971)

DEGREE OF PREPYLORIC MUSCLE HYPERTROPHY	NO. OF CASES	PYLORIC APERTURE RELAXED TO:—			
		2 cm. Diameter	1–2 cm. Diameter	1 cm. Diameter	< 1 cm. Diameter
None	32	28	4	—	—
Less than 50 per cent increase	25*	7	10	5	1
50 per cent increase	19†	2	3	7	6
100 per cent increase or more	8	0	0	4	4
Not recorded	3	2	1	—	—

* 2 cases were not recorded.
† 1 case was not recorded.

Table XI.—OBSERVATIONS OF DUODENAL ULCERATION MADE DURING 87 CHOLECYSTECTOMIES (MID-1969 TO MID-1971)

DEGREE OF DUODENAL ULCERATION	NO. OF CASES	PYLORIC APERTURE RELAXED TO:—				ASSESSMENT OF PREPYLORIC MUSCLE HYPERTROPHY			
		2 cm. Diameter	1–2 cm. Diameter	1 cm. Diameter	< 1 cm. Diameter	None	< 50 per cent Increase	50 per cent Increase	100 per cent or more Increase
Active duodenal ulcer	2	0	0	0	2	0	0	0	2
Duodenal ulcer scar with marked pyloric stenosis	2	0	0	0	2	0	0	0	2
Duodenal ulcer scar	6	2*	0	3	1	0	2	3	1
Total	10	2	0	3	5	0	2	3	5

* Some thickening of the pyloric ring.

e. Pylorospasm seen in 'fat-intolerant' patients.—Two 'fat-intolerant' patients operated upon in the past year had suffered from flatulent dyspepsia with epigastric pain, belching, acidity, and nausea and vomiting of bile during attacks. The cholecystograms were normal in both cases. A barium-meal examination was normal in the woman but in the man showed deformity of chronic or recurring duodenal ulceration. The patients were symptom-free while they adhered to the F.F.D. At laparotomy the gall-bladder, common bile-duct, and pancreas were normal in both cases. The pylorus appeared to be normal most of the time; the pyloric aperture relaxed to 2 cm. diameter, with no thickening of the prepyloric muscle, and there was no evidence of past or present peptic ulceration. However, in both patients spasms lasting for a minute or more at a time occurred intermittently, converting the pyloric antrum, prepyloric region, pyloric ring, and the duodenal cap into a rocky-hard mass which whitened with contraction. When the spasm ceased the whole area again relaxed widely and appeared to be normal. No operative procedure was performed. The patients were discharged on the F.F.D. more than 1 year ago and have remained symptom-free while on the F.F.D., but since the woman has been using non-milk-fat milk she has had indigestion and pain.

f. Barium-meal examination in biliary tract Disease.—During the survey of dyspeptic patients seen and treated during the years 1950–9 I noted the frequency of evidence in routine barium-meal examinations in patients suffering from disease or disorder of the biliary tract of abnormality at the oesophageal hiatus and the pylorus. Hiatus hernia was demonstrated in more than 11 per cent of 379 patients proved to have gall-stones, while abnormality was demonstrated at the pylorus in 17 per cent of 379 cases with proved gall-stones, and in 15 per cent of 342 cases diagnosed clinically to have gall-stones but in whom the cholecystogram was negative (*Table XII*).

Table XII.—BARIUM-MEAL EXAMINATION IN BILIARY TRACT DISEASE

TYPE OF BILIARY TRACT DISEASES	NO. OF CASES	PREOPERATIVE BARIUM MEAL		DEFORMITY OF DUODENAL CAP	PYLOROSPASM	DUODENAL ULCER
		No.	Percentage Abnormal			
Non-malignant surgical disease of biliary tract	379	202	17	23	12	1
Clinical diagnosis of surgical disease of biliary tract: cholecystogram negative	342	342	15	29	16	4
Total	721	544	17	52	38	5

2. *Discussion*.—The normal pylorus does not control emptying of the stomach but prevents reflux during duodenal cap systole (Martin and Burden, 1928; Johnson, 1961). Keet (1962) showed that in a relaxed state in normal persons the pyloric aperture was 1·5–2·0 cm. in diameter, while the canalis egestorius was 4–8 cm. diameter when completely relaxed. My own observations are in agreement with

those of Keet that the normal relaxed pylorus is one in which there is no increase in thickness of the circular muscle layer in the prepyloric region as it nears the pyloric ring and that the ring itself relaxes to give an aperture of 2 cm. diameter. Any increase in thickness of the circular muscle layer in the prepyloric region as compared with the pars media and any restriction of relaxation of the pyloric ring itself must be pathological.

When dyspeptic patients have been followed over many years successive barium-meal examinations have shown a progression of changes from irritability of the duodenal cap or intermittent pylorospasm in the early years, through a stage of more persistent spasm, sometimes with initial delay in the commencement of emptying of the stomach, to a stage of deformity of the duodenal cap, perhaps with prepyloric deformity but with no ulcer crater, finally to the demonstration of an ulcer crater. Many of these patients have suffered from flatulent dyspepsia and complained that 'fats' aggravated or precipitated their symptoms. I have been convinced in many cases that the symptoms were related to the biliary tract despite repeated negative cholecystograms. Eventually, however, duodenal ulceration has been proved, and at operation a definite feature has always been marked hypertrophy of the prepyloric muscle.

I have no statistically significant series of patients suffering from peptic ulceration who have been treated by the fat-free diet, but the results in cases so treated have been consistent with the thesis that excess dietary fat is an important aetiological factor in peptic ulceration. In early cases pylorospasm is still reversible and symptoms have been completely controlled by the F.F.D., as in the 2 cases cited in (*e*) above. In established cases in which prepyloric muscle hypertrophy, fibrosis, and even active ulceration have been present the appetite has been regained and dyspeptic symptoms other than pain have been relieved by the F.F.D. during the waiting period before operation.

An association between dietary fat intake and disease or disorder of the biliary tract is generally accepted. I have found an undoubted association between biliary tract abnormality and peptic ulceration. Twelve of 76 patients who underwent operation for duodenal ulcer also required operation on the biliary tract (*Table VIII*) and 6 of 57 patients who required sphincterotomy of the sphincter of Oddi also suffered from duodenal ulcer, while gross prepyloric muscle hypertrophy required operation in 5 others. The incidence of fat intolerance in cases of duodenal ulceration (*Table VIII*), the frequency of changes at the pylorus, limitation of relaxation of the pyloric ring, and hypertrophy of prepyloric circular muscle found in patients who have proved gallstones (*Tables X, XI*), and the incidence of radiological evidence of abnormality at the pylorus in cases of disease or disorder in the biliary tract (*Table XII*) make it difficult to believe that there is not a close link between biliary tract and pyloric disorders, and I suggest that the dietary fat intake is the link between the two parts of the digestive system.

Just as it causes spasm of the sphincter of Oddi I believe that an excess of dietary fat intake can stimulate pylorospasm. Crohn and Reiss (1920) showed that milk was a strong acid-producing stimulant and was only slowly emptied through the pylorus, and that the combination of milk and egg was a very powerful stimulant to gastric secretion causing hyperacidity and hypersecretion with prolongation of the emptying time. Waldron (1971), when combining cholecystograms and barium-meal examinations, found that the fat stimulus given to stimulate gall-bladder contraction delayed stomach emptying appreciably. The fat stimulus used was Prosparol, 50 per cent being ground nut oil—a vegetable fat. Spasm narrows the pyloric lumen but the pylorus becomes normal again when the spasm ceases. If pylorospasm is frequent or persistent prepyloric muscle hypertrophy may result and the lumen becomes permanently narrowed by the rigid, thickened muscle layer. The rate of stomach emptying, as measured by barium-meal examination, is rarely altered in these cases. If the lumen is narrowed but the rate of emptying remains the same the flow of gastric (or duodenal) contents through it must be faster and more forceful, in fact a 'jet'. Capper (1967) demonstrated that a reflux 'jet' of alkaline duodenal contents caused atrophic gastritis and gastric ulceration; a 'jet' of acid gastric contents, impinging always on one or two localized areas of duodenal mucosa before mixing with and being neutralized by duodenal contents, must cause localized duodenal ulceration. If the pylorus is incompetent as well as narrowed a jet can 'squirt' in both directions and cause coexisting duodenal and gastric ulcers. Pylorospasm may persist long enough for a duodenal ulcer to develop; if the pylorus then relaxes completely the ulcer can heal and the pylorus appears normal with only a healed scar remaining, but if fibrosis develops as the ulcer heals it may constrict the lumen and cause recurrence of ulceration. The extent of narrowing of the lumen owing to fibrosis of a healed ulcer or to moderate hypertrophy of the prepyloric muscle consequent upon repeated or persistent spasm may not be enough by itself to cause 'jet' formation but it might do so if further spasm was superadded. This hypothesis explains why pyloroplasty alone cures both duodenal and gastric ulcers and fails to do so when the lumen of the pyloroplasty does not remain widely patent.

Martin and Burden (1928) arraigned 'pyloric achalasia' as the cause of chronic dyspepsia, of ulcer symptoms in the absence of peptic ulcer, and of the development and chronicity of the peptic ulcer. They recognized that failure of cure by pyloroplasty was due to incomplete abolition of sphincter activity at the pylorus or to postoperative narrowing of the pyloroplasty. Farris and Smith (1961, 1963, 1966) accepted that the cure of anatomical obstruction by the pylorus was the most important factor in the cure of gastric ulcer. These authors, however, feared that the duodenal ulcer might develop if vagotomy was not performed in addition to pyloroplasty. This does not happen if the pylorus remains wide and incompetent, and indeed duodenal ulcers also heal when the pylorus remains wide and incompetent.

III. DIARRHOEA

A. The Evidence.—Patients known to have gallstones have frequently complained of disturbance of bowel habit in association with attacks of biliary tract pain. Some patients have attacks of diarrhoea or looseness of the bowels related to the ingestion of particular foods, and most of the fat-containing foods forbidden in the F.F.D. have been incriminated in this way at one time or another. When attacks of 'biliary colic' have been controlled by the F.F.D. associated bowel symptoms also have been cured. Some of the patients who had undergone cholecystectomy complained of attacks of diarrhoea and often also of flatulent dyspepsia when they had returned to a full diet; both the diarrhoea and dyspepsia were cured by the F.F.D.

Four hundred and twenty-five of 532 dyspeptic patients seen in the past 3 years were unequivocally fat intolerant (*Table XIII*). Bowel disturbance apparently related to fat intolerance and controlled by the F.F.D. was present in 161. Looseness and increased frequency of bowel action accompanied fat-intolerant dyspeptic pain in 82 cases. Attacks of looseness or diarrhoea unrelated to any other disease or condition but sometimes occurring in patients who also suffered from flatulent dyspepsia and often precipitated by a particular fat-containing food were controlled by the F.F.D. in 24 cases. There were 12 patients in whom left iliac fossa pain, probably due to spasm in the sigmoid colon, was relieved by the F.F.D.

Barium-enema examination when carried out in these cases showed either no abnormality, or areas of transient or persistent spasm, or diverticular disease of the bowel, or a tube-like appearance of the bowel with loss of haustrations called 'colitis' by radiologists (*Table XIII*). Spasm and loss of haustrations were sometimes found in the same patient, while diverticular disease occurred in isolation or in association with spasm, or with loss of haustrations, or with both. Motions were watery, often containing slime or mucus, and were passed one to six or more times in 24 hours. They were often 'explosive' and urgent, preceded by large-bowel colic; several motions were passed in quick succession in some patients, while the action of eating precipitated bowel movement in others.

B. Discussion.—In all the cases described above the bowel symptoms were cured when the patient adhered to the F.F.D. which was in many cases prescribed primarily for the dyspeptic symptoms. It became apparent that the symptoms and signs of bowel disturbance were in fact a syndrome of fat intolerance, and the F.F.D. was prescribed and was effective treatment for those cases of fat-intolerant diarrhoea in which dyspeptic symptoms did not require it.

The barium-enema examination showed progression of changes. The earliest evidence of abnormality was spasm, transient or persistent, affecting the sigmoid colon most frequently and seen at sigmoidoscopy invariably to affect the rectosigmoid junction. When diverticular disease was present with hypertrophy of the circular muscle layer and some loss of ability of the bowel to relax, areas of spasm were often also demonstrated radiologically. It is likely that hypertrophy is the result of repeated or persistent spasm. Loss of haustrations was also frequently associated with areas of spasm. In ulcerative colitis shortening of the colon and loss of haustrations are the result of a muscle abnormality which Morson (1968) described as more in the nature of a contracture or a maintained contraction than a spasm, while strictures in ulcerative colitis are due to thickening of the muscularis mucosae as well as the muscularis propria and are found in any part of the rectum and colon (Goulston and McGovern, 1969; Morson, 1970).

Table XIII.—BOWEL DISTURBANCE IN 'FAT-INTOLERANT' PATIENTS, 1969-71

TYPE OF BOWEL DISTURBANCE	TOTAL NO. OF CASES	TYPE OF FAT-INTOLERANT DYSPEPSIA			BARIUM-ENEMA EXAMINATION FINDINGS						OTHER COEXISTING DISORDERS								
		Gall-stones proved	Post-cholecystectomy	Fat-intolerant Dyspepsia: Cholecystogram negative	Not done	N.A.D.	Spasm	Loss of Haustration	Proctocolitis	Diverticular Disease	Previous Vagotomy and Pyloroplasty for D.U.	Dyspepsia but not investigated	Hiatus Hernia	Gall-stones proved	Hypertrophy of Sphincter of Oddi	Duodenal Ulcer	Abnormal Duodenal Cap	Gastric Ulcer	Diabetes
Looseness of bowel or diarrhoea associated with 'attacks' of dyspeptic pain	27	178	—	—	24	—	—	1	—	—	2	—	13	—	2	7	14	2	3
	14	—	77	—	5	2	3	2	—	2									
	41	—	—	170	28	—	6	—	—	7									
Principal complaint looseness of bowels or diarrhoea	24	—	—	—	5	4	7	6	2	—	—	4	—	2	—	—	2	—	1
Diverticular disease of bowel (not included in above cases)	43	—	—	7	—	—	—	—	—	43	—	3	7	5	—	—	1	—	—
Left iliac fossa pain	12	—	—	—	2	4	4	2	—	—	—	1	—	—	—	—	1	—	2
Total	161	—	—	—	64	10	20	11	2	54	—	—	—	—	—	—	—	—	—

Looseness of the motions or diarrhoea is 'triggered' by a high dietary fat intake and occurs in 37 per cent of patients who are recognized on other evidence as fat-intolerant. The bowel symptoms and signs are cured by the F.F.D. Spasm of circular smooth muscle in the bowel wall, especially in the area of the rectosigmoid junction but also elsewhere, is the earliest abnormality seen; this spasm is no longer present when the patient has been cured by the F.F.D. There is no clear-cut line between these patients and those with loss of haustrations or with established diverticular disease of the bowel. Even in the presence of diverticular disease with hypertrophy of the circular muscle and some rigidity and loss of distensibility of the bowel, patients are usually cured by the F.F.D. If they are not, Reilly's operation of sigmoidomyotomy is necessary (Reilly, 1966).

I have not had enough experience of the use of the F.F.D. in florid cases of ulcerative colitis to draw firm conclusions. It is very difficult, however, to separate from a true ulcerative colitis the fat-intolerant 'colitis' with spasm, loss of haustration, and a 'tube-like' radiological appearance of the bowel in which the mucosa is oedematous and pouring forth a copious mucoid and watery fluid. It could be significant that Truelove (1967) found that 9 per cent of cases were 'sensitive' to milk and derivatives of milk; he suspected that the protein of milk was responsible but was never able to detect any antibodies. I think that in any patient suffering from ulcerative colitis a prolonged trial of the effect of the F.F.D. must be carried out.

IV. FAT-INTOLERANT CHILDREN

Children as well as adults can eat too much fat. During the past 3 years I have seen 17 cases in which abdominal pains were associated with excess dietary fat intake. Ten of these children have been on the F.F.D. for more than 6 months and no longer suffer recurrent attacks of pain; 5 others have had no further pain during 3 to 6 months' follow-up.

All the children, 11 boys and 6 girls, aged 7 to 16 years (14 cases were aged 10–15 years), were 'plump' and 3 were much overweight. Pain had occurred in 'attacks' on and off for periods of a few months to 4 years but had recently become more frequent and even daily in some cases. In 3 cases fat had been identified as the cause of pain, which in 13 of the 17 cases was primarily epigastric, radiating as shown in *Table XIV*. The pain was described as aching in 5, colicky in 4, and both aching and colicky in 8 cases. Other symptoms are listed in *Table XIV*. The gall-bladder was markedly tender on palpation in 3 cases. The excess dietary fat intake was high in all the cases; in 1 it was more than 1250 cal. per day, and in 3 other cases was more than 800 cal. per day.

This group of patients is important because the children had often been labelled 'emotionally disturbed'. There was lethargy and 'lack of interest' in almost all of the children, but when the F.F.D. had cured them of their pain they became normal once more. In 8 of the cases the mothers commented spontaneously that their children were brighter and more lively. The provisional diagnosis is made on the history and clinical presentation. There may be some dyspepsia or disturbance of the bowels and even recognized fat intolerance. The diagnosis can only be confirmed by prescribing the F.F.D. and assessing the benefit after at least 3 months.

V. DIETARY FAT INTAKE AND GLUCOSE TOLERANCE

The effect of the F.F.D. on glucose tolerance (G.T.) has been investigated in 134 patients who required treatment by the F.F.D. An initial oral glucose-tolerance test (G.T.T.) was performed on each patient before prescribing the F.F.D. and was

Table XIV.—FAT INTOLERANCE IN 17 CHILDREN

Symptom	*No. of Cases*
Pain	
Site:—	
Epigastric	13
Central abdominal	3
Left iliac fossa	1
Radiation:—	
Right hypochondrium	9
Left hypochondrium	9
Interscapular region	2
Right iliac fossa	2
Left iliac fossa	1
Associations:—	
After food	2
Woke at night	1
After fat	3
Related to exertion	5
Other Symptoms	
Anorexia	3
Belching	1
Nausea	9
Vomiting	2
Bowels, more frequent, loose (watery and urgent in 1)	3

Table XV.—INDICATIONS FOR F.F.D. IN THE 65 CASES INCLUDED IN THE SERIES OF G.T.T.S WHICH WAS SUBMITTED TO STATISTICAL ASSESSMENT

DIAGNOSIS ON WHICH F.F.D. WAS PRESCRIBED	NO. OF CASES	OTHER CONDITIONS COEXISTING
Overweight	12	Inguinal hernia, 4. Dyspepsia, 2. Varicose veins, 1. Migraine, 1. Nodular goitre, 1. Diabetes, 2
Gall-stones	12	Diverticulitis, 1. Diabetes, 2. (Cholangitis positive bile-culture)
Post-cholecystectomy symptoms	7	'Colitis', 1. Diabetes, 1. Stone in common bile-duct, 1. 'Stenosis' of sphincter of Oddi, 1
Dyspepsia (including 'biliary colic' in 3 cases); cholecystogram and barium-meal examinations negative	15	Previous vagotomy and pyloroplasty, 1. Diabetes, 2. Migraine, 2. Spastic, irritable duodenal cap, 1. 'Colitis', 3 (including 1 case who had been on a low-carbohydrate diet). Prepyloric muscle hypertrophy, 1. Stenosis of sphincter of Oddi, 1
Duodenal ulcer	3	
'Spasm of colon'	4	Dyspepsia, 1. Diabetic, 1 (had been on low-carbohydrate diet)
Diverticulitis	4	
Undiagnosed abdominal pain	3	One case had been on low-carbohydrate diet
Migraine	1	Post-cholecystectomy dyspepsia, 1
Fat intoxication	3	Post-cholecystectomy, 1
Diabetes	1	Presented with 'prostatic' symptoms

repeated at intervals while the patient was on the diet; 433 separate tests have been carried out (*see* Appendix 3). The change in G.T. has been analysed statistically in a series of 65 consecutive patients.

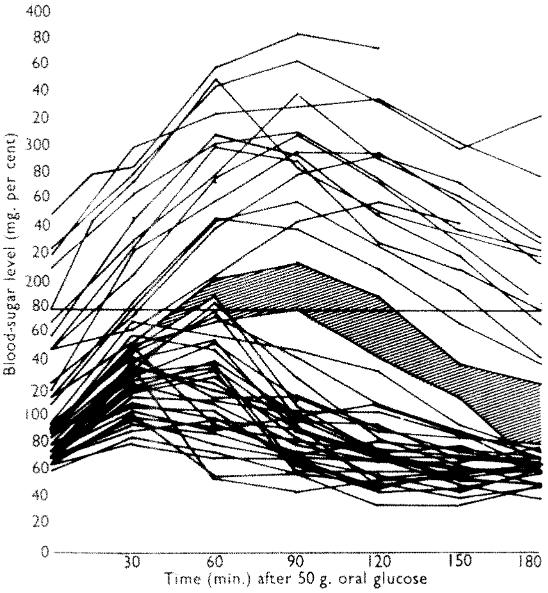

FIG. 4.—Initial G.T. curves. Representative selection (7 of 13 cases from group 1; 24 of 43 cases from group 2; 15 newly diagnosed diabetic cases) which demonstrates the 'hiatus' between high hyperglycaemic and diabetic curves, but continuous rise from 'normal' to hyperglycaemic curves.

The diseases or disorders afflicting these patients and any other coexisting diseases or disorders were representative for all the patients investigated by the G.T.T. (*Table XV*); so also was the range of variation found in the initial G.T. curves (*Fig.* 4).

A. The Results.—*Fig.* 4 shows a demarcation between diabetic and non-diabetic curves; no such 'hiatus' exists between any of the non-diabetic curves and it is impossible to define a level at which a normal G.T. curve becomes hyperglycaemic. A visual survey of all the initial and final G.T. curves in the 'statistical series' showed that if the initial curve rose at any point above the 100 mg. per cent level the G.T. increased on the F.F.D.; if the initial curve never rose above 100 mg. per cent changes in the G.T. showed no constant trend. The initial curves were therefore divided into three groups:—

Group 1 (13 cases; average age, 42 years): Not hyperglycaemic. Initial G.T. curve never rose above 100 mg. per cent.

Group 2 (43 cases; average age, 52 years): Hyperglycaemic. Initial G.T. curve rose above 100 mg. per cent but not above 180 mg. per cent (i.e., not diabetic).

Group 3 (9 cases; average age, 59 years): Diabetic.

Clinically it had proved to be impossible to assess the effect of the F.F.D. on symptoms in less than 3 months on the diet. There was often an immediate benefit, but this might not be noticeable for 2 or 3 weeks and the full effect was sometimes more delayed. Likewise, no fixed interval between the initial and final G.T.T. could be laid down as standard; th longer a patient adhered to the F.F.D. the mor certain it was that the G.T. would increase. Othe factors such as initial level of G.T., activ weight-loss, strictness of adherence to the diet, an intercurrent infection or disease all influenced tl time needed.

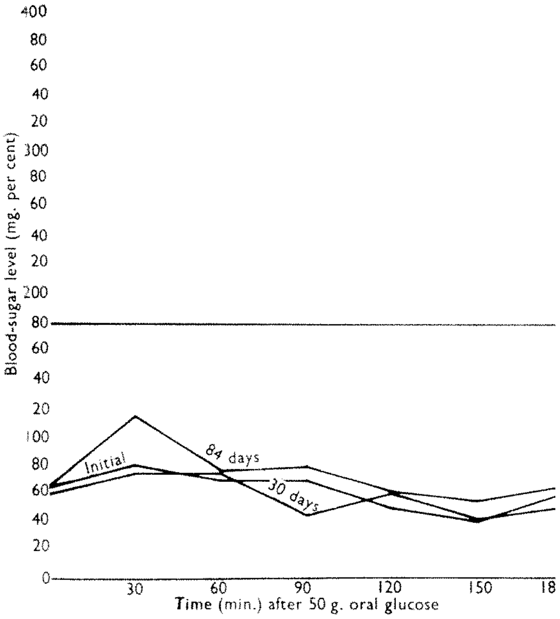

FIG. 5.—*Case* 1. Female, aged 47 years, with gall-stones. Dietary intake before F.F.D.: fat, 800 cal. per day; carbohydrate, 500 cal. per day. After F.F.D.: carbohydrate, plus 100 cal. per day. Initial weight was 126 lb.; after 30 days, 121 lb.; and after 84 days, 114 lb.

1. *Statistical Assessment of Change in G.T. wh on the F.F.D.* (*see* Appendix 4).—The G.T. curv of 65 consecutive patients before and after they ha been on the F.F.D. were assessed statistically b Mr. Niall Clinton, Lecturer in Statistics, Plymout Polytechnic. The series was divided on the basis the initial G.T. curves into the groups defined abov Mr. Clinton concluded:—

'The area under a G.T. curve (which is, in fact, broken-line graph) appears to be a reasonable ar objective measure of the glucose tolerance. If v accept this area as a measure of G.T., then tl following points emerge:—

1. The G.T. of patients in group 1 has not chang significantly.
2. The G.T. of patients in both groups 2 and has increased significantly (at 1 per cent level significance).
3. The G.T. of patients in group 3 has increas more than that in group 2.
4. The reactions of patients in group 3 are mo variable than the reactions of patients in either of tl other groups. However, there is a small number people in group 3, and there are large variations the reactions of patients within all the group Possibly these large variations are due to lar variations in weight changes, days between test etc.

'In short, using the area under the G.T. curve as measure of G.T., we conclude that the patients in roups 2 and 3 have significantly increased their .T. after being on the F.F.D.' (*Table XVI.*)

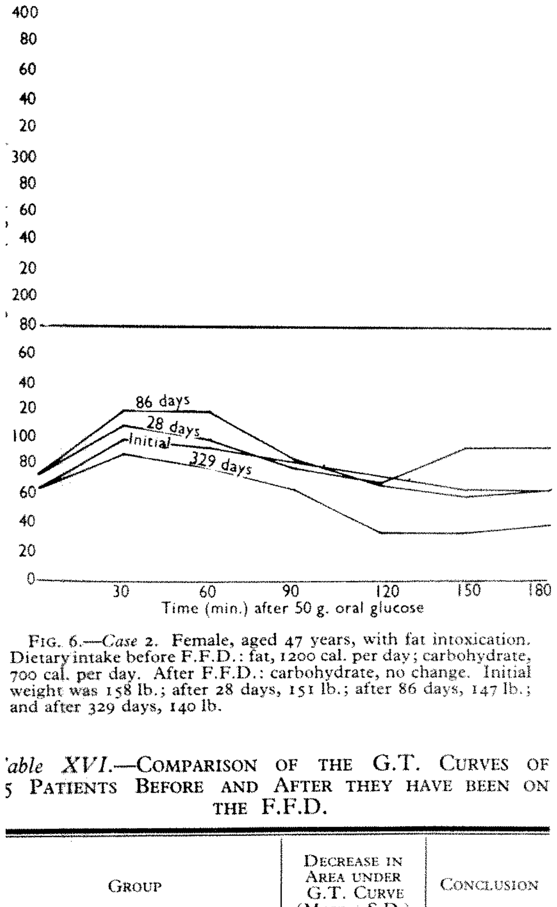

FIG. 6.—*Case* 2. Female, aged 47 years, with fat intoxication. Dietary intake before F.F.D.: fat, 1200 cal. per day; carbohydrate, 700 cal. per day. After F.F.D.: carbohydrate, no change. Initial weight was 158 lb.; after 28 days, 151 lb.; after 86 days, 147 lb.; and after 329 days, 140 lb.

able XVI.—COMPARISON OF THE G.T. CURVES OF 5 PATIENTS BEFORE AND AFTER THEY HAVE BEEN ON THE F.F.D.

GROUP	DECREASE IN AREA UNDER G.T. CURVE (Mean ± S.D.)	CONCLUSION
13 cases. Blood-sugar never more than 100 mg. per cent in initial curve	28·27 ± 86·37	No significant difference
43 cases. Blood-sugar level rose to more than 100 mg. per cent but never more than 180 mg. per cent in initial curve	89·59 ± 79·48	Difference significant ($P = 0·01$)
9 cases. Initial curve was a diabetic curve	449·16 ± 203·99	Difference significant ($P = 0·01$)

Conclusion of statistical analysis of the results by Mr. Niall Clinton, .Sc., Lecturer in Statistics, Plymouth Polytechnic.

2. *Individual Cases illustrating the Effect of the .F.D. on G.T.*

a. Group 1.—No increase in G.T. was expected these cases because they showed no initial impairent. In *Case* 1 an initial curve of group 1 type ecame group 2 type after 84 days (*Fig.* 5). The me change occurred in *Case* 2 after 86 days, but e G.T. was greater after 329 days than it had been initially (*Fig.* 6). *Case* 3 shows impaired G.T. at 28, 86, and 140 days, but little change from the initial level after 205 days (*Fig.* 7). The G.T. in all these cases was impaired during a period of active and appreciable weight-loss and recovered when the weight was stabilized.

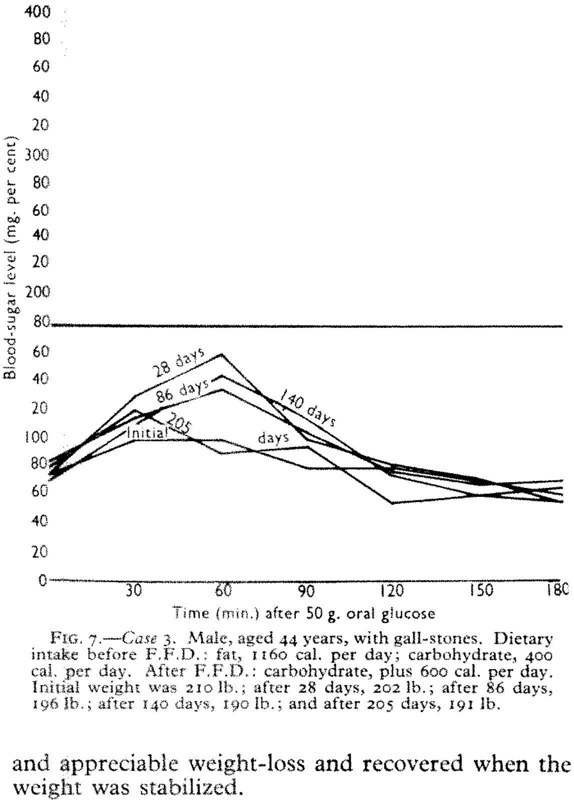

FIG. 7.—*Case* 3. Male, aged 44 years, with gall-stones. Dietary intake before F.F.D.: fat, 1160 cal. per day; carbohydrate, 400 cal. per day. After F.F.D.: carbohydrate, plus 600 cal. per day. Initial weight was 210 lb.; after 28 days, 202 lb.; after 86 days, 196 lb.; after 140 days, 190 lb.; and after 205 days, 191 lb.

b. Group 2.—The G.T. was impaired during active weight-loss in some cases in this group but there was finally always an overall increase in G.T. In *Cases* 4 and 5 initial curves of group 2 type were converted to group 1 type (*Figs.* 8, 9). Initial impairment in G.T. was not always detected and *Cases* 6–11 showed increased G.T. when the patients were on the F.F.D. (*Figs.* 10–15). In *Cases* 12–14 the initial G.T. curves were markedly hyperglycaemic; the longer the patients adhered to the F.F.D. the greater was the increase in G.T. (*Figs.* 16–18). After an initial weight-loss *Case* 14 gained weight but the G.T. showed a further increase despite this (*Fig.* 18).

c. Group 3: *diabetic patients.*—*Cases* 15–17 are diabetic patients who were cured by the F.F.D. (*Figs.* 19–21). *Case* 15 now weighs the same as when treatment started although her weight had decreased at one period. The G.T. is increasing steadily on the F.F.D. in *Cases* 18 and 19 (*Figs.* 22, 23), and *Case* 20 also shows an increase (*Fig.* 24). *Cases* 15–20 were diabetic and were treated only by the F.F.D.

Case 21 is an example of 'cure' of 'diabetes' by the F.F.D. in a patient who had been on chlorpropamide, 250 mg. daily, and a 12-portion diet for 8 years (*Fig.* 25). He was instructed to stop doing so. When, 75 days after starting the F.F.D. the G.T.T. was performed on *Case* 22 the patient was still in error taking tolbutamide. His G.T. initially became impaired, but after 252 days his G.T. curve was hyperglycaemic only. The impairment present again at 371 days was due to non-adherence to the F.F.D. (*Fig.* 26). *Case* 23 also illustrates the effect of dietary fat intake on G.T. The curve at 189 days shows no improvement over that at 77 days; the patient had been eating butter, bacon, cake, and fish paste (*Fig.* 27). In *Case* 24 impairment of G.T. between 229 and 320 days was due to fat-containing foods ingested at Christmas, while that between 460 and 579 days was due to a 3-week holiday in a bed-and-breakfast boarding house when no control over diet

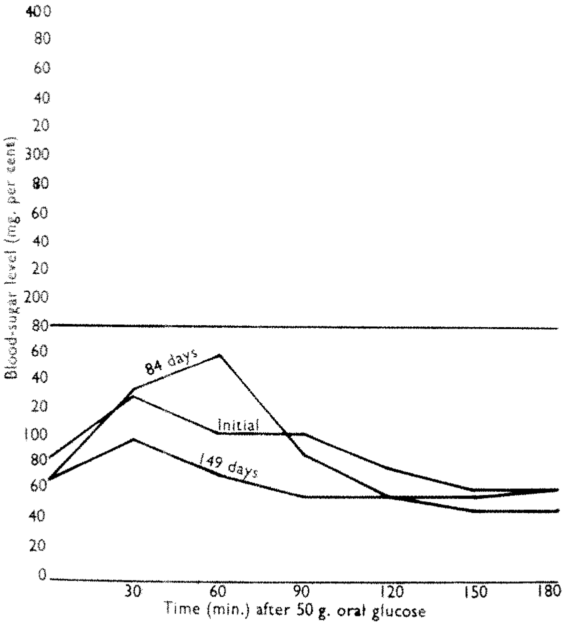

FIG. 8.—*Case* 4. Male, aged 32 years, with a duodenal ulcer. Dietary intake before F.F.D.: fat, 950 cal. per day; carbohydrate, 950 cal. per day. After F.F.D.: carbohydrate, no change. Initial weight was 149 lb.; after 84 days, 139 lb.; and after 149 days, 137 lb.

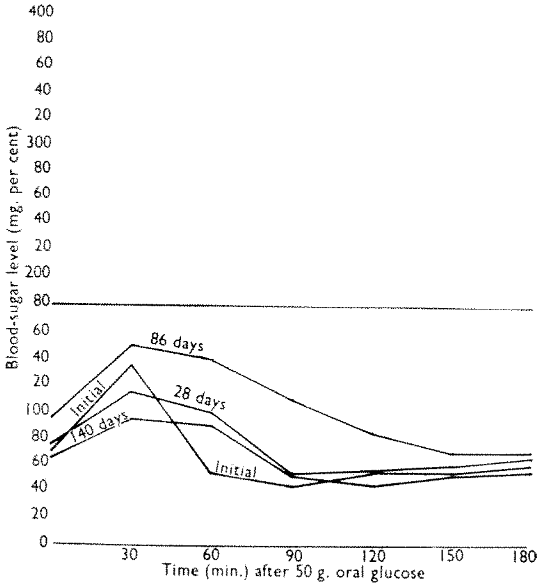

FIG. 9.—*Case* 5. Male, aged 45 years, with gall-stones. Dietary intake before F.F.D.: fat, 1200 cal. per day; carbohydrate, 720 cal. per day. After F.F.D.: carbohydrate, plus 130 cal. per day. Initial weight was 157 lb.; after 28 days, 140 lb., after 86 days, 135 lb.; and after 140 days, 136 lb.

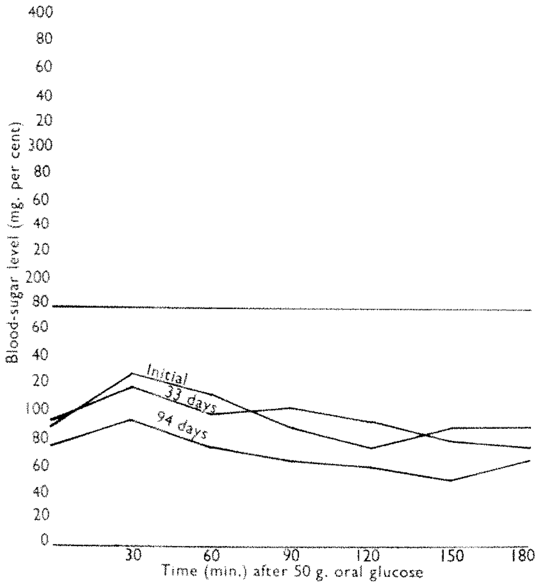

FIG. 10.—*Case* 6. Female, aged 49 years, with 'biliary colic'. The cholecystogram was negative. Dietary intake before F.F.D.: fat, 700 cal. per day; carbohydrate, 160 cal. per day. After F.F.D.: carbohydrate, plus 400 cal. per day. Initial weight was 138 lb.; after 33 days, 135 lb.; after 94 days, 130 lb.

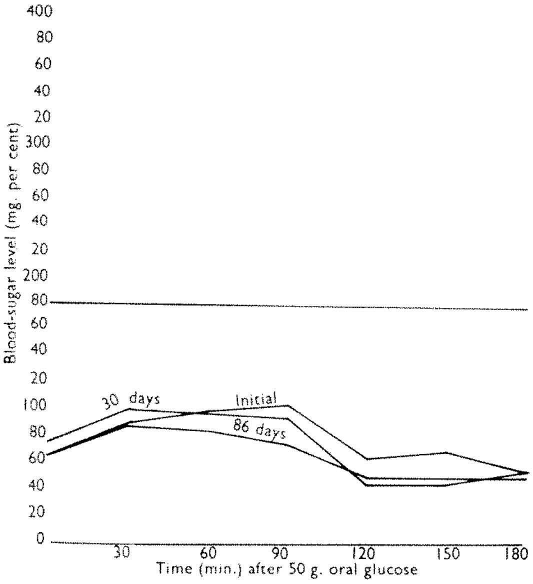

FIG. 11.—*Case* 7. Female, aged 37 years, with gall-stones. Dietary intake before F.F.D.: fat, 720 cal. per day; carbohydrate, 320 cal. per day. After F.F.D.: carbohydrate, plus 160 cal. per day. Initial weight was 138 lb., and after 86 days, 119 lb.

was possible (*Fig.* 28). The G.T. of *Case* 25 was increased after 60 days on the F.F.D.; at 119 days it was decreased after eating 12 eggs per week and other fat. There was improvement after 208 days, but by 327 days the curve reflected the fact that she was again eating fat (*Fig.* 29). The wife of *Case* 26 was a diabetic under orthodox treatment; my patient's G.T. had improved after 120 days on the F.F.D. but he had to abandon the diet to keep the peace at home, and his G.T. returned to its original level (*Fig.* 30).

Ten out of 23 patients who were diabetic when they started on the F.F.D. diet are no longer diabetic.

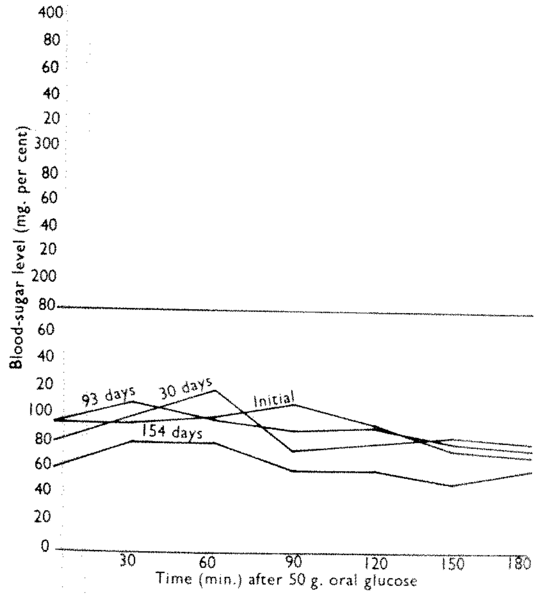

FIG. 12.—*Case* 8. Female, aged 57 years, with hypertrophy of the sphincter of Oddi and of the prepyloric muscle. Dietary intake before F.F.D.: fat, 1080 cal. per day; carbohydrate, 600 cal. per day. After F.F.D.: carbohydrate, plus 300 cal. per day. Initial weight was 126 lb.; after 30 days, 119 lb.; after 93 days, 105 lb.; and after 154 days, 98 lb.

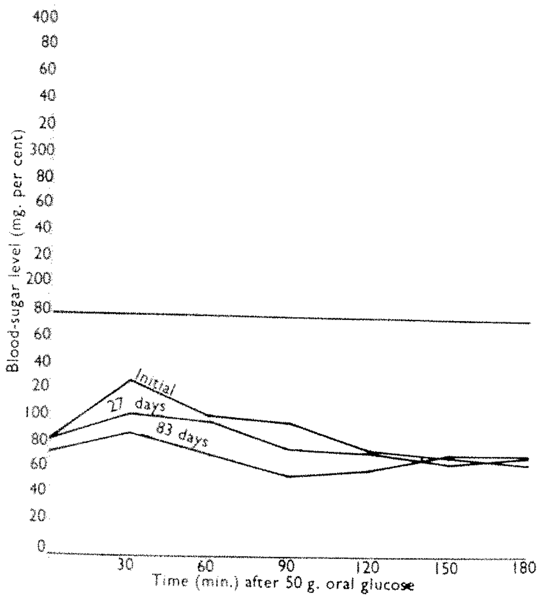

FIG. 13. *Case* 9. Male, aged 44 years, who was overweight. Dietary intake before F.F.D.: fat, 800 cal. per day; carbohydrate, 920 cal. per day. After F.F.D.: carbohydrate, plus 100 cal. per day. Initial weight was 189 lb.; after 27 days, 182 lb.; and after 83 days, 169 lb.

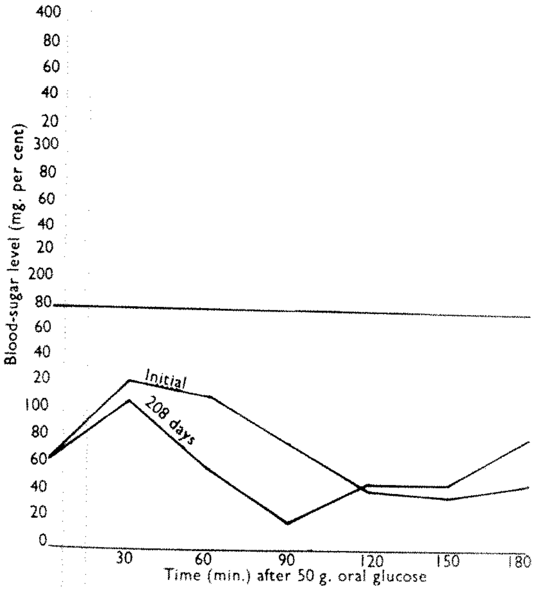

FIG. 14.—*Case* 10. Male, aged 19 years, with flatulent dyspepsia and who was overweight. Initial weight was 196 lb., and after 208 days 189 lb.

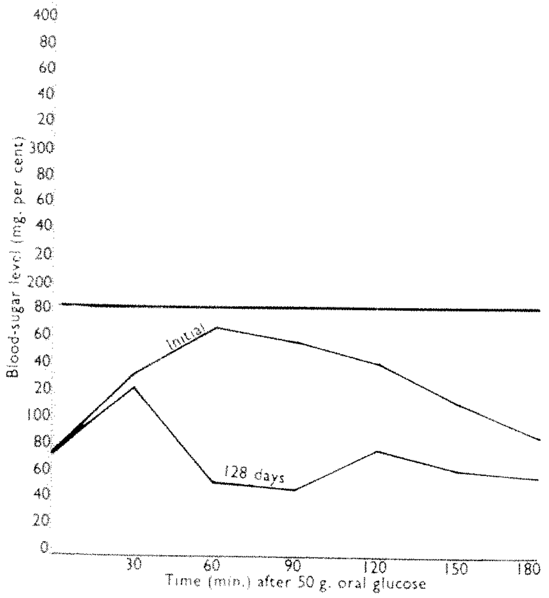

FIG. 15.—*Case* 11. Male, aged 58 years, with occasional glycosuria and an inguinal hernia. Initial weight was 168 lb., and after 128 days, 161 lb.

Three have at some time been hyperglycaemic only but have reverted to diabetic curves after taking fat. Two others whose G.T. had improved while they adhered to the F.F.D. reverted to their previous impairment when they took fat again. It is too early to assess the results in 6 patients; in 2 cases the G.T. is at present increased, in 2 it is impaired, and in 2 only the initial test has been performed. In 2 cases after initial improvement there has been no further increase in G.T.: 1 case appears to have reached the limit of increase in G.T.; the other patient does not adhere strictly to the F.F.D. (*Table XVII*).

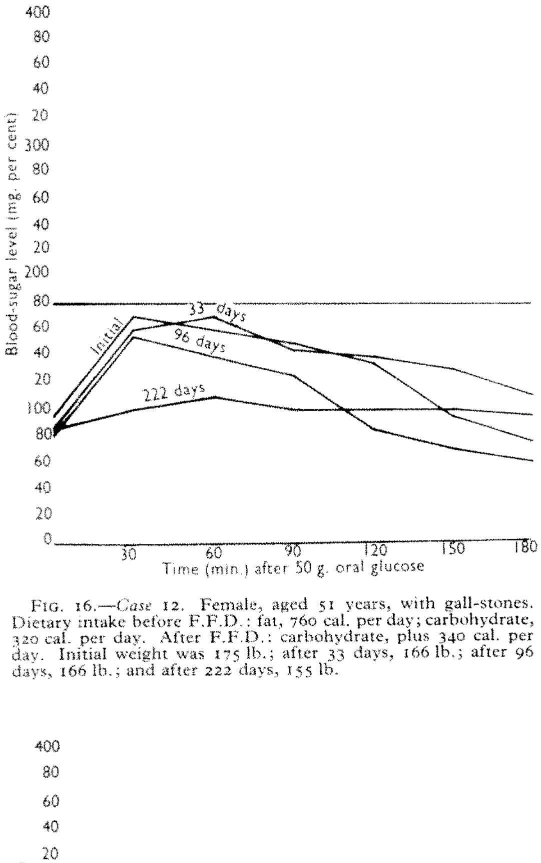

FIG. 16.—*Case* 12. Female, aged 51 years, with gall-stones. Dietary intake before F.F.D.: fat, 760 cal. per day; carbohydrate, 320 cal. per day. After F.F.D.: carbohydrate, plus 340 cal. per day. Initial weight was 175 lb.; after 33 days, 166 lb.; after 96 days, 166 lb.; and after 222 days, 155 lb.

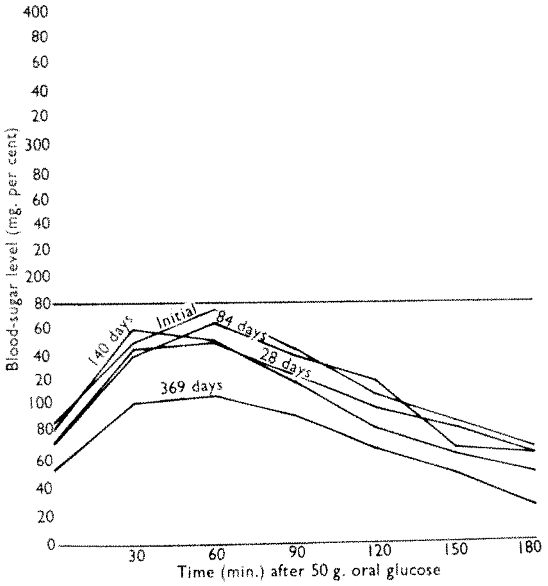

FIG. 17.—*Case* 13. Female, aged 71 years, with postcholecystectomy symptoms. Dietary intake before F.F.D.: fat, 500 cal. per day; carbohydrate, 720 cal. per day. After F.F.D.: carbohydrate, plus 100 cal. per day. Initial weight was 108 lb.; after 28 days, 102 lb.; after 84 days, 97 lb.; after 140 days, 93 lb.; and after 369 days, 88 lb.

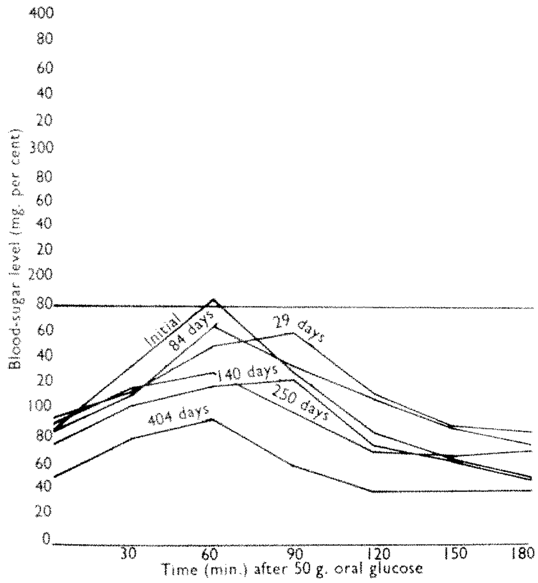

FIG. 18.—*Case* 14. Male, aged 53 years, post-cholecystectomy, with fat intoxication. Dietary intake before F.F.D.: fat, 1350 cal. per day; carbohydrate, 400 cal. per day. After F.F.D.: carbohydrate, plus 650 cal. per day. Initial weight was 205 lb.; after 84 days, 199 lb.; after 140 days, 194 lb.; after 250 days, 194 lb.; and after 404 days, 199 lb.

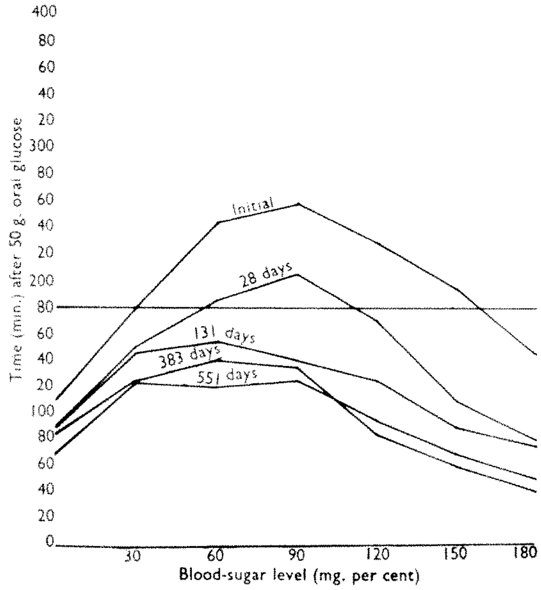

FIG. 19.—*Case* 15. Female, aged 59 years, with gall-stones and diabetes. Dietary intake before F.F.D.: fat, 1450 cal. per day; carbohydrate, 800 cal. per day. After F.F.D.: carbohydrate, plus 400 cal. per day. Initial weight was 125 lb.; after 28 days, 119 lb.; after 131 days, 113 lb.; after 383 days, 125 lb.; and after 551 days, 123 lb.

B. Discussion.—The F.F.D. resulted in increased G.T. in all the patients who adhered to it strictly, provided that it was possible to demonstrate impairment of G.T. initially. It has been impossible to define the level of a normal G.T. curve; in some cases with group 1 type initial curves the only change demonstrated after 80–100 days on the F.F.D. was slight impairment of G.T., but in all the cases from this group which were tested after a much longer period on the diet (more than 200 or even 300 days) no change or even increased tolerance was found. However, the frequency with which it has been

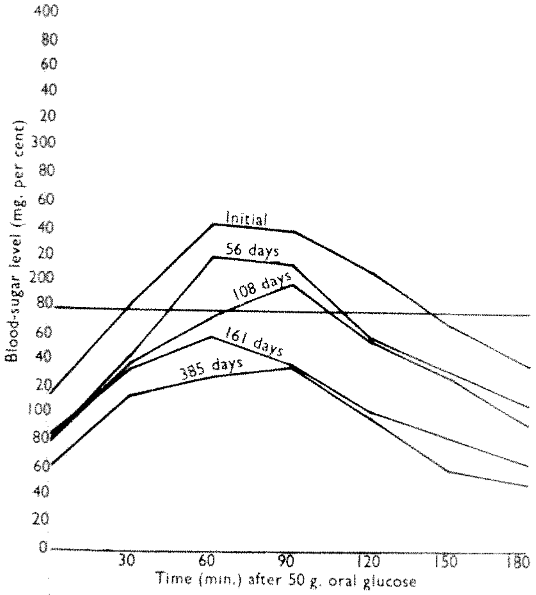

FIG. 20.—*Case* 16. Male, aged 27 years, who was overweight. He had an inguinal hernia and diabetes. Dietary intake before F.F.D.: fat, 720 cal. per day; carbohydrate, 790 cal. per day. After F.F.D.: carbohydrate, plus 50 cal. per day. Initial weight was 152 lb.; after 56 days, 150 lb.; after 108 days, 147 lb.; after 161 days, 143 lb.; and after 385 days, 140 lb.

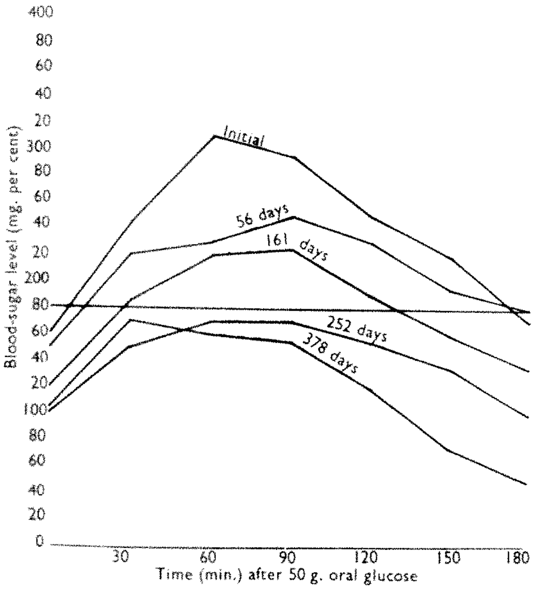

FIG. 21.—*Case* 17. Female, aged 64 years, with spasm in the colon and diabetes. Dietary intake before F.F.D.: fat, 860 cal. per day; carbohydrate, 650 cal. per day. After F.F.D.: carbohydrate, plus 150 cal. per day. Initial weight was 188 lb.; after 56 days, 176 lb.; after 161 days, 168 lb.; after 252 days, 157 lb., and after 378 days, 149 lb.

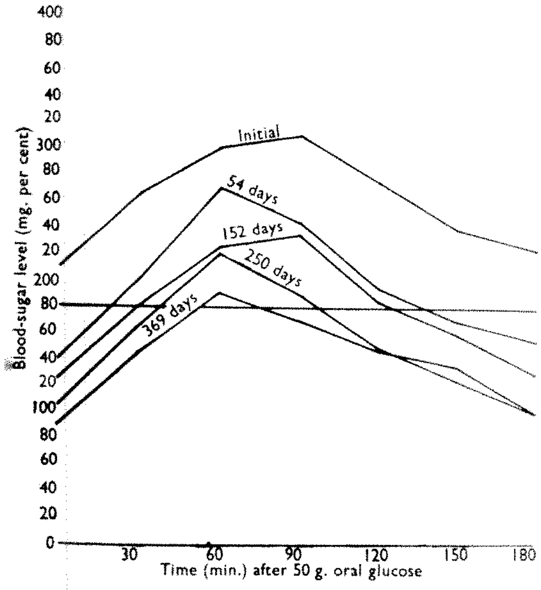

FIG. 22.—*Case* 18. Male, aged 57 years, with an inguinal hernia and diabetes. Dietary intake before F.F.D.: fat, 1030 cal. per day; carbohydrate, 1160 cal. per day. After F.F.D.: carbohydrate, no change. Initial weight was 206 lb.; after 54 days, 194 lb.; after 152 days, 196 lb.; after 250 days, 180 lb.; and after 369 days, 183 lb.

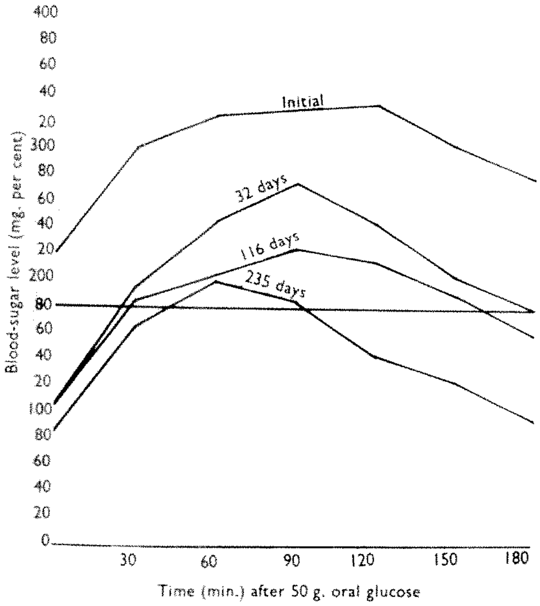

FIG. 23.—*Case* 19. Female, aged 70 years, with polycystic disease of the kidneys and diabetes. Initial weight was 195 lb.; after 32 days, 187 lb.; after 116 days, 168 lb.; and after 235 days, 164 lb.

possible to show increased G.T. is important. Analysis of 65 consecutive cases in which the F.F.D. was necessary treatment showed that the increase in G.T. was statistically significant in all except the 13 cases in group 1, which were not considered to have any impairment of G.T. when they w placed in this group.

There is no constant duration of the F.F which results in increase in G.T., but the longe patient is on the diet the more the G.T. increa

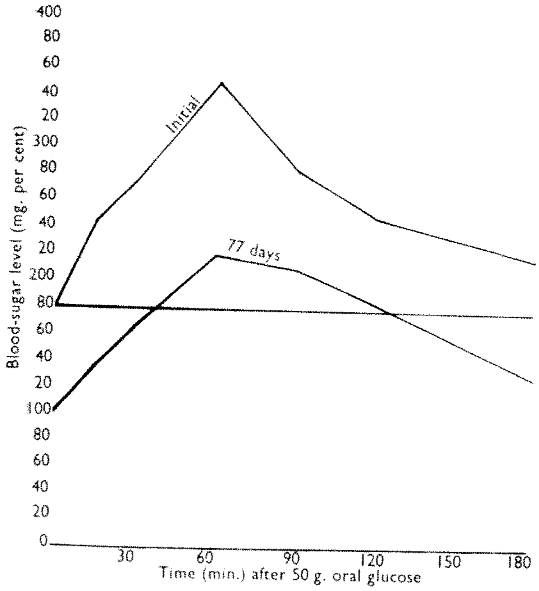

FIG. 24.—*Case* 20. Male, aged 60 years, with prostatic hypertrophy and diabetes. Initial weight was 132 lb., and after 77 days, 126 lb.

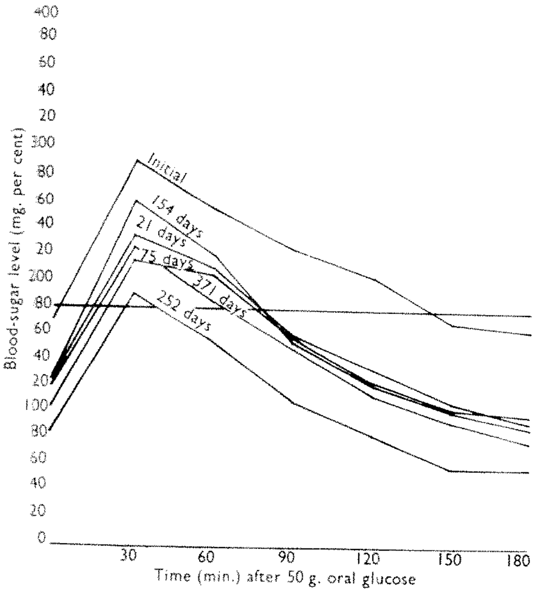

FIG. 26.—*Case* 22. Male, aged 51 years, with 'biliary colic', jaundice, diarrhoea, and diabetes. The diabetes had been diagnosed 6 years earlier on the occasion of vagotomy and pyloroplasty for a duodenal ulcer. The patient has suffered three myocardial infarcts since then. The diabetes had been treated initially by chlorpropamide, 250 mg. daily, and a 12-portion diet. Recently tolbutamide had been prescribed. Random blood-sugar had been 115–145 mg. per cent, and the weight 160–170 lb. The initial weight at the present time was 151 lb.; after 21 days, 143 lb.; after 75 days, 143 lb.; after 154 days, 131 lb.; after 252 days, 135 lb.; and after 371 days, 144 lb.

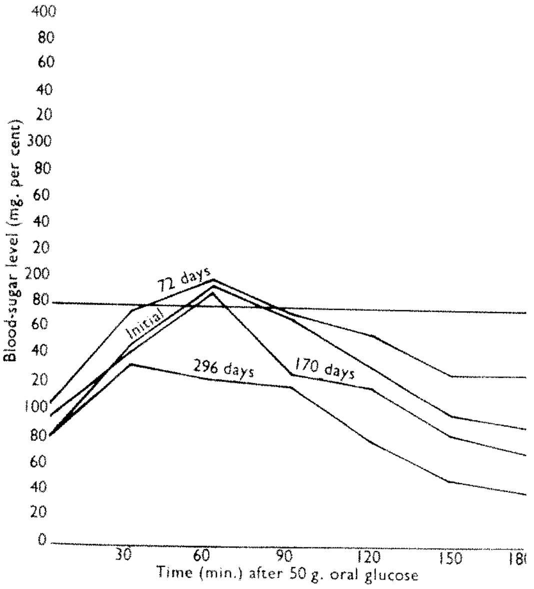

FIG. 25.—*Case* 21. Male, aged 63 years, with 'colitis' and diabetes. The diabetes had been diagnosed 8 years earlier and had been treated by chlorpropamide, 250 mg. daily, and a 12-portion diet. Random blood-sugars had been 210–250 mg. per cent and the weight 167–176 lb. The initial weight at the present time was 167 lb.; after 72 days, 145 lb.; after 170 days 138 lb.; and after 296 days, 126 lb.

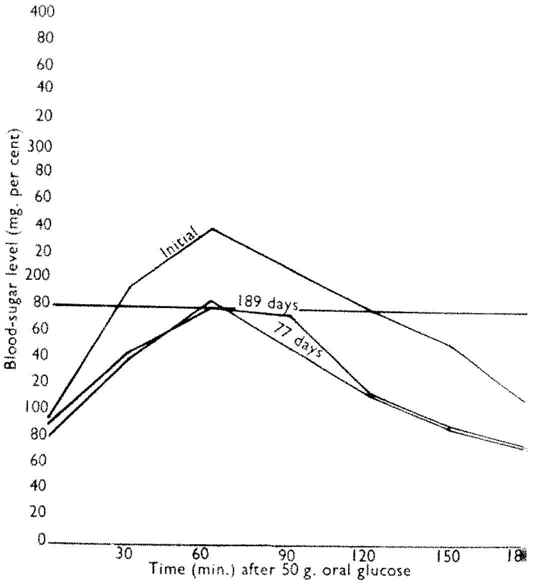

FIG. 27.—*Case* 23. Male, aged 58 years, post-cholecystectomy, with diabetes. The diabetes had been diagnosed 1 year earlier (after cholecystectomy). Previously he had been on steroids for arthritis. He had been weaned from these and prescribed a 10-portion diet. Random blood-sugars had been 105–200 mg. per cent and the weight 200–203 lb. The initial weight at the present time was 203 lb.; after 77 days, 196 lb.; and after 189 days, 197 lb

towards whatever can be termed a normal level, while there may be initial impairment before increased tolerance is established. Such impairment has been demonstrated during periods of active weight-loss. This could be due to catabolism of the patient's own adipose tissue flooding the body with fatty acids; the same process could explain occasional complaints while on the F.F.D. of 'attacks' of biliary tract pain during the period when patients are still losing weight. Initial impairment of G.T. was most obvious in the patients whose tolerance was already good, and much less evident in those whose initial G.T. curves were markedly hyperglycaemic or even diabetic. In the latter, increase in G.T. may be slow to appear; it may require 222 days (*Case* 12, *Fig.* 16), 399 days (*Case* 13, *Fig.* 17), or 404 days (*Case* 14, *Fig.* 18) to become normal.

Increase in G.T. has not been dependent upon a loss of body-weight. *Case* 15, a diabetic who became non-diabetic on the F.F.D., is the same weight now as when treatment started although she did lose weight initially. In the majority of cases the patients lost weight; during a period of active weight-loss G.T. might be impaired, but it increased when the weight became stabilized and continued to increase even when weight was gained while the patient was on the F.F.D. Obesity cannot be other than as

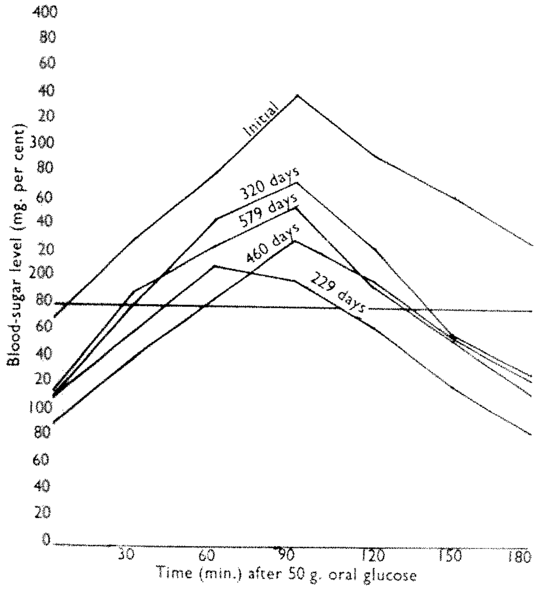

FIG. 28.—*Case* 24. Female, aged 74 years, with spasm in the colon and diabetes. Dietary intake before F.F.D.: fat, 1450 cal. per day; carbohydrate, 860 cal. per day. After F.F.D.: carbohydrate, plus 260 cal. per day. Initial weight was 149 lb.; after 229 days, 135 lb.; after 320 days, 146 lb.; after 460 days, 130 lb.; and after 579 days, 130 lb.

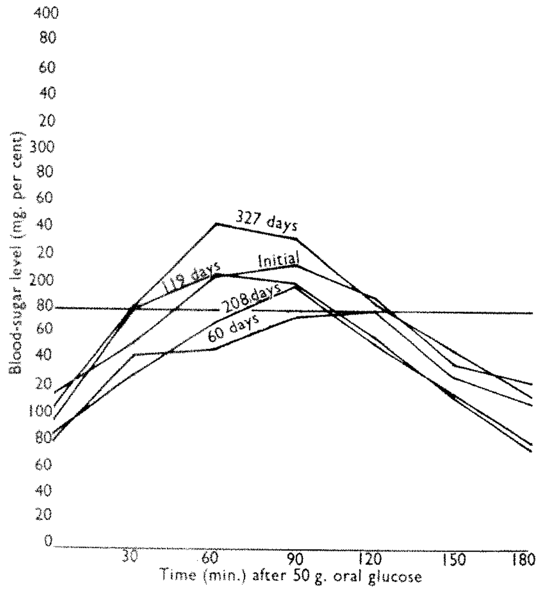

FIG. 29.—*Case* 25. Female, aged 58 years, with urinary infection and diabetes. Dietary intake before F.F.D.: fat, 1600 cal. per day; carbohydrate, 1800 cal. per day. Initial weight was 173 lb.; after 60 days, 168 lb.; after 208 days, 170 lb.; and after 327 days, 173 lb.

Table XVII.—RESULTS OF TREATMENT OF DIABETES BY F.F.D.

Results		*No. of Cases*
No longer diabetic		10
Low hyperglycaemic curve	6	
High hyperglycaemic curve	4	
Still diabetic		13
Have been hyperglycaemic only	3	
Improved G.T., now reverted	2	
'Stuck'—won't stay on F.F.D.	1	
Just 'stuck'	1	
Too early to assess	6	
G.T. impaired	2	
G.T. improved	2	
Only 1 G.T.T.	2	
Total No. now under treatment		23

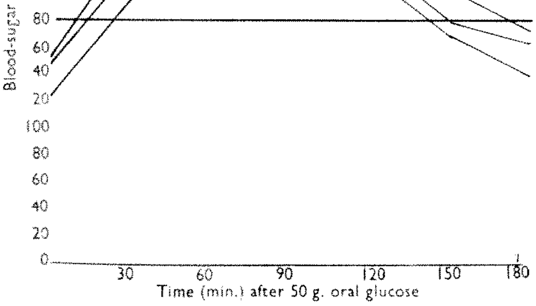

FIG. 30.—*Case* 26. Male, aged 60 years, with symptoms of prostatism and diabetes. Dietary intake before F.F.D.: fat, 1000 cal. per day; carbohydrate, 560 cal. per day. After F.F.D.: carbohydrate, plus 200 cal. per day. Initial weight was 147 lb.; after 120 days, 138 lb.; and after 351 days, 146 lb.

much a symptom of fat intolerance as is impaired G.T. There are at least two types of obesity:—

i. Obesity due to excess dietary fat intake and associated with impairment of G.T. In this type of obesity impairment of G.T. and loss of normal weight regulation are both corrected by the F.F.D.

ii. Obesity not associated with excess dietary fat intake. There is no impairment of G.T. in these cases. These patients do not complain of symptoms of the diseases and disorders discussed earlier in this paper. This type of obesity is not apparently of any sinister import, and if weight must be lost in these patients the calorie intake must be decreased dramatically.

Increase in G.T. on the F.F.D. is not related to previous carbohydrate intake (*Fig.* 1), although there is some evidence that the G.T. is more likely to have been impaired if the carbohydrate intake has been low because in such a diet the fat intake is proportionally higher. At least 3 of the 65 patients in the statistical series presented with symptoms directly attributable to their having attempted to lose weight on a low-carbohydrate diet (*Table XV*). Increase in G.T. on the F.F.D. was independent of change in the carbohydrate intake. There have been no restrictions of or instructions concerning carbohydrate intake on the F.F.D.; in the majority of cases it was increased (*Fig.* 2).

The total number of patients in each of the three different groups of the 'statistical' series was too small for accurate assessment of the relationship of the type of the initial G.T. curve and age. However, the average age of group 1 cases was 42 years, of group 2 52 years, and of group 3 59 years. There were some anomalous cases, but in the series of cases as a whole there appeared to be greater impairment of G.T. as the age of the patient increased. The dietary fat intake tended to be higher in many of the older patients and in those with the greater impairment of G.T.

Himsworth (1933) clearly always suspected that dietary fat played an important part in the causation of diabetes. It is unfortunate that in his studies of the influence of different diets on G.T. he only allowed 5 days for adjustment to diets. It is necessary to allow as long as is necessary for the G.T. to increase on the F.F.D. Himsworth (1935b) suggested that prediabetic obesity was an effect of the type of diet eaten. Himsworth and Marshall (1935) found that diabetics ate more fat than non-diabetics and concluded that this was because they were diabetic. In fact, my findings indicate that they are diabetic because they eat more fat. Himsworth (1935b) suggested that a relatively low carbohydrate diet was a factor determining the onset of diabetes in individuals with a predisposition to the disease, and that if a high-carbohydrate diet was taken a considerable proportion would not develop the disease. However, he concluded that the sugar tolerance of the healthy individual was determined solely by the carbohydrate content of the diet that he received; unfortunately again he only allowed 1 week for a diet to produce an effect (Himsworth, 1935a). In 1939 he stated that the sole dietary factor governing sugar tolerance was the absolute amount of carbohydrate in the preceding diet (Himsworth, 1939). In 1949 he reconsidered the role of fat. He pointed out that the diabetic death-rate tended to fall during wars owing to the food shortage. He could not say that fat was the deleterious factor but found that fat consumption was the dietetic factor most closely related to diabetic mortality (Himsworth, 1949).

My own studies demonstrate that diabetic patients become non-diabetic when they adhere to the F.F.D. and that they revert to the diabetic state when they take fat again. It appears that it is the dietary fat intake that is significant; it does not matter whether the fat is of animal or vegetable in origin because both animal and vegetable fats impair G.T. The length of time during which a high dietary fat intake is present appears to be significant. Butterfield, Hanley, and Whichelow (1965) concluded that obesity was an important factor in the development of diabetes and that carbohydrate tolerance diminished as the duration of obesity increased. However, evidence from the investigation of G.T. reported above points to obesity as merely another symptom of excess dietary fat intake and the duration of obesity must therefore be a measure of the duration of excess dietary fat intake; thus carbohydrate tolerance diminishes as the duration of the excess dietary fat intake increases. This is consistent with my own findings that impairment of G.T. tends to increase with age.

Maturity-onset of diabetes mellitus as seen in this series appears to be an acquired disorder of the metabolism resulting from an excess dietary fat intake over a period of time. It has proved to be reversible if the patient adheres to the F.F.D. and the most dramatic results are those in diabetics who have not had any previous treatment (*Figs.* 19–24). It appears from my investigation in 134 patients that as a consequence of prolonged excess dietary fat intake, probably over many years, with the fat intake also possibly increasing as the years pass, the G.T. gradually becomes more and more impaired till it reaches the stage shown in the initial curve of *Case* 14 (*Fig.* 18). There can be little doubt that if he had continued his high dietary fat intake this patient would have 'jumped the hiatus' noted in *Fig.* 3 and would have become diabetic. At some point a 'breakdown' of some kind must occur (perhaps a switch in metabolic pathways or a change from glucose to fatty acid as the substrate for oxidation—*see below*) and the hyperglycaemic non-diabetic becomes diabetic. No such 'hiatus' in the distribution of the G.T. has been seen during the recovery process when diabetics are becoming non-diabetics.

VI. DISCUSSION

Yudkin (1963) concluded that all species of animals are adapted anatomically, physiologically, and biochemically to a particular sort of diet, i.e., to a particular combination of foods, and that 100,000 years was too short a time for measurable adaptive change from man's early diet. He suggested that a surfeit of calories resulting from increased consumption of carbohydrate was a factor causative of obesity and other diseases in man. Cleave, Campbell, and Painter (1969) blamed refined carbohydrates. Howell and Wilson (1969), however, were not convinced by the evidence and considered that other foodstuffs must play an important role. The evolutionary approach of Yudkin (1963) and of Cleave and others (1969) is attractive and acceptable, but among the patients suffering from dyspepsia, diarrhoea, and lately diabetes whom I have seen and treated carbohydrate was not a causative factor in any. It has always been fat which has caused symptoms or precipitated 'attacks' of pain, and the F.F.D. which has cured symptoms, prevented attacks of pain, been accompanied by weight-loss, has increased G.T. and cured diabetes. In this country for several years before the Second World War fat provided 39 per cent of the total energy of the diet. During the war this figure fell and was 33 per cent in 1947; it rose to 39 per cent in 1954 and to 42 per cent in 1967 (Davidson and Passmore, 1969). The F.F.D. removes on average at least 950 calories of excess dietary fat from the diet per day, while the carbohydrate intake may be unchanged or decreased, but is usually increased. Eighty-six per cent of the excess fat withdrawn from the food intake by the F.F.D. is derived from two domesticated animals, the cow and the pig. The cow has been selectively bred to give a high butter content in milk, and the pig to be fat. These two animals provide a relatively cheap source of energy, and when this is available the human animal takes much more than its metabolic pathways and enzyme systems have been evolved to deal with. Too much vegetable fat is just as poisonous to the human animal; G.T. is impaired and symptoms of dyspepsia and diarrhoea are caused as readily by vegetable fats as by animal fats.

Shipp, Opie, and Challoner (1961) showed that glucose was replaced by fats as the substrate for oxidation in the perfused beating heart when the fatty-acid concentration in the perfusing fluid was raised. Fritz, Davis, Holtrop, and Dundee (1958) found that the rate of oxidation of fatty acids by liver and muscle *in vitro* was roughly proportional to the concentration of fatty acids in the medium. Nestel and Steinberg (1963) demonstrated a similar relation between the concentration and rate of oxidation of fatty acids in the perfused liver, while Challoner and Steinberg (1966) showed the same relationship in the perfused heart. Myant (1968), writing on the subject of the control of cell metabolism, pointed to 'the many cases in higher organisms where enzyme formation is modified by hormones, or by substances which evoke the secretion of hormones, or by metabolites unrelated to the pathway in which the enzyme operates'. He referred to the true induction or repression of many enzymes in animal tissues known to occur in response to changes in the diet, or in the amount of substrate present, or in the balance of hormones. He indicated that the rate of a metabolic process may be influenced by competition between two or more substrates for the same cofactor, and suggested that fatty acids and glucose may compete for a common cofactor. The withdrawal of at least 950 calories of fat (more than 100 g.) from the metabolism each day must clearly have a marked effect on the rate and direction of metabolic reactions and on the availability of pathways. This is the effect of the F.F.D. It must be remembered that the opposite change has taken place, perhaps more gradually, as the excess dietary fat intake was built up.

Clinically, the effect of the F.F.D. is marked by the cure of symptoms, as described earlier in this paper, by appreciable weight-loss in most patients, an average loss of 9 kg. per patient occurring in a series of 50 patients who suffered from gall-stones, and by increased G.T. The patient experiences a subjective 'change' often ascribed to but not satisfactorily accounted for by weight-loss; this 'change' occurs in those who do not lose weight and consists of loss of 'tired feeling', of 'feeling more alive', and of 'feeling better in all ways and able to do and cope with more'. I have investigated only a very small part of the whole metabolism and have shown that G.T. is increased by the withdrawal of excess dietary fat. All metabolic processes are interdependent to a greater or lesser extent, and this change in carbohydrate metabolism must reflect a change in the whole balance of metabolism. As has already been mentioned, there must be a chain reaction of changes throughout the metabolic processes of the whole body until a new state of homeostasis with the new G.T. is reached. The extent of change in each individual must depend upon that individual's gene constitution and the adaptability of metabolic control mechanisms. How far G.T. returns to normal must depend to some extent upon what permanent damage has been done during the period of impaired tolerance and disturbed metabolism, what enzymes have been suppressed, and perhaps how quickly enzymes can be synthesized. Change in the metabolism may act upon control mechanisms by altering the hormone metabolism, or peripherally by altering the individual cell metabolism and perhaps thereby modifying cell function. Almost all patients who adhere to the F.F.D. rapidly lose the desire for fat; many acquire distaste for it. This constant effect of the diet indicates a change in the 'chemistry' of the patient, as does the clinical fact that when a patient who has adhered to the F.F.D. does take fat a very much smaller quantity stimulates symptoms than was the case before dieting.

It cannot be coincidental that the patients in whom I found impaired G.T. and even diabetes were those who were complaining of dyspepsia or diarrhoea or both, or that the F.F.D. cured symptoms and increased G.T. in the same patients at the same time. Nor can it be coincidence that the primary lesion in cases of dyspepsia and diarrhoea is spasm of circular smooth muscle at the site of sphincter action—at the sphincter of Oddi, the pylorus, and the recto-sigmoid junction—or hypertrophy following upon repeated or chronic spasm; or that when limited relaxation of these sphincters results from pathological changes in the muscle layer, thereby preventing complete cure by the F.F.D., a similar operation, sphincterotomy, pyloroplasty, or sigmoidomyotomy, by restoring an adequate lumen in each site cures those cases not cured by the F.F.D.

I have not discussed a series of isolated and independent diseases in this paper, for intolerance is a disorder caused by excess dietary fat intake and characterized by disturbance of the whole metabolic balance. It may present as one or more syndromes in each patient. Diabetes itself is an extreme manifestation of the disordered metabolism, perhaps, as suggested earlier, a 'breakdown' when limits of adaptability have been reached and metabolic pathways have switched or the substrate for oxidation changed. In the digestive system fat intolerance may present as flatulent dyspepsia, or with symptoms and signs referable to the biliary tract, peptic ulceration, or the lower levels of the large bowel. The onset of spasm is often sudden, as in acute attacks of biliary pain; this again suggests a 'breakdown'. (It is interesting and perhaps relevant that an essential lesion in migraine and in coronary artery disease is spasm of circular smooth muscle.) This hypothesis is compatible with the association of dyspepsia and diarrhoea with hormonal changes and with stress noted clinically in so many cases. Wynn and Doar (1966) measured impairment of G.T. caused by the 'pill'. Stress alters hormone levels, mobilizes body fats, and causes spasm (Oliver, Kurien, and Greenwood, 1968).

Treatment of these conditions should, it seems, be directed to the restoration of a more normal metabolism by restricting severely the excess dietary fat intake, rather than by administering drugs to treat individual symptoms such as raised blood-sugar, acidity, or diarrhoea. Surgery should be reserved for those cases which are not cured by the F.F.D. and should be directed at the proper lesion; no purpose is served by removing a gall-bladder if an obstructing or hypertrophic sphincter of Oddi is not also relieved, while pyloroplasty does not require the addition of vagotomy, the latter being merely an attack upon a symptom, and is unnecessary if obstruction at the pylorus is efficiently relieved.

The human animal is adaptable, but there is a limit to adaptation. Farmers have changed the cow and the pig from the animals they once were. By excess dietary fat intake the human animal has been changed from the animal it should be. In the case of the cow and the pig genetic selection has produced new animals. The excess dietary fat-eating human has been changed chemically and not genetically and can only adapt so far and for a time; when the limit of adaptability is reached the diseases and disorders that I have discussed in this paper become apparent.

CONCLUSIONS

1. Fat intolerance is a metabolic disorder associated with impairment of G.T. and caused by excess dietary fat intake.
2. The syndromes of fat intolerance are not different diseases but are due to dysfunction in different parts of the body in response to the same metabolic abnormality which may present as flatulent dyspepsia, surgical disease or disorder in the biliary tract, peptic ulceration, diarrhoea (associated with spasm of the colon, colitis, or diverticular disease), abdominal pain (in children), or diabetes mellitus. One, two, or more of these syndromes may occur in the same patient at the same or different times.
3. The F.F.D., as defined, cures symptoms in the majority of cases and the G.T. is significantly increased on it.
4. The abnormal metabolism of fat intolerance causes spasm of smooth muscle and affects especially the circular muscle-fibres at sphincter sites—the sphincter of Oddi, the pylorus, and the rectosigmoid junction. Spasm is reversible by the F.F.D. When permanent restriction of relaxation is caused by hypertrophy or fibrosis, surgery is necessary for a cure. If hypertrophy or fibrosis of the sphincter of Oddi interferes with the emptying of the gall-bladder or the free drainage of the common bile-duct, sphincterotomy of the sphincter of Oddi is required. When surgical treatment is required for duodenal or gastric ulcer, pyloroplasty alone cures the ulcer. Vagotomy is unnecessary and can be detrimental to the patient.
5. Increase in G.T. results from decrease in dietary fat intake and is independent of the previous carbohydrate intake, of change in the carbohydrate intake, and of weight change. In many cases obesity is only another symptom of fat intolerance.
6. Ten out of 23 diabetic patients have, to the present date, become non-diabetic on the F.F.D. without any other treatment. Diabetes mellitus (maturity-onset) appears to be an acquired metabolic disorder caused by excess dietary fat intake and is reversible; glucose tolerance increases progressively on the F.F.D., and the extent to which recovery is retarded or limited is dependent only on the previous duration of the diabetes and previous treatment by drugs provided that the patient adheres to the diet.
7. Eighty-six per cent of the excess dietary fat intake is derived from cow's milk and the pig which have been selectively bred to produce a high butterfat content in milk and a 'fat' animal respectively.
8. Vegetable fat causes fat intolerance and all its syndromes as readily as animal fat.
9. No evidence has been found that carbohydrate in any form is the cause of symptoms or disease.

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APPENDIX 1: TECHNIQUE OF SPHINCTEROTOMY OF THE SPHINCTER OF ODDI

The following technique has proved to be simple to perform, effective, and free from complications.

The duodenum is mobilized, if necessary, by incising the peritoneum on its lateral border. A longitudinal incision is made in the common bile-duct just below the junction with the cystic duct in the free border of the lesser omentum. A 6/10 urethral sound (Clutton's) is passed down the duct and is gently levered so that the ampulla of Vater, or the tip of the sound if it actually passes through the sphincter and ampulla, can be readily identified through the anterior wall of the second part of the duodenum. An oblique incision, 2·5 cm. long, is made in the anterior wall of the duodenum over the ampulla, which is then delivered by further gentle leverage on the sound. The duodenal mucosa is incised over the tip of the sound; if the tip is already presenting the opening in the mucosa is enlarged by incising against the sound on its right anterolateral aspect for a distance of 2–3 mm. Gentle retraction of the mucosa by dry gauze will then expose the lowermost fibres of the sphincter stretched upon the sound. These fibres are incised against the sound on the right anterolateral aspect until the sound slips through easily. The sound is then withdrawn and replaced by one of size 8/12. Further fibres of the sphincter are incised as above, and the manœuvre is repeated with larger sizes of sounds until a 16/20 sound can slip through the sphincter easily. The lumen is then more than 5 mm. in diameter and the sphincterotomy is complete. The sound is withdrawn, the incision in the duodenum is closed by a single layer of interrupted Dexon sutures, and the incision in the common bile-duct is closed around a T-tube.

If pyloroplasty is necessary at the same operation the sphincterotomy can be performed through the pyloroplasty incision.

APPENDIX 2: TECHNIQUE OF PYLOROPLASTY

The following technique has been found to be most satisfactory.

The duodenum is mobilized, if necessary, by incising the peritoneum along its right lateral border. A long incision is made through all the layers on the anterior surface of the pylorus extending far enough on to the antrum and the duodenum to divide any rigid or constricting segment to decompress the antrum and to prevent duodenal cap systole. The incision is centred on the pyloric ring and extends an equal distance proximally and distally to it. The incision is sewn up transversely (in relation to the lumen) with a single layer of interrupted Dexon sutures placed 0·32–0·64 cm. apart. The lumen of the resulting pyloroplasty must 'take three fingers' when completed. Omentum should be interposed between the pyloroplasty and the under-surface of the liver and the gall-bladder or the gall-bladder bed.

APPENDIX 3: THE ORAL GLUCOSE-TOLERANCE TEST

The test was performed as an out-patient investigation in most cases. The patients were instructed not to eat or drink anything after 9.00 p.m. on the evening before the test. They attended hospital at 8·45 a.m. on the day of the test, and a specimen of blood (for the fasting blood-sugar level) was taken just before 9·00 a.m. Each patient then drank, in turn, a solution of 50 g. glucose dissolved in 500 ml. water. Specimens of blood were taken from each patient at 30-minute intervals for the next 3 hours. Each blood specimen was taken by venepuncture, and estimation of the blood-sugar level was carried out on a Technicon Auto-Analyser by the alkaline ferricyamide technique.

APPENDIX 4: A COMPARISON OF THE GLUCOSE TOLERANCE CURVES OF PATIENTS BEFORE AND AFTER THEY HAVE BEEN ON A FAT-FREE DIET

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Two G.G.T.s were carried out on each of 65 patients. For each patient test 1 was carried out before the patient went on the F.F.D. and test 2 was performed after the patient had been on the diet for some time.

The patients were divided into three groups. Group 1 contained 13 patients whose G.T. at test 1 was considered normal, while group 2 contained 43 patients whose G.T. at test 1 was low, and group 3 contained 9 patients who were diabetic at the time of test 1.

It is required to determine if the F.F.D. has increased the G.T. of the patients and also if the patients in the different groups respond differently to the diet.

Analysis.—A quantity proportional to the area under the G.T. curve was found for each test as it affords a measure that takes into account all the readings of a test. If x_1, x_2, x_3, x_4, x_5, x_6, x_7 are the readings of a test (in the order in which they are obtained), then the quantity found was

$$A = x_2 + x_3 + x_4 + x_5 + x_6 + \tfrac{1}{2}(x_1 + x_7).$$

Since the time interval between each adjacent pair of readings is the same (30 minutes) for comparison

Table IA.—SCORES FOR EACH PATIENT

CASE	SCORE 1: FASTING	SCORE 2: 30 MIN.	SCORE 3: 60 MIN.	SCORE 4: 90 MIN.	SCORE 5: 120 MIN.	SCORE 6: 150 MIN.	SCORE 7: 180 MIN.	SCORE 8: AREA
1	−10·0	−15·0	−5·0	0·0	10·0	−20·0	−10·0	−40·0
2	−25·0	−20·0	−60·0	−35·0	−35·0	−25·0	−10·0	−192·5
3	0·0	−35·0	−5·0	−10·0	−10·0	−15·0	−5·0	−87·5
4	−15·0	−20·0	−5·0	−25·0	−25·0	−15·0	−15·0	−105·0
5	15·0	0·0	−15·0	−10·0	10·0	15·0	15·0	15·0
6	10·0	5·0	15·0	0·0	15·0	−10·0	15·0	37·5
7	0·0	5·0	25·0	25·0	−5·0	0·0	0·0	50·0
8	5·0	−5·0	−35·0	−10·0	5·0	−15·0	−5·0	−60·0
9	−15·0	−10·0	−25·0	−30·0	−25·0	−30·0	−15·0	−135·0
10	−20·0	0·0	0·0	−10·0	0·0	−5·0	−5·0	−27·5
11	5·0	35·0	10·0	15·0	−5·0	−20·0	−5·0	35·0
12	5·0	−10·0	−45·0	−35·0	5·0	10·0	5·0	−70·0
13	−10·0	−20·0	−25·0	0·0	10·0	5·0	0·0	−35·0
14	10·0	25·0	20·0	40·0	35·0	25·0	15·0	157·5
15	0·0	−45·0	−25·0	10·0	40·0	15·0	10·0	0·0
16	0·0	−10·0	−10·0	−10·0	30·0	20·0	−5·0	17·5
17	35·0	15·0	20·0	50·0	35·0	25·0	10·0	167·5
18	0·0	−15·0	−35·0	5·0	30·0	20·0	15·0	12·5
19	0·0	−35·0	−5·0	20·0	0·0	−5·0	0·0	−25·0
20	−5·0	45·0	30·0	−15·0	−15·0	−10·0	−10·0	27·5
21	0·0	0·0	15·0	30·0	15·0	20·0	5·0	82·5
22	−10·0	−20·0	10·0	60·0	−10·0	−10·0	−5·0	22·5
23	−5·0	−10·0	−25·0	−5·0	30·0	80·0	45·0	90·0
24	−20·0	0·0	−10·0	−10·0	5·0	15·0	5·0	−7·5
25	5·0	20·0	25·0	50·0	15·0	10·0	5·0	125·0
26	0·0	25·0	15·0	35·0	30·0	−10·0	−15·0	87·5
27	−5·0	−10·0	25·0	15·0	30·0	5·0	−5·0	60·0
28	5·0	−10·0	−5·0	20·0	10·0	0·0	−5·0	15·0
29	15·0	20·0	−15·0	−25·0	15·0	10·0	20·0	22·5
30	0·0	50·0	15·0	15·0	10·0	0·0	5·0	92·5
31	5·0	40·0	−35·0	−10·0	10·0	0·0	5·0	10·0
32	−5·0	5·0	40·0	20·0	0·0	10·0	15·0	80·0
33	15·0	−5·0	−55·0	15·0	20·0	15·0	15·0	5·0
34	10·0	40·0	30·0	40·0	15·0	0·0	−5·0	127·5
35	0·0	15·0	25·0	15·0	5·0	10·0	−5·0	67·5
36	15·0	35·0	40·0	25·0	15·0	40·0	25·0	175·0
37	0·0	−15·0	60·0	5·0	10·0	−5·0	−5·0	52·5
38	10·0	15·0	10·0	−15·0	−5·0	5·0	5·0	17·5
39	10·0	50·0	45·0	25·0	10·0	−5·0	0·0	130·0
40	15·0	30·0	60·0	20·0	30·0	15·0	25·0	175·0
41	15·0	−5·0	−25·0	20·0	5·0	15·0	10·0	22·5
42	10·0	35·0	10·0	5·0	10·0	5·0	0·0	70·0
43	0·0	15·0	0·0	−5·0	20·0	15·0	15·0	52·5
44	20·0	15·0	35·0	40·0	0·0	5·0	5·0	107·5
45	0·0	0·0	20·0	30·0	25·0	15·0	10·0	95·0
46	5·0	15·0	50·0	15·0	25·0	10·0	5·0	120·0
47	0·0	20·0	55·0	20·0	0·0	−20·0	15·0	82·5
48	−20·0	20·0	60·0	0·0	−10·0	−25·0	−30·0	20·0
49	15·0	30·0	30·0	5·0	−10·0	10·0	10·0	77·5
50	0·0	30·0	40·0	15·0	55·0	35·0	25·0	187·5
51	15·0	15·0	20·0	25·0	50·0	25·0	15·0	150·0
52	5·0	−10·0	25·0	25·0	25·0	25·0	20·0	102·5
53	5·0	25·0	95·0	50·0	40·0	25·0	20·0	247·5
54	−5·0	20·0	55·0	30·0	15·0	0·0	−20·0	107·5
55	10·0	45·0	50·0	−15·0	−20·0	−10·0	0·0	55·0
56	15·0	5·0	10·0	−20·0	−30·0	−5·0	−20·0	−42·5
57	35·0	45·0	70·0	40·0	50·0	40·0	45·0	285·0
58	70·0	65·0	30·0	65·0	80·0	70·0	70·0	380·0
59	45·0	55·0	45·0	65·0	70·0	60·0	70·0	352·5
60	30·0	35·0	40·0	50·0	30·0	30·0	10·0	205·0
61	60·0	70·0	70·0	140·0	130·0	145·0	145·0	657·5
62	45·0	55·0	95·0	130·0	195·0	195·0	170·0	777·5
63	80·0	80·0	95·0	110·0	100·0	85·0	125·0	572·5
64	25·0	25·0	85·0	45·0	10·0	35·0	35·0	230·0
65	25·0	55·0	90·0	125·0	125·0	130·0	90·0	582·5

purposes the use of A is equivalent to the use of the actual areas under the G.T. curves, and in the following we shall refer to A as the area.

For each patient the results of test 2 were subtracted from the corresponding results of test 1, giving eight scores for each patient. Thus, the first score for a particular patient is the decrease in the fasting blood-sugar level over the period that the patient was on the diet, the second score is the decrease in the blood-sugar level at the 30-minute stage of the tests, etc., and the eighth score is the decrease in the area under the patient's G.T. curve. Of course a negative decrease is an increase. The scores for all the patients are given in *Table IA* and the means and standard deviations of the scores for each group are given in *Table IIA*.

Table IIA.—MEANS AND STANDARD DEVIATIONS FOR THE SCORES OF EACH GROUP

GROUP		SCORE 1: FASTING	SCORE 2: 30 MIN.	SCORE 3: 60 MIN.	SCORE 4: 90 MIN.	SCORE 5: 120 MIN.	SCORE 6: 150 MIN.	SCORE 7: 180 MIN.	SCORE 8: AREA
1	Mean S.D.	−4·23 12·39	−6·92 17·14	−13·07 24·37	−9·61 18·31	−3·84 15·83	−9·61 13·76	−2·69 9·70	−46·53 71·64
2	Mean S.D.	4·41 10·18	12·32 22·36	18·48 30·83	15·46 20·72	14·30 18·47	9·76 17·76	5·69 13·95	75·40 64·09
3	Mean S.D.	46·11 19·96	53·88 17·09	68·88 24·97	85·55 40·19	87·77 57·01	87·77 57·06	84·44 53·17	449·16 203·99

Table IIIA.—VARIANCE RATIOS FOR COMPARING THE SCORES OF THE GROUPS IN PAIRS

GROUPS COMPARED	SCORE 1: FASTING	SCORE 2: 30 MIN.	SCORE 3: 60 MIN.	SCORE 4: 90 MIN.	SCORE 5: 120 MIN.	SCORE 6: 150 MIN.	SCORE 7: 180 MIN.	SCORE 8: AREA
1 and 2	1·48	1·70	1·60	1·28	1·36	1·67	2·07	1·25
2 and 3	3·74*	1·71	1·52	3·76*	9·58*	10·32*	14·53*	10·13*

* Significantly different from unity.

Table IVA.—TEST STATISTICS FOR COMPARING THE MEAN SCORES OF THE GROUPS IN PAIRS

GROUPS COMPARED	SCORE 1: FASTING	SCORE 2: 30 MIN.	SCORE 3: 60 MIN.	SCORE 4: 90 MIN.	SCORE 5: 120 MIN.	SCORE 6: 150 MIN.	SCORE 7: 180 MIN.	SCORE 8: AREA
1 and 2	2·464	2·764	3·265	3·790	3·093	3·941	1·950	5·675
2 and 3	C = 0·948 V = 6·104	4·990	4·359	C = 0·947 V = 5·092	C = 0·979 V = 3·824	C = 0·980 V = 4·061	C = 0·986 V = 4·412	C = 0·979 V = 5·440

To test for differences between the three groups a one-way analysis of variance was performed for each of the eight scores. The mean square ratios in all of these were very large, indicating that there were in fact differences for all of the scores. The groups were then compared in pairs and for this it was decided to test the hypotheses that the means for group 2 were significantly larger than those for group 1, and that the means for group 3 were significantly larger than those for group 2. First, the appropriate variance ratios were found and these are given in *Table IIIA*, the starred ratios being those that are significantly different from unity. To compare the means of the pairs associated with the starred ratios Welch's test was used, and for the means of the pairs associated with the other variance ratios, which were not significantly different from unity, t tests were used. The required test statistics are shown in *Table IVA*. Where Welch's test has been used the notation is that used by *Biometrika Tables for Statisticians* (Pearson and Hartley, 1966). The tests show that we can accept the above hypotheses at the 5 per cent level of significance.

The question still remains as to whether the average scores for each group are significantly greater than zero. Here again t tests were used, all at the 1 per cent level, and the test statistics are given in *Table VA*. It was found that none of the scores for group 1 was significantly greater than zero. Since it was considered that the patients in this group had normal G.T. curves initially it may be more appropriate to test the hypotheses that the average scores are different from zero rather than just greater than zero. The result was still not significant for this test. It was found, however, that all the mean scores for both group 1 and group 2 were significantly greater than zero.

Conclusion.—The above tests indicate that while the fat-free diet appears to have had little or negligible effect on the blood-sugar levels of the patients whose G.T. was normal, there is strong evidence to suggest that the patients whose initial G.T. was low had increased their G.T. significantly after they had been on the diet. Moreover, greater increases in G.T. were shown by the diabetic patients. Also the diabetic patients showed more variability in their reactions to the diet than did the other groups of patients.

The question arises as to what constitutes an increase in G.T. Possibly the best measure of G.T. is the area under the G.T. curve and then an increase in the G.T. is represented by a decrease in the area under the curve. There may be a dilemma if some of the first seven scores are significantly greater than zero and some are not, because the interpretation of the results then becomes difficult if it is considered that these seven scores are the important ones. However, the problem does not arise here as all the eight scores give the same result.

Table VA.—Test Statistics for testing the Hypotheses that the Mean Scores for Each Group are Greater than Zero

Group	Score 1: Fasting	Score 2: 30 Min.	Score 3: 60 Min.	Score 4: 90 Min.	Score 5: 120 Min.	Score 6: 150 Min.	Score 7: 180 Min.	Score 8: Area
1	−1·23	−1·45	−1·93	−1·89	−0·87	−2·51	−1·00	−2·34
2	2·84	3·61	3·93	4·89	5·07	3·60	2·67	7·71
3	6·92	9·45	8·27	6·38	4·61	4·61	4·76	6·60

Table VIA.—Further Scores for Some Patients

Case	Score 1: Fasting	Score 2: 30 Min.	Score 3: 60 Min.	Score 4: 90 Min.	Score 5: 120 Min.	Score 6: 150 Min.	Score 7: 180 Min.	Score 8: Area
12	−5	−20	10	−15	25	10	−5	5
13	0	10	15	20	40	30	25	127·5
18	10	−40	−30	45	45	40	35	82·5
33	15	30	30	45	20	5	0	137·5
51	10	70	50	50	35	−5	−20	195
52	35	45	65	50	40	40	45	280
54	35	55	90	70	45	25	10	307·5
56	0	−10	−5	20	−15	−15	−65	−57·5

Table VIIA.—New Means and Standard Deviations for the Scores of Each Group

Group		Score 1: Fasting	Score 2: 30 Min.	Score 3: 60 Min.	Score 4: 90 Min.	Score 5: 120 Min.	Score 6: 150 Min.	Score 7: 180 Min.	Score 8: Area
1	Mean	−4·23	−5·38	−5·77	−6·54	0·00	−7·69	−1·54	−28·27
	S.D.	12·05	17·73	23·44	18·41	21·02	17·27	12·31	86·37
2	Mean	5·81	15·58	22·67	20·12	15·70	10·00	15·23	89·59
	S.D.	11·85	26·12	31·16	23·13	18·57	19·06	18·58	79·48
3	Mean	46·11	53·88	68·88	85·55	87·77	87·77	84·44	449·16
	S.D.	19·96	17·09	24·97	40·19	57·01	57·06	53·17	203·99

APPENDIX 4A: ANALYSIS WITH NEW DATA

Table VIA gives the new scores for the patients with additional data. *Table VIIA*, which corresponds to *Table IIA* of the previous analysis, gives the new means and standard deviations for the scores in the three groups. The other tables of test statistics, etc., have also changed but these have not been included as I feel that a statement of the procedures adopted and not all the details of them is sufficient.

Analysis.—The same procedures as before were used with the new data. To test if the mean scores of each group were greater than zero t tests were used. Also as before t tests and Welch's test were used to compare the mean scores of the groups.

Conclusions.—The conclusions have not changed, but for the sake of clarity let us go into these in a little more detail.

It was pointed out before that the area under the G.T. curve (which is, in fact, a broken-line graph) appears to be a reasonable and objective measure of G.T. Then the area under a patient's before F.F.D. curve minus the area under the patient's after F.F.D. curve is a measure of the patient's increase in G.T. after being on the diet. This measure is, in fact, score 8 in the tables. If we do accept the area as a measure of G.T., and it seems difficult not to, then the following points emerge:—

1. The G.T.s of patients in group 1 have not changed significantly.
2. The G.T.s of patients in both groups 3 and 2 have increased significantly.
3. The G.T.s of patients in group 3 have increased more than those of patients in group 2.
4. The reactions of patients in group 3 are more variable than the reactions of patients in either of the other groups. However, there is a small number of people in group 3 and there are large variations in the reactions of patients within all the groups. Possibly these large variations are due to the large variations in weight changes and days between tests, etc.

In short, using the area under the G.T. curve as a measure of G.T. we conclude that the patients in groups 2 and 3 have significantly increased their G.T.s after being on the F.F.D.

It is notable also that the same conclusions are reached even if it is demanded that significant results should be obtained for each of the first seven scores.

Note on the New Data.—The conclusions have not changed with the new data, as was mentioned above, except that the results for some individual patients are more encouraging. The differences we are trying to detect were marked with the original data, so that the new results on a few patients have not had any large affect.

It is surprising to note that patient 56 has indicated an even greater decrease in G.T. after the longer period on the F.F.D.

Possibilities for Further Analysis.—It would be interesting to pursue the idea that there might be relations between the variables measured on each patient. Also for the patients on which a series of G.T. tests have been done it may be possible to find relations between G.T. and the time on the F.F.D. and to compare these for different patients.

Acknowledgement.—I would like to thank E. C. Tapper, B.Sc., A.F.I.M.A., for the computer programming he has done in connexion with this work.

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THE ORIGIN OF PHLEBOLITHS

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SUMMARY

Phleboliths originate as thrombi in the pelvic veins and are the result of injury to the vein wall.

Although in children the pelvic veins and venous plexuses may be protected by valves, these have disappeared in adult life. In 20 dissections in adult cadavers remnants of osteal valves were sometimes seen, but a functioning bicuspid valve was noted only once.

These unprotected veins are subjected to large and abrupt rises in pressure during normal acts of coughing and straining. Because of this the veins are distended and damage to the intima with the formation of a protective thrombus can occur.

A locally high concentration of phosphatase in the perivesical tissues would explain why these thrombi become calcified in the pelvis and why phleboliths are so rarely found elsewhere.

PHLEBOLITHS are commonly seen in radiographs of the pelvis but their origin has so far remained a mystery. That they are calcified thrombi inside pelvic veins has been known for many years, but what causes such frequent thrombi and why they should become calcified has never been explained.

The aim of the present study was first to ascertain whether the pelvic veins had the protection of valves. Having verified their absence, the next objective was to discover whether there were sufficient pressure changes inside the pelvic veins to damage the vein wall and thus initiate a thrombus. Finally an explanation of why thrombi once formed at this site should, so unusually, become calcified was sought.

HISTORICAL REVIEW

Early anatomists and pathologists (Rokitansky, 1852; Balogh, 1861) had observed the presence of calcified intravenous nodules in their dissections of the human pelvis. Before long it was established that these phleboliths were harmless calcified thrombi in dilated veins (von Recklinghausen, 1883). From then on there was little interest in the subject and phleboliths were forgotten.

With the discovery of X-rays in the early part of the twentieth century phleboliths attracted attention once more. At first radiologists were at a loss to explain the presence of calcified rounded opacities so often seen in radiographs of the pelvis. Many theories were proposed as to their nature. Leonard (1902) suggested that they were due to intestinal concretions and foreign bodies. Von Albers-Schönberg (1906) thought that they were caused by calcification in pelvic ligaments and he mentioned the fruitless discussion on the subject at the Roentgen Congress of 1905. In 1907 a warning was given by Beckett that unnecessary operations were being carried out on phleboliths. He pointed out, as did Orton in 1908, the difficulty in distinguishing between renal stones and phleboliths and advised against operative treatment based on pelvic radiological shadow.

Clark (1909) firmly established the nature of these small opacities so frequently seen on pelvic radiographs. He proved beyond doubt that they were indeed the vein stones of the earlier pathologists. By taking radiographs of the pelvis before and after removal of the soft tissues he was able to show that the calcareous bodies lay outside the urinary tract and were inside the veins. They might be found anywhere in the pelvis but especially close to the line of the lower ureter. They were usually round or oval in shape, varying in number and size, and often bilateral. They were always intravenous, attached to the intima, and surrounded by a thin membrane. He found them to be composed of concentric calcified strata around a central kernel.

The microscopic appearances of phleboliths were described by Ribbert in 1917. He showed all the stages from freshly made thrombi in the periprostatic veins forming a central calcified nucleus to final complete calcification by layers of the whole thrombus.

Culligan reviewed the subject in 1926. He found phleboliths in 39 per cent of 1555 consecutive radiographs of the pelvis. He thought that they were more common in males, but Bützler (1934) and Dovey (1966) disputed this and there is probably little difference in prevalence between the sexes. In Culligan's (1926) series the average age of patients with phleboliths was 37 years; he found none in any patient below the age of 16. The number of phleboliths varied and up to 20 might be present. There was an average size of 4 mm. with variations between 1 and 10 mm. Culligan noted a tendency for the phleboliths to appear in chains.

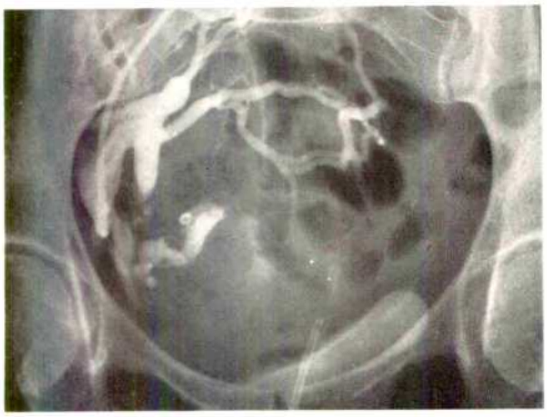

FIG. 1.—Radiograph showing contrast medium pooled in the pelvic veins.

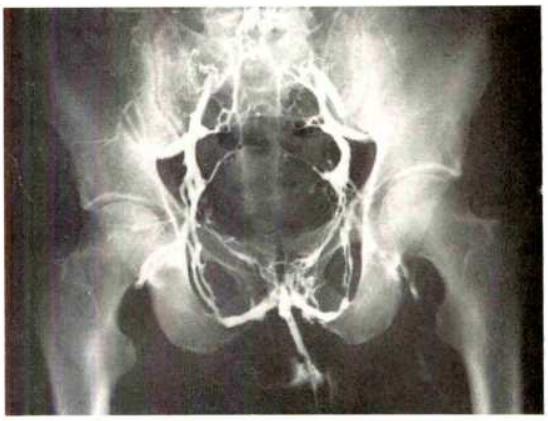

FIG. 2.—Radiograph showing the injection of contrast medium into the deep dorsal veins of the penis.

In the recent series the incidence of phleboliths in the adult population has been estimated at between 30 and nearly 50 per cent (Dillon and Cody, 1928; Dovey, 1966; Green, 1967), the prevalence increasing with age up to the sixth decade but falling slightly thereafter. Significantly Dovey (1966) found no progressive increase in the size of phleboliths in the patients that he followed for up to 9 years. Green (1967), from his estimate of the size of phleboliths at different ages, concluded that phleboliths must form as the result of a process which can occur once or perhaps repeatedly during life, but which lasts a comparatively short time.

THEORIES OF ORIGIN

From the time that they were first described there has been speculation regarding the mode of origin of phleboliths.

Slowing of the blood-stream was the explanation usually given by pathologists in the nineteenth century. Balogh (1861), having examined phleboliths in a patient who died of carcinoma, concluded that malignancy might be a cause.

Clark (1909) gave various explanations: idiosyncrasy, lowered or impaired degree of local venous circulation, congestion, changes in the vessel wall from disease or age, phlebitis, and possibly inflammatory processes in neighbouring structures. He could offer no reason why one thrombus should undergo resolution and another calcification.

Culligan (1926) pointed out that thrombi in other parts of the body only rarely formed phleboliths. It is true that they have been reported occasionally in other sites—in the spleen (Barsony and Schültz 1931), in a varicocele (Sanazzari, 1927), and occasionally in angiomata—but these are exceptional findings. Culligan (1926) believed that stasis in pelvic venous plexuses favoured thrombus formation and he thought that secondary infection from prostatic ducts might play a part. Since the area was poorly nourished the thrombus would become calcified more easily. Dillon and Cody (1928) considered that phleboliths, being rare in patients under the age of 40 years, might indicate by their presence some past disease of the sex organs. Greenburg (1949) mentioned phlebitis as a cause of pelvic thrombi and warned that phleboliths might become dislodged to form emboli. From studies on venograms Dovey (1966) concluded that valves are present in pelvic veins, and that phleboliths might form from non-specific valvulitis.

None of these explanations appears to be convincing. The fact that the blood flows slowly in the pelvic venous plexuses was confirmed during the course of the present investigations. Radio-opaque dye injected directly into the internal iliac veins of patients could be seen pooled in the plexuses for several seconds on the radiographic screen (*Fig.* 1). A sluggish blood-flow could hardly by itself initiate a thrombus, and therefore there would need to be some other factor.

It seems unlikely that infection in the pelvis or genital tract has any large influence determining phlebolith formation. This would mean an unsuspected infection in nearly half the adult population, giving rise to thrombi which are always sterile. Clark (1909) could find no bacteria in any of the phleboliths that he examined.

A theory proposing non-specific inflammation of valves in the pelvic veins implies that valves are scattered throughout the pelvic plexuses. This point was investigated by reference to the literature and by post-mortem dissection of the pelvic veins.

ANATOMY OF THE PELVIC VEINS

Standard descriptions of the pelvic veins show that they consist of a number of intercommunicating plexuses surrounding the viscera. These veins are thin walled and are contained in loose connective tissue. From the plexuses blood drains into the internal iliac veins via the vesical, uterine, vaginal, and middle rectal veins.

VALVES IN THE PELVIC VEINS

It proved unexpectedly difficult to discover from the literature whether or not the internal iliac veins and pelvic plexuses contain valves. Many of the standard works on anatomy either are contradictory or make no mention of this point. Most studies on the iliac veins and their valves seem to have concentrated only on the common and external veins.

Quain (1892) states that there are no valves in the internal iliac veins. Testut (1921) makes no mention of the presence or absence of valves in these veins. Fredreich (1881) states that valves in the common iliac vein are excessively rare, having been found in 4 subjects in 185 examinations. In *Gray's Anatomy* (1967) and Cunningham's *Textbook of Anatomy* (1964) the point is not mentioned.

Fredreich (quoted by Franklin, 1927) stated that no valves are present in the internal iliac veins but that they do exist in their ramifications, opinions differing as to their presence either at their terminations or in the path of these vessels beyond the pelvic confines. Opinions were also divided about the existence of valves in the various venous plexuses such as the middle and inferior haemorrhoidal, vesical, pudendal, and uterovaginal.

Fenwick (1885) remarked on the difficulty in obtaining anatomical preparations of the pelvic venous plexuses. He dissected the pelvic veins in 50 subjects (foetuses, children, and young adults). He insisted that after the age of 25 pathological changes set in altering the anatomy with enlargement of existing veins or the formation of new channels.

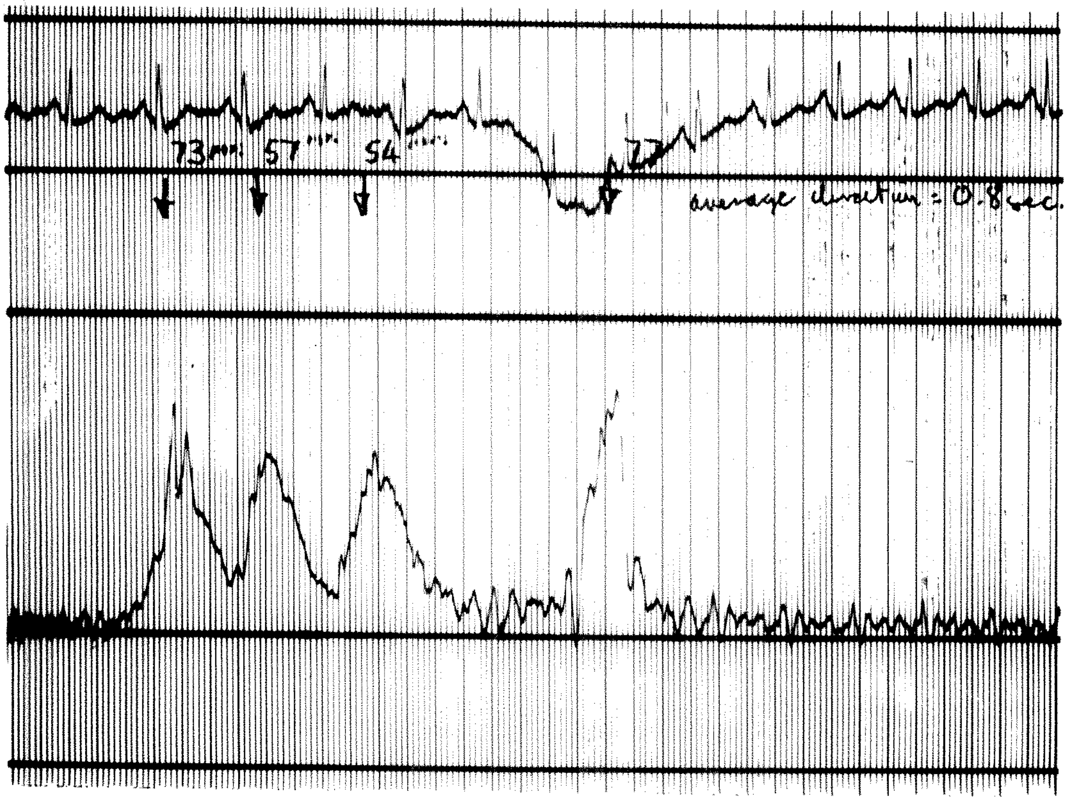

FIG. 3.—The pressure rises in the pelvic veins caused by coughing.

Fenwick concentrated on the vesicoprostatic plexuses in his young subjects and found valves in all parts; one group behind the pubis, another set guarding reflux from the internal iliac vein, and a third set which was less constant and apt to degenerate about the middle of the tract. He recorded that by the age of 38 many of the valves had atrophied and in old age the pelvic veins that he dissected were valveless.

Dodd and Cockett (1956) stated: 'Valves are not described in the internal iliac vein but are said to be found in its tributaries'.

Batson (1942) demonstrated the pelvic plexuses radiographically by post-mortem injection of radio-opaque dye into the deep dorsal vein of the penis. He saw no valves and showed that there was a flow of contrast from the deep dorsal vein into the pelvic plexuses and so into the inferior vena cava. He could not find valves when he dissected the venous plexuses in male and female subjects. His experiment, injecting contrast medium into the deep dorsal vein of the penis in post-mortem subjects, has been repeated in the present study. The radiographs (*Fig.* 2) show excellent filling of the prostatic plexus and of all the tributaries of the internal iliac veins, but no valves could be made out.

In recent years various methods have been used to demonstrate the pelvic veins radiographically. From the evidence of these radiographs it has sometimes been claimed that the internal iliac veins and their tributaries contain valves in almost all cases.

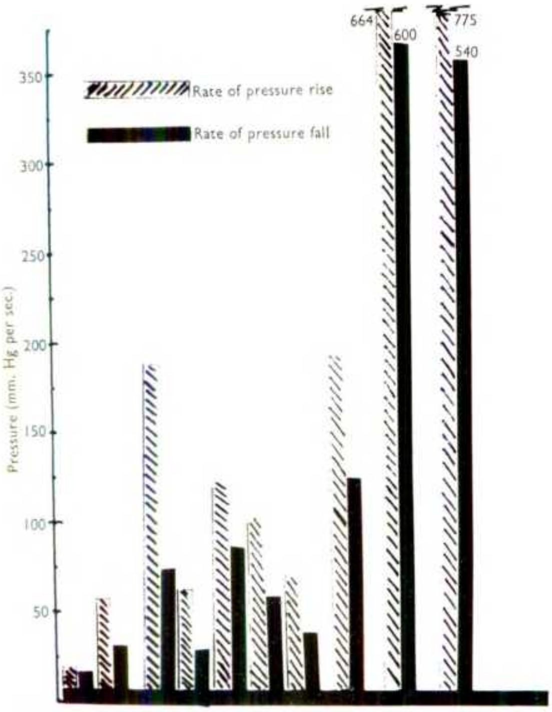

FIG. 4.—The rates of pressure changes in the pelvic veins during coughing and straining.

Helander and Lindbom (1959) injected contrast medium into the external iliac vein bilaterally in 304 patients using abdominal compression to occlude the inferior vena cava. By this means they were able to fill the internal iliac veins by back-flow. In about one-third of their cases the pelvic plexuses were filled and appeared dilated. When the contrast medium was held up in a vessel it was assumed that the block was caused by a valve. Helander and Lindbom considered valves were likely in the internal iliac veins or their branches in 85 per cent of the cases.

Dovey (1966), using retrograde inferior vena cava injection at autopsy on 10 cases, was able to fill the common and internal iliac veins. In all except 1 case the contrast would not flow beyond the internal iliac vein and its tributaries would not fill. He concluded that valves were therefore present, and demonstrated the valves in a few cases by dissecting the main draining veins.

Excellent pictures of the pelvic veins have also been obtained by intra-osseus pubic phlebography (Lea Thomas, Fletcher, Andress, and Cockett, 1967).

The recent studies of pelvic venography apparently contradict the findings of the anatomists, who were unable to demonstrate valves in the internal iliac vein or its tributaries in the pelvis in adults.

In order to settle the question the pelvic veins were dissected in 20 subjects at autopsy. The dissections were carried out mainly on elderly subjects, none being younger than 25 years.

DISSECTIONS

The inferior vena cava was opened and the dissection extended downwards into the pelvis, opening the common and internal iliac veins on each side. At this point the visceral contents of the pelvis were removed *en bloc* and the tributaries of each internal iliac vein were dissected as far as the pelvic viscera.

No valves or remnants of valves were seen in the common or internal iliac veins in any subject. Every tributary of the internal iliac vein entered it at an oblique angle, tending to provide it with a valvular type opening. Were this oblique entrance protected by a fold of intima it could act as an osteal valve. In the subjects dissected no osteal valves were seen, but sometimes a thin crescent of intima betrayed the presence of a possible osteal valve which had atrophied. In 1 subject only a bicuspid valve was discovered in the vesical tributary of the right and left internal iliac veins. No valves of any kind, osteal or bicuspid, were seen in the pelvic plexuses. These veins varied in size along their course, in some places being dilated and in others narrowed. Occasionally the intima appeared rippled or scarred, the possible site of previous intimal damage.

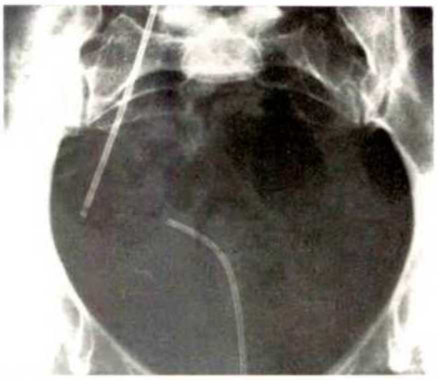

FIG. 5.—Radiograph showing catheters inside the internal iliac vein and the bladder.

It seemed likely that since in adults the pelvic venous plexuses are not protected by valves they might be subject to gross variations of intraluminal pressure.

PHYSIOLOGICAL STRESSES ON THE PELVIC VEINS

Alterations in pressure in the inferior vena cava can be transmitted directly downwards to the pelvic veins. This could not happen in the veins of the legs since the abdominopelvic venous blood-pressure is always shut off from that of the lower extremity by efficient valves (Fenwick, 1885).

Sudden alterations in venous pressure normally and frequently happen in coughing and straining. Franklin (1927) noted this in the efforts of difficult defaecation, micturition, parturition, or violent coughing. Halpern, Selman, Shaftel, Samuels, Shaftel, and Kuhn (1959) recorded the venous pressures in the limbs during the act of straining at defaecation. They observed that with controlled straining efforts the venous pressure in the extremities rose in proportion to the magnitude of the strain. Sharpey-Schafer (1960) has noted pressures reaching 400 mm. Hg in the vena cava of strong males with coughing.

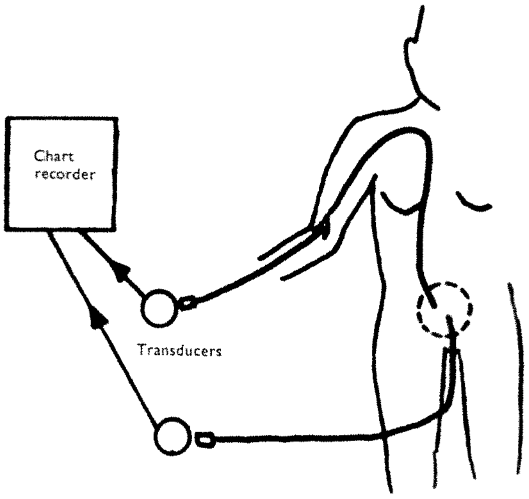

FIG. 6.—Diagram of the experiment recording pressures in the internal iliac vein and the bladder.

It seemed possible that in the pelvic veins without valvular protection, pressure changes on muscular effort might be sudden and dramatic. These veins are thin walled, tortuous, and poorly supported by the surrounding tissues. They are thus ill equipped to withstand alteration in venous pressure except by distension.

EXPERIMENTS ON PELVIC VENOUS PRESSURES

The first experiments to record pelvic venous pressures were carried out by inserting a catheter in the internal iliac vein and connecting it to a transducer. In order to achieve this a No. 7 Goodale-Lubin plastic catheter used during the course of cardiac catheterization was inserted into the right brachial vein under a local anaesthetic. The patient was supine and conscious but under light sedation. The catheter was advanced into the superior vena cava through the right auricle and down the inferior vena cava. Guiding the catheter under radiographic control the tip was seen to reach the internal iliac vein where it was arrested.

A continuous recording was made of the pelvic venous pressure with the patient supine, first at rest and then during the acts of coughing and straining (*Fig.* 3).

From the graph obtained (*Fig.* 4) it was seen:—

1. There is a sudden abrupt rise in the pelvic intravenous pressure during the act of coughing or straining.

2. The height of pressure is proportional to the magnitude of the effort, up to 140 mm per cent Hg being recorded with a violent cough.

3. As soon as the strain is over the pressure returns to normal, but the rate of descent is always slower than the rise, indicating distension of the venous bed.

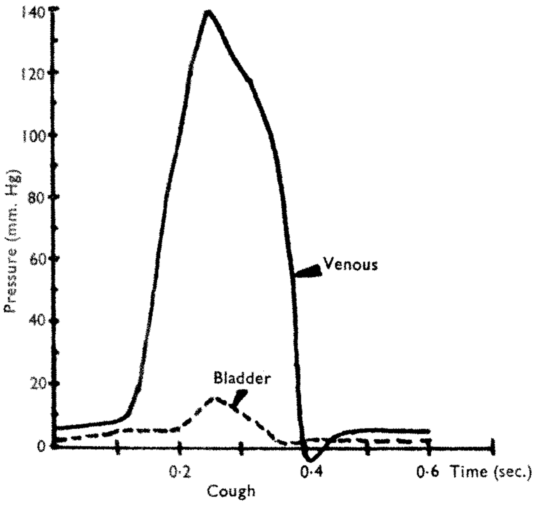

FIG. 7.—Simultaneous pressure recordings from the internal iliac vein and the bladder during coughing.

These recordings of pressure variations inside the pelvic vein give no information of the tension or pressure gradient on the vein wall since intravenous pressures might be protected by equivalent pressures in the pelvis generally. To obtain the pressure gradient on the vein wall, measurements of the pressures inside the vein must be matched with those outside in the pelvic cavity recorded simultaneously. In order to achieve this the second experiments were carried out with a catheter in position in the internal iliac vein as before, but this time with an identical Goodale-Lubin catheter in the bladder (*Fig.* 5). It was assumed that the pressure inside the undistended bladder would be that of the pelvic cavity.

In another set of experiments simultaneous pressure tracings were again taken from the intravenous and bladder catheters with the patients supine, at rest and then during acts of coughing and straining. This time twin transducers were used (*Fig.* 6).

The graph (*Fig.* 7) shows that in every case the pressure in the pelvic veins rose much higher and more quickly than that in the bladder during efforts of coughing and straining.

RESULTS

The experiments appear to prove the following:—

1. There is a large and abrupt rise in pelvic intravenous pressure during normal acts of coughing and straining.

2. There is a pressure difference across the vein wall since the pressure outside does not match the intravenous pressure.

3. The pelvic veins are distended by these pressures.

It is known that violent coughing or forcible straining at defaecation can cause overdistension and even rupture of the inferior haemorrhoidal tributaries of the rectal plexus, resulting in a visible perianal haematoma.

It seems likely that similar events occur in the intrapelvic venous plexuses as a result of sudden muscular strains. The delicate vein wall is overdistended and the intima is damaged, resulting in an intramural thrombus. The thrombus formation is a protective reaction to a wound inflicted upon the vascular wall, and the characteristic of the condition is that the thrombus remains localized and does not increase in size (Franklin, 1927).

Thrombi are frequently formed in the pelvic venous plexuses, and the most likely cause would appear to be venous damage brought on by straining at defaecation, by violent coughing, or at parturition. The thrombus may be large or small but it is symptomless and it would form only in adults since in children the pelvic veins have the protection of osteal valves.

CALCIFICATION

It has never been explained why the thrombi in the pelvic veins become calcified. Clots in this situation apparently remain localized and exhibit dystrophic calcification. This deposition of lime in dead and dying tissue is dependent on local conditions and is not initiated by the state of calcification in the circulating blood (Barr, 1932).

Of the many theories suggesting a cause for dystrophic calcification, that of a locally high concentration of phosphatase (Robinson, 1923) would best explain the formation of phleboliths.

Huggins (1931) found that transplants of bladder mucosa stimulated bone formation in the connective tissues of dogs and rabbits. This did not happen when other tissues were transplanted. He showed also that when cysts were formed by bladder-mucosa transplants the cyst fluid contained much more calcium and phosphorus than did the blood-serum. Huggins explained this by assuming the presence of a phosphatase in higher concentration in the bladder mucosa and perivesical tissues than elsewhere.

If, as Huggins's (1931) experiments appear to show, there is an increased amount of phosphatase in the tissues near the bladder this would account for the surprisingly regular deposition of calcium in the thrombi in the pelvic veins.

Acknowledgements.—I am indebted to Dr. Alan Johnson for allowing me to make recordings during the course of cardiac catheterization, and I am grateful to those patients who gave their informed consent for the additional tests to be carried out. I also wish to thank Mr. Robert David Chase, of the department of Electronics, Southampton Chest Hospital, for his help with the preparation of graphs and diagrams.

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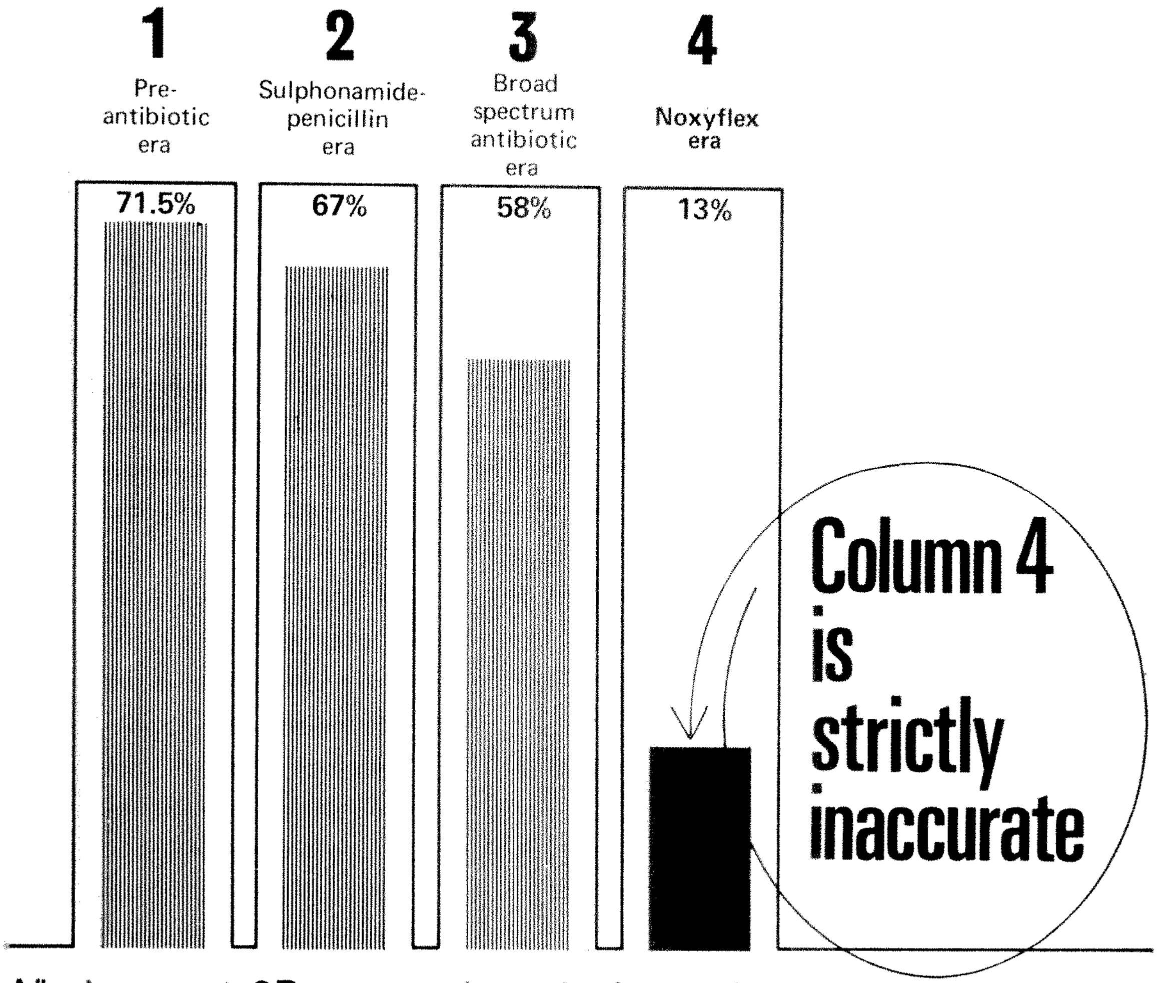
The graph below compares mortality rates due to faecal peritonitis, era by era.
It is not pedantically accurate because its sources differ. But the point is fairly made.



Column 4 is strictly inaccurate

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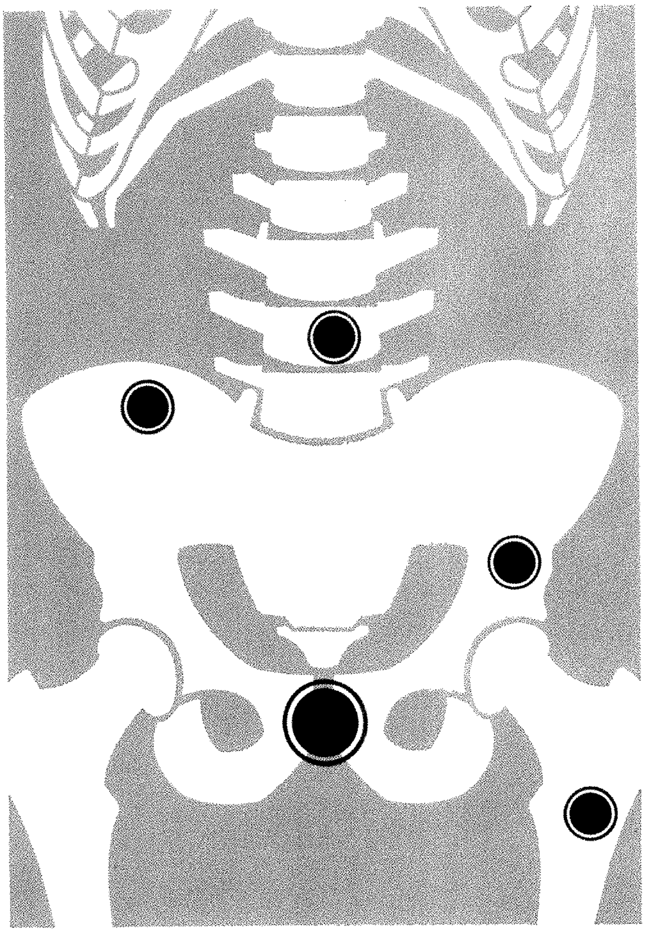

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FEMORO-FEMORAL CROSS-OVER GRAFTS

A REPORT OF 7 CASES

By R. BAKER and E. J. C. PARKER
SURGICAL UNIT, THE LONDON HOSPITAL

SUMMARY

Seven patients who had femoro-femoral by-pass grafts are reported and the results are noted.

The value of the operation in poor-risk patients with unilateral disease and ischaemic rest pain is confirmed. It is suggested that the indications for doing this procedure could be extended.

FEMORO-FEMORAL cross-over grafts using either a Dacron prosthesis or autogenous saphenous vein have been successfully employed in a small number of patients over the past 10 years. They represent a useful palliative procedure in patients with unilateral iliac artery obstruction in whom poor general condition or the presence of local pathology renders major abdominal surgery unduly hazardous. This paper presents 7 patients who had cross-over grafts and suggests that the indications for the procedure might be extended.

TECHNIQUE

Under general anaesthesia both common femoral arteries were exposed and their branches controlled. A pre-clotted 8- or 10-mm. Dacron prosthesis or autogenous saphenous vein was passed subcutaneously above the pubis from one femoral artery to the other, and end-to-side anastomosis was performed using continuous 00000 Dacron. *Fig.* 1 shows a Dacron graft in situ.

RESULTS

The patients selected for the procedure all had ischaemic disease of the legs of a predominantly unilateral distribution. *Fig.* 2 shows the angiograms of *Case* 5, demonstrating a complete block of the left common iliac artery with comparatively little disease on the right side. All the surviving patients were seen for the purpose of this survey and the results are given in *Table I.* A graft was considered successful if it improved the perfusion of the affected limb without prejudicing the circulation in the donor limb. The graft produced a successful result in 5 patients, although in 1 of these (*Case* 3) infection and secondary haemorrhage necessitated its removal 5 months later. In a sixth patient (*Case* 1) the graft failed to maintain an effective circulation and this necessitated the only amputation in the series. It is possible that the insertion of the graft allowed this to be below the knee rather than above the knee. In only 1 patient (*Case* 7) did the graft have an adverse effect on the donor limb. In this man the recipient limb became warm and the rest pain was relieved although no pulses returned. The donor limb, however, developed severe rest pain on the sixth postoperative day which resolved over the succeeding 3 days. When seen in the out-patients' department 6 months postoperatively the recipient limb was symptom-free and had an ankle pressure of 130 mm. Hg with a systolic pressure of 160 mm. Hg, but no pressure could be recorded in the donor limb which claudicated at 10 yards.

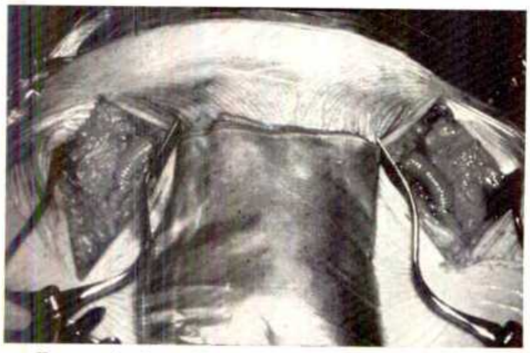

FIG. 1.—An 8-mm. Dacron femoro-femoral graft in situ.

DISCUSSION

History.—Since McCaughan and Khan recorded 2 successful cross-over grafts in 1960 this procedure has been recommended by a number of writers (Vetto, 1962; Papadopoulos, 1966; Warren and Fomon, 1966; Chavez, Hardy, and Tucker, 1967; Parsonnet, Alpert, and Brief, 1970) as a palliative procedure in poor-risk patients with unilateral disease of the lower limb.

The value of the procedure rests in the fact that it is a relatively minor operation which may be completed within an hour, especially if the two anastomoses are performed synchronously.

Indications.—These consist of the systemic conditions of previous cardiac infarction, severe bronchitis and emphysema, old age and debility, and the local problems of previous aorto-iliac surgery and retroperitoneal disease. It is also useful to revascularize the remaining limb of an amputee, provided that the femoral pulse is still present on the side of the amputation (Wertheimer, Sautot, Sisteron, and Descotes, 1963).

The Assessment of Patients.—Patients with arteriosclerosis rarely have unilateral disease, although its disposition is sometimes predominantly unilateral.

The major difficulty when considering a patient for this procedure lies in assessing the state of the circulation in the donor limb. It is of little value to revascularize one limb at the expense of the other, as happened to some extent in the present *Case* 7.

This 'steal' phenomenon cannot occur in health. Parsonnet and others (1970) have shown experimentally that the normal rate of flow through a healthy artery is capable of a tenfold increase; they have also demonstrated that if a recipient limb having the same flow resistance as a donor limb is connected to the donor inflow vessel, then the peripheral resistance presented to that vessel is halved and its flow rate doubled.

Clearly, however, it seems reasonable to accept some degree of proximal iliac disease on the donor side; the difficulty lies in determining how much is acceptable and in assessing the situation in the individual patient. Wertheimer and others (1963) stress the danger if the circulation of the donor limb is suspect, and Foley, Dow, and Fry (1969) report a failure in which the donor limb showed ischaemic changes preoperatively. The present *Case* 7 also demonstrates the dangers of a poor circulation in the donor limb. Preoperatively this man was noted to have no pulses

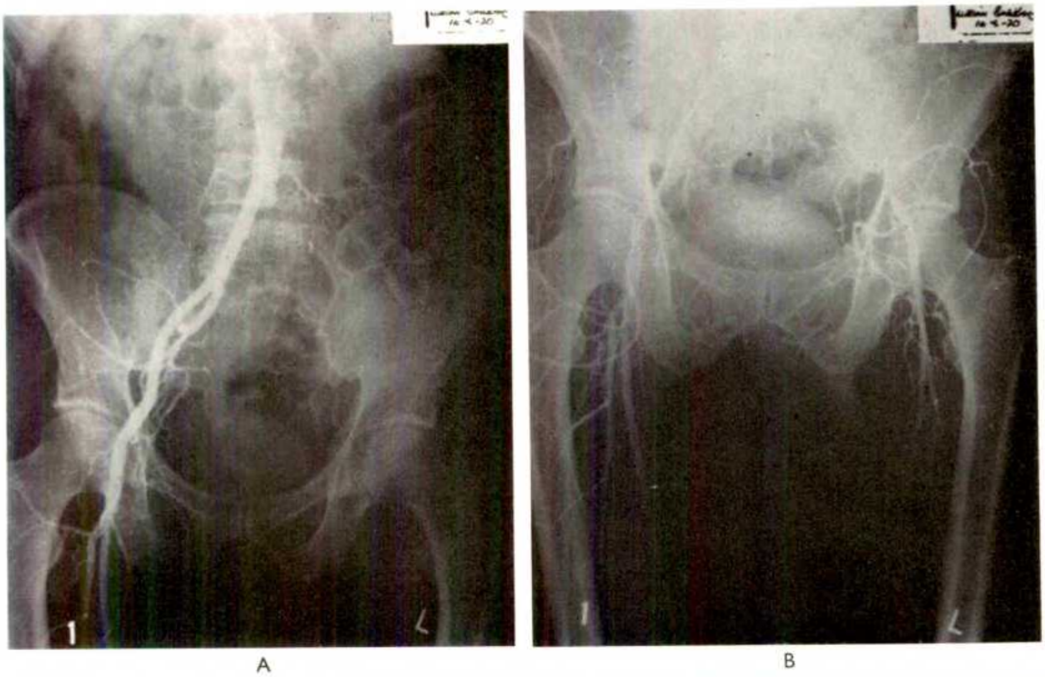

FIG. 2.—*Case* 5. Angiograms showing a complete block of the left iliac artery with retrograde filling of the left common femoral artery and comparatively little disease on the right side.

Table I.—DETAILS AND RESULTS IN

CASE NO. AND SEX	AGE AT OPERATION (years)	INDICATION FOR CROSS-OVER GRAFT RATHER THAN AORTO-ILIAC SURGERY	DISEASE OF RECIPIENT LIMB	DISEASE OF DONOR LIMB	RESULT
1 F.	54	Poor general condition	Total block of common iliac artery	Nil significant	Failure to preserve li knee amputation
2 M.	64	Ischaemic heart disease; cerebral emboli	Total embolic block of common iliac artery	Nil significant	Success
3 F.	57	Previous retroperitoneal disease and deep X-ray therapy to para-aortic nodes (secondary carcinoma of cervix)	Total block of common iliac artery (probably extrinsic)	Nil significant	Success (became infec to secondary haemo
4 F.	57	Ischaemic heart disease and previous aorto-iliac surgery	Stenosis of common iliac artery	Iliac disease and block of superficial femoral artery; 1 pedal pulse present	Success (rest pain relie claudicates at 100 yc later
5 M.	55	Recent cardiac infarction	Total block of common iliac artery	Moderate iliac disease, but all pulses present and full	Success (rest pain relie pressure 95 mm. Hg sides; systemic 145
6 F.	55	Retroperitoneal fibrosis and infection; operative trauma to common iliac artery	Ligation of common iliac artery	Nil significant	Success; walks > 1 mil pressure = systolic af
7 M.	78	Previous aorto-iliac surgery; chronic bronchitis	Occlusion of common iliac and superficial femoral artery	Iliac disease and block of superficial femoral artery; no pulses distal to diminished femoral	Partial success; recipie pressure 130 mm. H ankle pressure 0; sys sure 160/90

in the donor limb distal to a diminished femoral and this probably represented a contra-indication to the procedure. The only other patient in our series with clinically detectable disease in the donor limb was *Case* 4, who had a superficial femoral block although the common femoral pulse was full and one pedal pulse was present. *Case* 5 had radiologically demonstrated donor iliac disease, but all the pulses were full on clinical examination. All the other patients had full donor pulses on clinical examination at rest. Preoperative angiograms were performed in *Cases* 2, 3, 4, and 5. Preoperative ankle pressures measured with the ultrasonic probe (Yao, Hobbes, and Irvine, 1969) were not taken, but we feel that these would have provided valuable information. Postoperative pressures in all the surviving patients are given in *Table I*.

Choice of Material.—Saphenous vein-grafts were used in 2 patients and Dacron in the remaining 5.

Saphenous vein-grafts have the advantage that there is less risk of infection and false-aneurysm formation, and the vein is more tolerant of angulation (Ehrenfeld, Levin, and Wylie, 1968). However, the vein may become involved in the occlusive process, and this may be a cause of late failure. In addition, dissection and removal of the saphenous vein increase the operating time significantly for poor-risk patients.

Dacron has the advantage that it can be put in quickly and in the series reported so far compares very favourably with saphenous vein-grafts, although the danger of infection and secondary haemorrhage is well illustrated by the present *Case* 3.

Factors which may affect Graft Survival.—Turbulence at the site of take-off and run-in of the graft may predispose to thrombosis. Ideally an angle of 15° for take-off gives the best flow pattern (Parsonnet and others, 1970), but this is technically difficult to achieve without the risk of angulation. Blaisdell (Vetto, 1966) has shown experimentally that proximal turbulence does not affect flow through the graft, which is governed more by the peripheral resistance, i.e., the run-off.

The success of these grafts may depend upon the profunda artery, which is usually patent even in severe arterial disease. Jepson, Harris, and Miller (1970) have stressed this and Vetto (1962) reports a case where a popliteal pulse reappeared following direct anastomosis of the graft to the orifice of the profunda artery.

Endarterectomy of the orifice of the profunda artery should be done if it is narrowed (Vetto, 1966). This was not necessary in any of our patients.

Despite the disadvantages of an implant of any foreign material Dacron gives good results (Parsonnet and others (1970) report no late failures in 30 by-passes), possibly because the graft is relatively short and the prosthesis is wide and grafted between major arteries. The most likely causes of early failures are inadequate run-off, as may have happened in *Case* 1, and technical errors.

Late failure may be due to progression of the occlusive process in the donor iliac vessels. The disease may also progress in the distal recipient vessels, progressively reducing run-off. However, it has been suggested that distal disease in the donor limb may even be arrested owing to the altered haemodynamics following grafting in which there is increased linear blood-flow and decreased lateral wall tension (Vetto, 1966).

CONCLUSION

A cross-over femoro-femoral graft is a good treatment for poor-risk patients with rest pain. The risk of 'stealing' from the donor limb seems much less than might be expected, even in the presence of some

FEMORO-FEMORAL CROSS-OVER GRAFT

AFT	DURATION OF PATENCY	EFFECT ON DONOR LIMB	INDICATION FOR OPERATION	COMMENT
cron	Not known	Nil of clinical significance	Rest pain	The cross-over graft may have allowed a below-knee rather than an above-knee amputation
s vein	10 months (patient died)	Nil of clinical significance	Rest pain	Graft patent at death 10 months later of unrelated cause. Incipient gangrene relieved and amputation avoided. Good result
cron	5 months (graft removed—patient died following this)	Nil of clinical significance	Rest pain	Previous para-aortic disease, together with radiotherapy, would have made any transperitoneal surgery difficult. Pedal pulses returned following graft
s vein	Blocked at 3 months	Nil of clinical significance	Rest pain	Femoro-femoral by-pass clearly benefited this patient initially, although the sustained improvement following thrombosis of the graft must have been due to the development of further collateral vessels
acron	Patent at more than 7 months	Nil of clinical significance	Rest pain	A good result. Pre-gangrene in a patient who had had a recent infarct compelled surgical intervention under unfavourable conditions
cron	Patent at more than 23 months	Nil of clinical significance	Operative trauma	The left common iliac artery was injured at operation. Previous retroperitoneal infection and adhesions around the iliac vessels precluded prosthetic graft reconstruction in this area. No other procedure would have been of value
cron	Patent at more than 6 months	Claudication at 12 yd. (minimal previous symptoms)	Rest pain	This patient ultimately derived benefit from the operation in that he was relieved of rest pain. Normally the presence of severe ischaemia in the donor limb is a contra-indication to cross-over grafting (*see* Discussion)

proximal iliac disease (e.g., *Case* 5), and, as mentioned, it may even arrest the progress of distal disease. In view of this we suggest that the indications for this procedure might perhaps be extended, and that it should be considered as an alternative primary procedure in some patients who normally would undergo aorto-iliac surgery.

Acknowledgement.—We would like to thank Mr. D. G. A. Eadie for permission to report cases under his care.

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AXILLARY-FEMORAL BY-PASS GRAFTS IN THE TREATMENT OF AORTO-ILIAC OCCLUSIVE DISEASE[*]

BY A. V. POLLOCK
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SUMMARY

Seventeen patients with aorto-iliac occlusive disease have been treated by inserting a Dacron by-pass prosthesis subcutaneously from the axillary artery to the common femoral artery, with acceptable immediate and poor late results. Only 4 grafts remained patent for more than a year.

MANY patients who present with intermittent claudication and who are found to have an absent common femoral pulse are so little disabled that they are best managed conservatively. They are encouraged to stop smoking, to take regular walking exercise, and to avoid injury to the limb. In this way they can be maintained in reasonable comfort until death as a result of the visceral lesions of the underlying arteriosclerosis.

There are, however, certain patients with an absent common femoral pulse who have incapacitating claudication, rest pain, or gangrene, and for whom the surgeon must advise operation. For the relatively young, fairly fit patient with a short iliac occlusion, laparotomy and thrombo-endarterectomy may be the best treatment. When the occlusion is more extensive it is preferable to insert a synthetic prosthesis from the aorta or an iliac artery to one or both common femoral arteries.

Some patients have an iliac occlusion which is technically operable but their general condition is so poor that a major laparotomy is dangerous. If these patients complain only of claudication, however distressing, one cannot recommend operation. If, on the other hand, the patient presents with rest pain or gangrene, operation becomes mandatory. When gross ischaemia is the problem there is nearly always a coexisting superficial femoral or popliteal artery occlusion in addition to the iliac artery occlusion, but restoration of a full flow through the profunda femoris artery always improves these patients and usually allows healing of the gangrene (Foley and Fry, 1968).

Quite apart from the patient who may die as a result of exposure of his abdominal aorta, there are a few cases in which it may be technically inadvisable or impossible to use this vessel as the starting point of a by-pass graft. The aorta (or a previously inserted prosthesis) may be infected or it may be so heavily calcified as to defy surgery.

In all these conditions it is attractive to consider the possibility of revascularizing the common femoral artery without opening the abdomen.

Blaisdell and Hall (1963) and Louw (1964) published the first accounts of the use of a prosthesis to convey blood through a subcutaneous tunnel from the axillary artery to the common femoral artery.

The present author first employed the method in November, 1969, for a patient whose respiratory function was so poor that laparotomy was inadvisable, and has now used it 17 times. The indications for this relatively minor operation were extended so that even patients who were not at risk from a laparotomy but who required surgery were offered an axillary-femoral by-pass graft as an alternative to the more serious operations.

TECHNIQUE OF OPERATION

The common femoral artery on the ischaemic side is explored through a high oblique incision. Retraction of the lower leaf of this incision allows adequate exposure of the common femoral artery and its bifurcation. Approximately 3 cm. of the lower part of the artery are cleared, encircled with tape, and clamped. The superficial femoral and profunda femoris origins are also controlled and clamped. An incision into the vessel near the bifurcation allows inspection of the profunda origin. If the lumen at this point is compromised by an atheromatous plaque this is dealt with by endarterectomy. The end of a 6-mm. knitted, crimped, Dacron prosthesis 50 cm. long is bevelled and anastomosed to the common femoral artery. The femoral clamps are removed and the prosthesis is filled with blood and clamped near its insertion into the common femoral artery (*Fig.* 1).

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[*] This paper is based on a communication to the Vascular Surgical Society of Great Britain and Ireland in May, 1971.

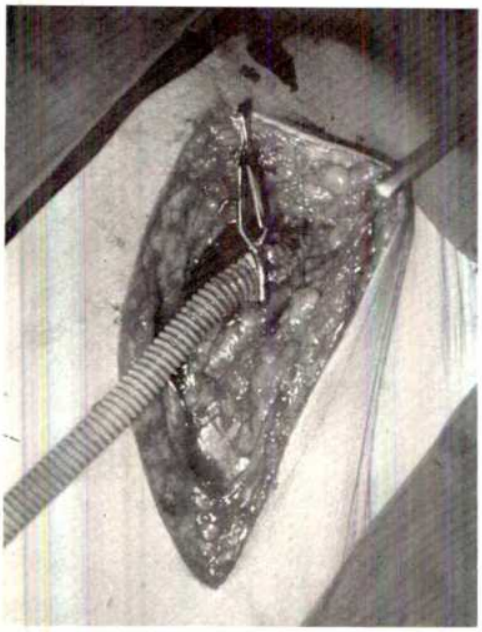

FIG. 1.—The completed anastomosis of the prosthesis to the right common femoral artery.

Table I.—DETAILS OF 17 CASES HAVING AN AXILLARY-FEMORAL BY-PASS GRAFT

Details	*No. of Cases*
Sex	
Male	15
Female	2
Age	
Under 60 years	5
60–69 years	7
70–79 years	5
Diabetic	2
Cigarette smokers	17
Occlusion of femoropopliteal artery on same side as iliac occlusion	15
Occlusion of femoropopliteal artery on opposite side to iliac occlusion	14
Presenting symptoms	
Incapacitating claudication	6
Rest pain or gangrene	11
Preoperative pulmonary function	
Good	7
Moderate	4
Poor	6
Preoperative cardiac function	
Good	9
Moderate	1
Poor	7
Condition of common femoral artery	
Fair	4
Poor	13
Condition of axillary artery	
Good	14
Fragile	3

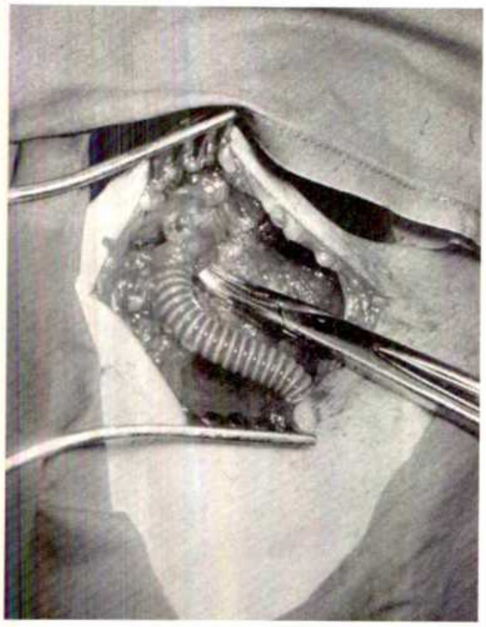

FIG. 2.—The completed anastomosis of the prosthesis to the axillary artery.

The first and second parts of the axillary artery on the same side are exposed by an infraclavicular incision. The fibres of pectoralis major are split or divided in the line of the incision and the clavipectoral fascia and pectoralis minor muscle are divided. The axillary vein is retracted and a 3-cm. length of the first and second parts of the axillary artery is cleared and controlled.

An oesophagoscope is thrust deep to the pectoralis major and through the subcutaneous tissue of the chest and abdomen until it emerges in the groin wound. The end of the prosthesis is grasped by biopsy forceps and drawn up to the axillary artery through the oesophagoscope. It must not be twisted. The oesophagoscope is withdrawn and the graft is trimmed to the correct length and anastomosed to the axillary artery (*Fig.* 2). We find that the resistance to tearing is much less in the axillary artery than in the femoral artery, though the former seldom shows signs of atherosclerosis.

As a rule heparin is not used but low-molecular-weight Dextran is infused during and after the operation. If the prosthesis clots the patient is given heparin and the clot is cleared by means of an embolectomy catheter.

The entire operation can be conducted with light general anaesthesia and spontaneous respiration. The patient soon recovers and shows little tendency to shock. Blood transfusion is seldom necessary.

After operation the graft pulse can usually be felt quite easily but sometimes it can only be detected by a stethoscope or an ultrasonic flow detector.

CASE MATERIAL

Details of the 17 cases which had an axillary-femoral by-pass graft are shown in *Table I*.

In 7 patients an embolectomy catheter had to be employed to clear a blocked prosthesis soon after operation. In each case it was successful and the graft did not immediately occlude again. One of these patients died 3 days after operation of a coronary artery occlusion, and 5 of the remaining 6 grafts occluded again within 6 months. Three patients suffered intimal damage to the axillary artery with resultant thrombosis of the artery beyond the site of the graft. There were no ischaemic manifestations in the hand in any of these patients.

RESULTS

Postoperative complications were few and there were 2 deaths. One patient became temporarily uraemic, 1 groin wound developed a minor *Escherichia coli* infection, and 3 patients had coronary thromboses from which 2 made satisfactory recoveries and 1 died on the third postoperative day. The other death was from coma due to treated cardiac arrest associated with diabetic acidosis 24 hours after operation. All except 3 patients were discharged from hospital in less than 14 days. These 3 patients were delayed up to 20, 32, and 35 days for the treatment of uraemia, pre-existing gangrene of the heel, and coronary thrombosis respectively. All the grafts were patent at the time of discharge.

The follow-up period was from 13 to 32 months.

The symptoms of claudication or rest pain and gangrene were improved in all the cases by operation. In 6 patients the graft clotted within 3 months and 5 of these were re-explored. In 1 case a further profunda endarterectomy has relieved the ischaemia of the lower limb and no further treatment is contemplated. In the others the clot was quite easily removed from the graft and the patients were maintained on heparin for a week but patency was not maintained. The sixth patient is not living in the area and further treatment was undertaken locally.

In addition to these failures 5 grafts clotted within a year without causing disabling ischaemia, and another patient had an amputation because of spread of infection from a gangrenous toe although his by-pass graft was working. A further patient had the opposite leg amputated for gangrene. Four patients have died since discharge from hospital, 3 from cardiac failure and 1 from carcinoma of the bronchus. The first graft was still patent when last seen 22 months later.

DISCUSSION

In order to make a comparison with this series of axillary-femoral grafts the author has reviewed 63 of his own cases of aorto-iliac occlusion in all of which major surgery was indicated.

Nine out of the 63 cases were rejected after cardiac and respiratory assessment. Of the remaining 54 cases, 9 females were operated on, with 1 death from shock and haemorrhage soon after operation, and 45 males with 9 deaths—1 from shock and haemorrhage soon after operation, 5 from coronary thromboses proved at post-mortem examination (on the first, fourth, ninth, twenty-eighth, and eightieth postoperative days respectively); 1 from bilateral bronchopneumonia on the eighth day, 1 from intestinal obstruction on the tenth day, and 1 from hemiplegia on the nineteenth day.

There were 23 patients under 60 years of age, 23 between 60 and 69 years, and 8 over 70 years.

Of the operations carried out, there were 2 aorto-iliac by-pass grafts, 7 iliofemoral by-pass grafts 7 aorto-femoral by-pass grafts, and 38 endarterectomies.

Postoperative complications were uraemia (2) wound infections (5), chest complications (19), fata coronary thrombosis (5), burst abdomen (14), shock and haemorrhage (2), paralytic ileus (5), and 1 each of the following: Gram-negative septicaemia, intestina obstruction, lymph fistula (groin), and hemiplegia There were 4 subsequent amputations, 12 early failures, and 5 late failures.

Twenty-five patients presented with incapacitating claudication and there were 2 deaths. Twenty-nine patients presented with rest pain or gangrene and 8 of these died.

The most important factor which influenced the mortality-rate was the preoperative condition of the heart and lungs. All the patients were assessed as good, moderate, or bad risks on the basis of the history, physical examination, electrocardiograph chest radiograph, and, in some cases, ventilatory function tests (*Table II*).

The 54 patients were divided into two groups There were 44 patients in the good or moderate cardiac and pulmonary group with 1 death, and 10 patients in the poor cardiac or pulmonary group with 9 deaths (*Table III*).

Compared with the rather dismal postoperative picture resulting from major laparotomies in poor-risk

Table II.—BASIS OF PREOPERATIVE CARDIAC AND PULMONARY ASSESSMENT

	ASSESSMENT		
	Good	Moderate	Poor
Cardiac	No history of coronary insufficiency No cardiac failure No atrial fibrillation No E.C.G. changes	One previous cardiac infarct, no residual angina No present treatment for cardiac failure Minor E.C.G. changes	Two or more cardiac infarcts Angina of effort Continuous treatment required for cardiac failure Gross E.C.G. changes
Pulmonary	No chronic cough No dyspnoea	History of recurrent bronchitis Dyspnoea on moderate exertion Ventilatory function more than half predicted normal	Chronic cough Dyspnoea on slight exertion Ventilatory function less than half predicted normal

patients, axillary-femoral by-pass grafts cause few major complications, but the incidence of graft clotting is much higher in the prostheses which are seldom less than 40 cm. long.

Table III.—A COMPARISON OF THE MORTALITY RATES OF AORTO-ILIAC SURGERY AND AXILLARY-FEMORAL BY-PASS GRAFTS

PATIENTS	AORTO-ILIAC SURGERY		AXILLARY-FEMORAL GRAFTS	
	Total No. of Patients	No. of Deaths	Total No. of Patients	No. of Deaths
Good-risk Good or moderate cardiovascular assessment, and good or moderate pulmonary assessment	44	1	7	1
Poor-risk Poor cardiovascular assessment, or poor chest assessment	10	9	10	1

Graziano, Lal, and Dobrin (1970) reported 14 males treated by axillary-femoral by-pass grafts. Of these, 11 had superficial femoral artery occlusions in addition, and there were 3 postoperative deaths. One graft clotted at 3 months and the other results were good in 7 patients, fair in 2, and poor in 1. Mannick and Nabseth (1968) reported 17 poor-risk male patients treated by this operation with 1 postoperative death, 1 primary failure, and 2 secondary failures. Urdaneta, Visudh-Arom, Delaney, and Castenada (1969) reported a patient whose bilateral axillary-femoral by-pass grafts were still patent at 35 months.

This operation offers a simple method of by-passing an aorto-iliac occlusion. It appears to be relatively free from early complications, but the late clotting rate is far too high. It might be thought that an 8- or 10-mm. graft would offer a greater chance of success. The diameter of the common femoral artery is, however, seldom greater than 6 mm. and it is thought that the continued patency of the graft is partly determined by the adequacy of the outflow tract. If the profunda femoris is able to take the full flow of the graft, secondary clotting is less likely.

Various agents have been shown to diminish coagulability, platelet stickiness, or blood viscosity, or to increase fibrinolysis. If a safe and effective drug can be found which will ensure the long-term patency of long prosthetic grafts a major drawback of this operation will have been removed.

In his case Louw (1964) used an autogenous saphenous vein-graft. An adequate length of saphenous vein, however, can be obtained only in two ways: either by removing the vein from the groin to below the knee where its calibre is often disappointingly small or by using the long saphenous veins from both sides and joining them. On the whole, autogenous veins do not recommend themselves for this purpose. However, Stipa (1971) has reported 4 cases treated with saphenous, cephalic, or basilic veins with apparent success.

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NEUROLOGICAL COMPLICATIONS OF RUPTURED ABDOMINAL AORTIC ANEURYSM

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SUMMARY

Two cases of neurological complications of abdominal aortic aneurysm are described, with a brief review of the other neurological complications of this condition.

NEUROLOGICAL complications are a not-infrequent manifestation of dissecting aneurysm of the aorta producing either cerebral, spinal, or, rarely, peripheral nerve lesions (Moersch and Sayre, 1950; Condon and Rose, 1969). These complications may also occasionally occur following abdominal (McAfee, 1957) or thoracic (Abrams, 1957) aortography. We report here 2 unusual neurological presentations of ruptured abdominal aortic aneurysm and add a brief review of the literature.

CASE REPORTS

Case 1.—A 63-year-old male presented to the surgical out-patients' department complaining of symptoms suggestive of a urinary-tract infection. Direct questioning revealed that he also suffered from intermittent claudication in the right calf. On examination a large abdominal aortic aneurysm was noted and both the common and external iliac arteries also felt aneurysmal. Femoral and popliteal pulses were palpable on both sides but the posterior tibial and dordalis pedis pulsations were impalpable on the right side.

The patient was admitted for assessment. An ejection systolic murmur was audible over the precordium and there was clinical and radiographic evidence of left ventricular enlargement. Neurological examination revealed no abnormality in the central or peripheral nervous systems. The blood-urea was 35 mg. per 100 ml. A microscopic examination of the urine showed innumerable pus cells with a heavy growth of coliform organisms. Intravenous pyelography showed no renal function on the left side and no definite left renal outline.

An elective operation was planned, but on the night prior to surgery the patient complained of severe lower abdominal pain of sudden onset and within 10 minutes he had developed a complete paraplegia below the level of T.V. 10. His lower limb pulses were unchanged and initially there was no abdominal tenderness or hypotension. However, rupture of the aneurysm was suspected and whilst being transferred for emergency operation he developed a tachycardia and his blood-pressure fell to 70 mm. Hg. At operation a large retroperitoneal haematoma was found and the diagnosis of aneurysmal rupture was confirmed. The aneurysm extended from 1 cm. below the origin of the right renal artery and involved both common iliac arteries. Neither the left renal artery nor the left kidney was seen or felt. After proximal and distal control had been obtained, the aneurysm was incised, the lumber vessels oversewn from within, and a bifurcated Teflon graft was sutured in place. The atherosclerotic internal iliac arteries were ligated without macroscopic effect on the colon. The time of aortic cross-clamping was 2 hours and 40 minutes.

Postoperatively the paraplegia was unchanged. The patient developed acute renal failure and haemodialysis was instituted. The abdomen became distended and bloody diarrhoea ensued, presumably due to ischaemic colitis. On the fifth postoperative day the right lower limb became cold and pulseless. His condition deteriorated progressively and he died on the seventh postoperative day. At post-mortem examination the vascular suture lines were intact. No major left renal artery was identified although there was a small atretic left renal element at the level of the pelvic brim. The right kidney was enlarged and pale. The wall of the colon showed patchy discoloration without blood in the lumen or perforation. Both femoral arteries were atheromatous but no definite premortem thrombosis was noted. The spinal cord was not examined.

Case 2.—A 68-year-old male was admitted following a fall. For a year he was known to have had an aortic aneurysm but he had been advised by his general practitioner to leave well alone. For the fortnight preceding his admission his wife had noticed him dragging his right foot on walking and he himself had noticed weakness in his right big toe. Immediately prior to admission, whilst out walking, he stumbled on his right lower limb and fell directly on to his abdomen. He had immediately developed severe abdominal pain. On admission he was extremely pale and shocked (the peripheral pulses were impalpable and the blood-pressure was unrecordable before resuscitation). A large tender swelling was palpable in the left iliac fossa and a provisional diagnosis of ruptured aortic aneurysm was made. Examination of his right lower limb revealed that it was slightly dusky. There was a foot-drop with no active dorsiflexion at the ankle and loss of extension of the hallux as well as sensory loss on the anterolateral aspect of the leg and on the dorsum of the foot. Passive movements at the ankle-joint were full. He was considered to have a right, lateral, popliteal nerve palsy. After a short period of resuscitation operation was performed. A large aneurysm of the abdominal aorta was found commencing 2 cm. below the origin of the renal arteries and involving both common iliac vessels. The aneurysm had ruptured on its left side. A bifurcated Teflon graft was sutured in place. The duration of aortic cross-clamping was 2 hours and 20 minutes.

Postoperatively the patient's condition improved. However, the right leg still showed the signs of a lateral, popliteal nerve lesion and was now ischaemic. Arteriography via the right femoral artery revealed extensive peripheral vascular disease. The ischaemia progressed and a mid-thigh amputation was performed on the ninth postoperative day with secondary suture of the skin-flaps 8 days later. He recovered well and was discharged 24 days after admission. Three months postoperatively he was walking well with a prosthesis.

DISCUSSION

Although injuries of the spinal cord or the peripheral nerves are unusual complications of abdominal aortic aneurysm, both have been recorded.

The rarity of spinal cord damage following abdominal aortic surgery is surprising as the arteria radicularis magna of Adamkiewicz is said to arise in the lumbar region in 50 per cent of cases (Adams and Van Geertruyden, 1956). This vessel is the largest of the segmental reinforcements of the anterior spinal artery. However, Adams and Van Geertruyden (1956) point out that when the arteria radicularis magna originates in the lumbar region there is also a constant large segmental contribution to the anterior spinal artery from a low thoracic spinal vessel. Presumably paraplegia can only occur if this thoracic vessel is absent or blocked as well as the lumbar arteria radicularis magna. This combination appears to be infrequent since spinal cord damage is a very rare sequel of excision of abdominal aortic aneurysm and, indeed, was not recorded in a review of 14,000 cases (DeBakey, Crawford, Cooley, Morris, Royster, and Abbott, 1964). Eight cases of spinal cord damage have been described (Hara and Lipin, 1960; Mehrez, Nabseth, Hogan, and Peterling, 1962; Coupland and Reeve, 1968; Skillman, Zervas, Weintraub, and Mayman, 1969) and a further 2 cases are mentioned in the correspondence following the communication of Skillman and others (1969). Paraplegia has also been reported in a patient with thoracic aortic aneurysm without rupture where recovery occurred following excision of the sac (Davie, 1963).

A review of the literature has failed to reveal a case where paraplegia developed as the initial sign of rupture of an abdominal aortic aneurysm. It seems likely that the paraplegia in our patient developed as a result of spinal cord ischaemia consequent upon occlusion of a major artery arising from the aneurysm and supplying the cord. This occlusion may have been related to dissection of the vessel wall or to embolism associated with the rupture.

Although interference with the abdominal component of the autonomic nervous system is a well-recognized complication of abdominal aortic surgery (May, De Weese, and Robb, 1969), autonomic lesions have not been commonly recorded in association with rupture of an abdominal aortic aneurysm. Eastcott and Gardner (1969) have, however, reported a case of autosympathectomy following extension or leakage of an aneurysm behind the vena cava.

Peripheral nerve lesions too may complicate abdominal aortic aneurysm, and femoral neuropathy following rupture of an aneurysm into the psoas sheath has been recorded (Razzuk, Linton, and Darling, 1967). Recently Kubacz (1971) has reported a case of combined femoral, obturator, and sciatic palsy in a limb associated with a ruptured abdominal aortic aneurysm. The mechanism of the femoral neuropathy in these cases was considered to be pressure produced as a result of rupture of the aneurysm into the tight fascial compartment of the psoas and iliacus muscles. The cause of the sciatic palsy was attributed to direct pressure of a common liac artery aneurysm impinging on the nerve trunks arising from L.V.4, L.V.5, S.V.1, and S.V.2.

It is interesting to speculate on the mechanism of the lateral popliteal palsy recorded in our second case. It seems unlikely that direct pressure on the nerve trunks in the pelvis can be held responsible since the medial popliteal component of the sciatic nerve was not involved. Ischaemic neuropathy is rare since nerves receive a blood-supply from several anastomosing vessels. However, the sciatic nerve is supplied by a named vessel, the arteria comitans nervi ischiadici. It is conceivable that sudden occlusion of this vessel by embolism or thrombosis might result in ischaemic damage of vulnerable nerve-fibres, particularly in a limb already the site of extensive peripheral vascular disease. Although it is possible that the lateral popliteal palsy in our second case arose from some other cause, its development in a limb with extensive peripheral vascular disease shortly before the rupture of an abdominal aortic aneurysm makes it very likely that the neurological signs were related to the arterial disease. It is tempting to suggest that the aneurysm produced the peripheral nerve lesion either via ischaemia or pressure and that the consequent foot-drop caused the fall which precipitated aneurysmal rupture.

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CRYOSURGERY IN THE TREATMENT OF HEAD AND NECK NEOPLASIA

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SUMMARY

The clinical and cellular changes which occur after cryosurgery are described. Its advantages as a form of therapy in the treatment of neoplasia are discussed, particularly with regard to pain relief in palliation. However, the limitations of the effectiveness of cryosurgery in cancer therapy are emphasized.

The results of cryosurgery are presented in 30 cases of recurrent or persistent neoplasia, which followed more formal treatment. In 5 cases healing appeared to be complete; good palliation was achieved in 6 cases, and useful palliation in 13 cases. There was no response in 6 cases.

DURING the past 5 years the results of treatment with cryosurgery have become available, and now the advantages and disadvantages can be more critically assessed. This is especially important with regard to neoplasia in order to avoid misconceptions about a new method of therapy. Although cryotherapy is being used with some success in the treatment of other conditions of the head and neck, such as allergic rhinitis and nasal polypi, pituitary ablation, Menière's disease and epistaxis, the purpose of this communication is to report on its use in the treatment of malignant lesions of the head and neck.

Both normal and neoplastic cells may be irreversibly damaged by extreme cold. The experimental evidence to support and demonstrate this is mainly from the work of Fraser and Gill (1967) in this country, and from that of Gage, Koepf, Wehrle, and Emmings (1965), Hill (1965), von Leden and Rand (1966, 1967), and Gage (1968) in the U.S.A. In using the technique for the destruction of cells the following criteria must be met: rapid repeated freezing and thawing to a temperature of at least −20° C. with sufficient duration of freezing for a good tissue ice-ball to form. The repeated rapid freezing and thawing probably causes rupture of nuclear and cellular membranes. Also contributing to cell death are: (*a*) alterations in the lipoprotein components of the cell membranes; (*b*) *p*H changes; (*c*) toxic concentration of electrolytes; (*d*) polymerization; (*e*) denaturation of proteins (Lovelock, 1957). Added to these, and considered to be of importance, are vascular stasis and microthrombi leading to ischaemia of the tissues.

Although the above hold true for normal tissues and benign tumours there is some doubt about the absolute destructive power on some malignant tumours, as certain paramorphic malignant cells have an inherent resistance to physical trauma (e.g., mesenchymal cells appear to be more resistant to cold than epithelial cells (Fraser and Gill, 1967)).

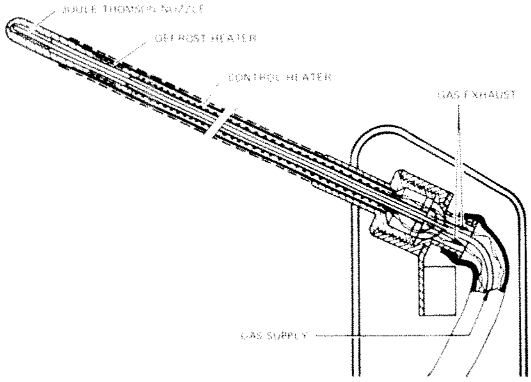

FIG. 1.—Section through a cryoprobe. The gas escaping through the narrow Joule-Thomson nozzle into the outer jacket creates the drop in temperature at the probe tip.

Other limitations of cryotherapy which must be borne in mind are: freezing is not selective—all frozen cells may die, including surrounding normal tissue; the area of destruction does not include adjacent non-frozen lymphatics and therefore treatment is only local and not regional; the vascularity of the area affects the speed and extent of freezing although temporary vasular occlusion, where possible, helps to reduce this.

However, in clinical work definite advantages of cryotherapy are apparent as an adjunct to other methods of treatment, and in certain cases it is the primary treatment of choice. Amongst the advantages of cryosurgical techniques can be listed the following features:—

1. Relative avascularity of the lesion produced with minimal or no bleeding postoperatively. This renders it very suitable for vascular tumours.

2. Cryosurgery evokes minimal tissue responses and only very slight oedema.

3. The destruction can be localized, the subsequent lesion being demarcated with some encapsulation and good healing.

4. Relative anaesthesia and relief of pain owing to the destruction of sensory nerve-endings is a particularly attractive feature when palliating for malignancy or if treating under a local anaesthetic.

5. Resistance of some tissues to freezing, such as bone, means that malignant cells invading bone can be destroyed without losing the bony architecture. Although frozen bone is devitalized malignant cells within it are destroyed.

6. There is some evidence that cryotherapy may render a tissue antigenic; since freezing may modify its antigenic structure slightly it could then behave as a foreign substance, eliciting an auto-antibody (Shulman, Yantorno, and Bronson, 1967). The antibody response appears to reach its maximum in 7–10 days, extending destruction beyond the areas initially frozen.

THE PRESENT INVESTIGATION

Cryotherapy has been used in a series of patient presenting at otorhinolaryngological department with inoperable cancers of the floor of the mouth oral cavity, pharynx (including nasopharynx), neck nasal cavity, and sinuses.

MATERIALS AND METHODS

The equipment consisted of the Amoils Cryo-unit (Amoils, 1968), modified by McKelvie and Shahee (1967), with insulated cryoprobes of varying size from 2 to 11 mm. in diameter, each with a reheatin circuit for rapid thawing and using nitrous oxide a a refrigerant. This gives rapid cooling and deal with a reasonably large volume of tissue. The working 'tip' temperature of −40° C. gives an averag 10-mm. ice-ball with a marginal temperature c −20° C. These temperatures are quite sufficient t produce the required tissue destruction. The fall i temperature is monitored by thermocouple needle around and deep to the lesion.

The majority of cases are treated under gener anaesthesia. The thermocouples are placed i position. The cryoprobe is pressed on to the lesio and freezing is commenced; it is important to plac the probe in the required position before allowing th gas to pass, as firmer adhesion is established and there i more certain rapid freezing of the tissues with les likelihood of insulated pockets. Freezing is continue until a good tissue ice-ball has formed. Ideally, th thermocouple thermometer will give an accurat indication, but this is not essential as one can soo learn to judge clinically when the tissue ice-ba has reached its maximum. The time required varie between 1 and 5 minutes, depending on the tissu vascularity and the size of the lesion. The gas flo is stopped and the reheating circuit rapidly thaws th ice. The probe can be removed in about 20 second and one can observe a crater where the probe wa placed (*Fig.* 1). As thawing continues the tissu swells again to fill the defect. The procedure i repeated in exactly the same site at least two or thre times, and then the adjacent area is treated in similar manner until one has dealt with the whol tumour (Holden, 1969).

Immediately following treatment the gross appear ance of the tissue is virtually unchanged, but durin the next 3 or 4 days necrosis occurs with superfici slough; gradually this separates to reveal clea granulations which slowly heal. If superficial bon has been treated it may become exposed and sequestrum formed, or the bare area becomes covere by granulation tissue and epithelization commenc from the edges. With normal tissues and benig lesions (particularly the vascular variety) it has bee noticed that the necrosis and sloughing are far le than with malignancies, fibrosis being the mai response. This observation supports histologic findings that peripheral fibroblastic activity occu early on the third day whilst organization in th treated area is prominent (Fraser and Gill, 1967). I these cases scarring is minimal.

Thirty cases with malignancy in the head and nec have been treated by cryotherapy, the majority aft

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* Developed by Spembley Technical Products Lt and supplied by C. Davis Keeler Ltd.

Table I.—DETAILS OF 30 CASES WITH MALIGNANCY IN THE HEAD AND NECK WHO WERE TREATED BY CRYOSURGERY

CASE	AGE AND SEX	TYPE AND SITE OF NEOPLASM	DURATION	OTHER TREATMENT	FOLLOW-UP AFTER CRYOTHERAPY (mth.)	RESULTS
. B.	33 M.	Recurrent transitional-cell papilloma of nasal septum	39 mth.	Wide excision with diathermy. Deep X-ray therapy	17	Some necrosis. Healed satisfactorily
. P.	55 F.	Recurrent carcinoma of maxilla	33 yr.	Maxillectomy in 1933	38	Healed satisfactorily
. W.	56 M.	Extensive carcinoma of pyriform fossa	20 mth.	Deep X-ray therapy and gold seeds to neck secondaries	7	Endoscopic cryo-application. Good pain palliation and swallowing possible until death
R. F.	80 M.	Recurrent carcinoma of tongue	6½ yr.	Deep X-ray therapy. Gold grains locally	6	Healed well. Tongue mobility improved
. B.	15 F.	Recurrent neurofibrosarcoma of pharynx and palate	9 yr.	Deep X-ray therapy and extensive excisions	5	Significant reduction in size. Improvement in voice. 4 applications
W. K.	64 M.	Persistent carcinoma of mandible and tongue	9 mth.	Deep X-ray therapy. Cytotoxic perfusion	2	Pain palliation only. 2 applications. Died
A. J. H.	63 M.	Recurrent carcinoma of floor of mouth	60 mth.	Deep X-ray therapy. Hemimandibulectomy. Cervical block dissection	24	Good remission and healing after first application. Lesser responses on 4 further applications, but pain relieved. Died
. B.	82 M.	Recurrent carcinoma of tongue	38 mth.	Partial glossectomy. Radium implant	15	2 applications. Complete healing
. M.	70 M.	Recurrent carcinoma of soft palate	40 mth.	Deep X-ray therapy	24	1 application. Complete healing
. D.	78 M.	Carcinoma of parotid into overlying skin (with secondaries in sternum)	10 yr.	Deep X-ray therapy to primary. Excision of secondary	13	Good regression of protruding part of tumour. 4 applications
. P.	49 M.	Recurrent carcinoma of larynx around tracheostome	14 mth.	Deep X-ray therapy. Laryngectomy. Cytotoxic drugs	1	Minimal healing only. Patient subsequently died
W. S.	55 M.	Recurrent subglottic carcinoma around tracheostome and in trachea	26 mth.	Laryngectomy. Deep X-ray therapy	5	Fairly good healing and permitted airway to be clear of proliferating tumour. Died of mediastinal extension. 3 applications
. H.	41 F.	Transitional-cell carcinoma of nasal septum	34 mth.	Excision and deep X-ray therapy (refused major surgery). Gold grains to cervical node	22	3 applications. Good local healing, some crusting. No local recurrence yet
. O.	49 M.	Persistent carcinoma of tongue	10 mth.	Radium implant. Hemiglossectomy	1	No palliation. Pain worse. Patient died
R. D.	47 M.	Carcinoma of mandible. Secondaries over buccal mucosa	37 mth.	Hemimandibulectomy. Cervical block dissection. Cytotoxic perfusion. Deep X-ray therapy	4	2 applications. Pain palliation for 3 months. Died
W. R.	62 M.	Recurrent carcinoma of floor of mouth	29 mth.	Deep X-ray therapy. 'Commando' operation. Methotrexate	14	Good pain palliation. Initial healing. 2 applications. Died with chest secondaries
. U.	56 F.	Recurrent carcinoma of palate	27 mth.	Deep X-ray therapy. Refused surgery	4	Some pain palliation only. Ulcer a little cleaner
. W.	61 M.	Recurrent carcinoma of tongue	17 mth.	Radium needles. Deep X-ray therapy	3	Good pain palliation. Ulcer smaller and cleaner. 2 applications
. L.	49 F.	Recurrent carcinoma of nasopharynx	10 yr.	Deep X-ray therapy. Cervical block dissection	32	Good tumour destruction and pain relief on each occasion. Conductive deafness improved
A. P.	68 F.	Carcinoma of left cheek	48 mth.	Surgery and deep X-ray therapy	14	Pain palliation only
. C.	54 M.	Carcinoma of floor of mouth	36 mth.	Laryngectomy and deep X-ray therapy previously. Perfusion of residual ulcer with methotrexate	12	Cryosurgery sole effective pain palliation
. S.	80 F.	Carcinoma of floor of mouth	38 mth.	Deep X-ray therapy	12	Arrest of growth. Partial resolution. Pain palliation

Table I (cont.).—DETAILS OF 30 CASES WITH MALIGNANCY IN THE HEAD AND NECK WHO WERE TREATED BY CRYOSURGER

CASE	AGE AND SEX	TYPE AND SITE OF NEOPLASM	DURATION	OTHER TREATMENT	FOLLOW-UP AFTER CRYOTHERAPY (mth.)	RESULTS
A. G.	68 F.	Carcinoma of floor of mouth	18 mth.	Deep X-ray therapy	9	Pain palliation for 3 months on each 3 occasions
A. H.	54 F.	Carcinoma in neck nodes. Ulcerated persistence	36 mth.	Resection and irradiation of laryngeal primary	12	Pain palliation only. Died of pneumon after 3 years. 4 treatments; no riv palliation
S. W.	61 M.	Carcinoma of maxillectomy cavity	14 mth.	Ineffectual cytotoxic perfusion	13	Pain palliation for 1 month. 3 applic tions
H. B.	55 M.	Carcinoma in neck nodes. Shallow ulcer on presentation	38 mth.	Deep X-ray therapy	11	Pain palliated for 1 month
A. H.	66 F.	Carcinoma of floor of mouth	37 mth.	Deep X-ray therapy	12	Relief of pain. Partial temporary resol tion. 3 applications
A. P.	55 M.	Carcinoma of upper jaw	22 mth.	Deep X-ray therapy and maxillectomy. Initial relief from Epodyl infusion	11	Pain palliation brief and poor. 2 applic tions in 2 weeks
S. H.	54 M.	Carcinoma of temporal bone	26 mth.	Deep X-ray therapy	11	Pain palliation brief and poor. Died inanition after 37 months
H. W.	64 M.	Carcinoma of cheek from maxillary cavity	17 mth.	Deep X-ray therapy and resection of maxilla	11	Pain controlled for 17 months. 3 applic tions. Little resolution

other forms of treatment had failed, hence the tumours were either persistent or were recurrences after a period of time. Unless otherwise stated the tumour was treated on one occasion only. *Table I* gives brief details of these cases and summarizes the results. This table can only give a general guide to the results, as the lesions differed greatly in size, time of presentation, and type of previous treatment. However, in 5 cases the healing was apparently complete, with no recurrence at the follow-up time specified. These tended to be small lesions or recurrences which were treated early.

There was good palliation in 6 cases, with relief of pain, some healing, or return of function.

The largest number of cases (13) can be described as having useful palliation, with relief of pain and arrest of growth. Often it was found that pain relief was better than would be achieved by drugs or other means.

In 6 cases there was either minimal or no response.

Secondary bleeding was rare and when it occurred was very minor. Freezing in the vicinity of large vessels did not cause any haemorrhage or other problems. The connective tissue remains intact and the endothelium, which is presumably destroyed, soon regrows from the unaffected part of the vessel.

In the light of these findings and other published results cryotherapy must now be considered seriously as an adjunct in the treatment of neoplasia. In this respect its status is between radiotherapy and diathermy. Even if it is finally accepted only as a tool of palliation there is enough evidence to demonstrate its worth as such, particularly as it gives the patient hope and the knowledge that he is not being neglected. Cryotherapy causes no extra discomfort and as it i almost invariably a safe and simple procedure th patient's stay in hospital can be minimal.

Cryotherapy may become the treatment of choic with recurrences of malignant growths in surgicall inaccessible places, or after radiotherapy, surgery, an cytotoxic measures have failed. These includ uncontrolled tumours of the oral cavity, pharyn nasal cavity, postnasal space, and sinuses which hav resisted surgical, radiotherapeutic, or cytotoxi management. In addition, inoperable tumours i which deep bone pain is a prominent feature ma profitably be palliated by cryotherapy.

Cryosurgical techniques should improve as ne refrigerants and modes of application become available. The suggested immunological aspect will nee elucidation.

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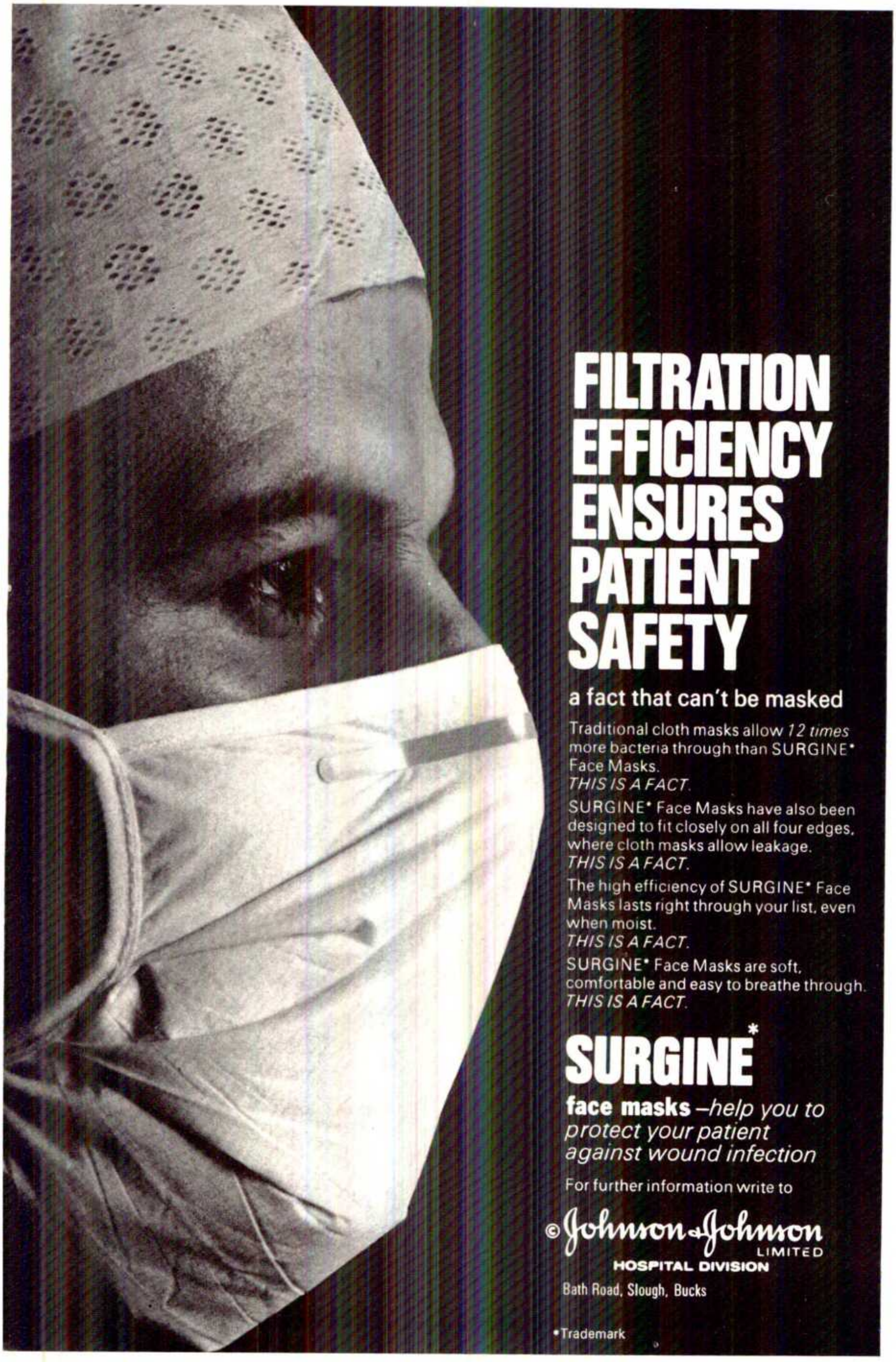

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VENOUS STASIS AND DEEP-VEIN THROMBOSIS[*]

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SUMMARY

A venographic technique for studying stasis in the deep veins of the legs of conscious patients is described. A second technique involving the clearance of radioactive material from the veins has been developed for use during operation. The results of the two methods correlate closely.

There is considerable stasis of the blood, particularly in the soleal veins, in conscious patients with the legs horizontal, and it is prolonged considerably during surgery. Using these new techniques the effectiveness of various methods said to prevent stasis has been assessed.

RECENT investigations using the ^{125}I-fibrinogen test have shown that the incidence of deep-vein thrombosis is high, not only in general surgical patients (30 per cent—Flanc, Kakkar, and Clarke, 1968; Negus, Pinto, LeQuesne, Brown, and Chapman, 1968; Kakkar, Nicolaides, Renney, Friend, and Clarke, 1970) but also in gynaecological patients (18 per cent —Friend, 1971), orthopaedic patients (50 per cent—Field, Kakkar, Nicolaides, and Renney, 1971), and urological patients (28 per cent—Nicolaides, Field, Kakkar, Yates-Bell, Taylor, and Clarke, 1972). In practically all instances the thrombosis started in the calf and particularly in the soleal veins (Nicolaides, Kakkar, Field, and Renney, 1971). Studies with the ^{25}I-fibrinogen test have also demonstrated that in urgical patients 50 per cent of the thromboses start during the operation (Flanc and others, 1968) and hat another 30 per cent occur during the subsequent 48 hours (Nicolaides, 1972). The majority of these hrombi remain localized in the calf or lyse spontaneously (Kakkar, Howe, Flanc, and Clarke, 1969); hey are harmless and do not produce emboli. Twenty per cent, however, extend proximally into and above the popliteal vein and are then liable to ragment and give rise to emboli. When thrombosis xtends as far as the pelvic veins the incidence of pulmonary embolism approaches 50 per cent (Kakkar and others, 1969).

The fact that thrombosis starts in the soleal veins at operation or soon afterwards means that the factors esponsible for intravascular coagulation produce heir maximum effect there at these particular times. mmediately after injury the various coagulation actors in an activated form have been shown to be irculating in the blood (Penick, Roberts, and Dejanor, 1965). Thrombosis has been shown to depend on the presence of such activated factors in the presence of stasis (Wessler and Yin, 1968). Thrombosis is not produced by stasis alone or by activated factors alone; it requires a combination of the two (Wessler and Yin, 1968).

It has been demonstrated already that stasis which occurs in the valve pockets and in the muscular veins of the calf in conscious and recumbent patients can be reduced by leg elevation and exercises (McLachlin, McLachlin, Jory, and Rawling, 1960). More recently several attempts have been made to prevent deep-vein thrombosis by preventing stasis in the leg veins. Many trials using the ^{125}I-fibrinogen test to detect the onset of deep-vein thrombosis in patients have been reported, but the results are inconclusive (Flanc, Kakkar, and Clarke, 1969; Browse and Negus, 1970; DeJode, Khurshid, and Walther, 1970; Rosengarten, Laird, Jeyasingh, and Martin, 1970; Hills, Pflug, Jeyasingh, and Calnan, 1971; Rosengarten and Laird, 1971; Sabri, Roberts, and Cotton, 1971).

The main aim of the present study is to determine the degree of stasis in the deep veins of the leg in conscious, recumbent patients and in those undergoing operation, and to assess the effectiveness of various methods believed to prevent stasis.

MATERIALS AND METHODS

The investigation was divided into three parts:—

1. Clearance of Radio-opaque Material from the Tibial and Soleal Veins.—A technique of venography has been used which consistently demonstrates the soleal veins in addition to the other deep veins of the leg. This has been described in detail elsewhere (Nicolaides, Kakkar, Field, and Renney, 1971). Briefly, the patient lies horizontal on the X-ray table. A scalp-vein infusion needle is introduced into a vein on the dorsum of the foot. A 5-cm. wide pneumatic cuff is placed at the ankle to prevent any filling of the superficial leg veins and a similar cuff is placed on the mid-thigh to occlude the femoral vein. In all patients the veins of the leg are first partially emptied by a lightly applied elastocrêpe bandage. The ankle cuff is then inflated to 120 mm. Hg and the mid-thigh cuff to 200 mm. Hg. This does not occlude the arterial blood-flow because of the narrowness of the cuff. The injection of 45 per cent sodium diatrizoate (Hypaque) is commenced and the bandage is removed. The contrast medium is seen on the image intensifier to ascend in the tibial veins and to fill the soleal veins in a retrograde fashion. After injecting 30 ml. of 45 per cent sodium diatrizoate and filling the soleal and tibial veins, the injection is stopped, the mid-thigh cuff is removed, and the time taken by the contrast medium to disappear from the soleal and tibial veins is measured using a stopwatch (Nicolaides, Kakkar, and Renney, 1971).

The clearance times of the radio-opaque material from the tibial and soleal veins have been determined in 46 conscious patients who had normal veins.

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[*] Based on three communications to the Surgical Research Society, in July, 1970, January, 1971, and January, 972, respectively.

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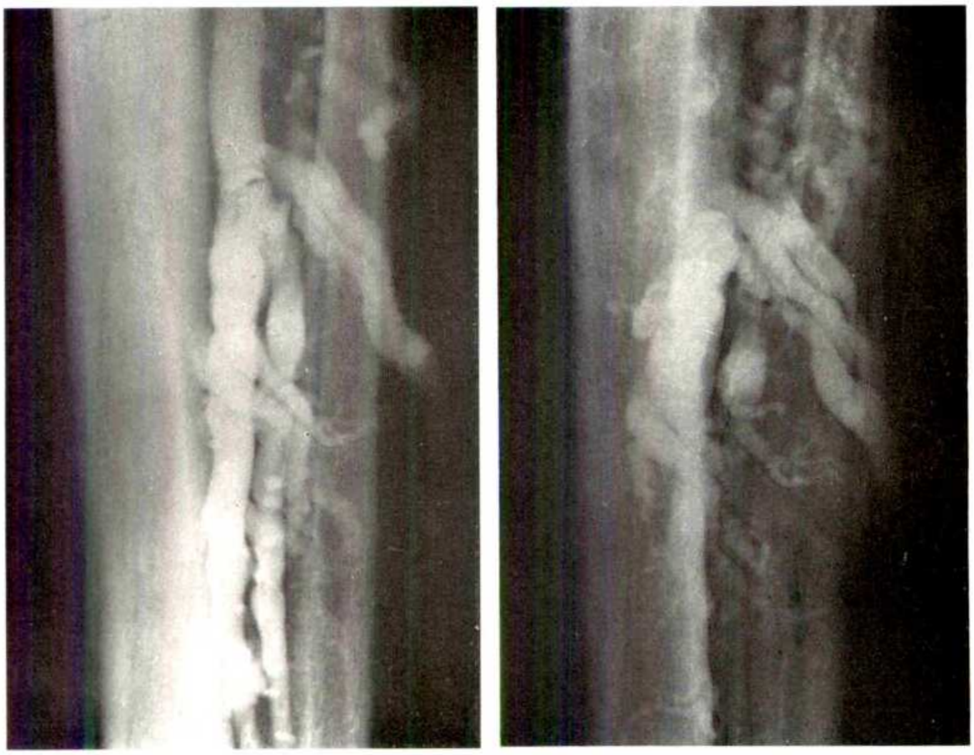

A B

FIG. 1.—A, The soleal and tibial veins filled with contrast medium just before releasing the mid-thigh cuff. B, One minute after the mid-thig cuff has been released. Contrast medium remains in the soleal veins.

Venography was performed in these patients in order to prove or disprove the clinical diagnosis of deep-vein thrombosis. Patients with thrombi, oedema, or cellulitis were excluded. The clearance times have been determined when the leg was horizontal (16 patients), when the leg was horizontal but with a full-length elastic stocking on (5 patients), when the leg was elevated 20° (10 patients), during active plantar flexion of the foot (5 patients), during electric stimulation of the calf muscles (5 patients), and during active plantar flexion of the foot againt resistance (5 patients) (Nicolaides, Kakkar, and Renney, 1971).

2. Simultaneous Clearance of Radio-opaque Material and ^{125}I-fibrinogen from the Soleal and Tibial Veins.—The technique described above has also been used to study the clearance of both radio-opaque material and ^{125}I-fibrinogen from the tibial and soleal veins simultaneously in 8 male volunteers with normal limbs prior to inguinal herniorrhaphy. First, the thyroid gland of these patients was blocked by the oral administration of 100 mg. of sodium iodide 24 hours prior to the test. Then 10 μc. of ^{125}I-fibrinogen mixed with 30 ml. of 45 per cent sodium diatrizoate were injected to fill the tibial and soleal veins. After releasing the mid-thigh cuff, a clearance curve of the ^{125}I-fibrinogen from the calf was obtained while the clearance of the sodium diatrizoate, as seen on the image intensifier, was timed. The clearance curve of the radioactive fibrinogen was obtained by placing the scintillation probe of a Pitman 235 isotope-localization monitor over the medial aspect of the calf at the site of the soleal vein and connecting the monitor to a pen recorder. Th scintillation probe was moved away from the le whenever the image intensifier was switched on t avoid damage to the probe from X-ray radiation. mark on the patient's skin ensured that the prob could be replaced at exactly the same position.

3. Clearance of ^{125}I-fibrinogen from th Soleal and Tibial Veins just before and durin Operation.—Thirty ml. of normal saline containin 10 μc. of ^{125}I-fibrinogen were injected into a vein o the dorsum of the foot and directed into the tibial an soleal veins using the technique described abov The mid-thigh cuff was then released and a clearanc curve obtained. This was performed just before th patients were anaesthetized and 20 minutes after th induction of anaesthesia while the operation was i progress.

The clearance times of ^{125}I-fibrinogen from th soleal and tibial veins have been determined ju before and during operation in 8 patients undergoin simple mastectomy with apparently normal limbs.

RESULTS

1. Clearance of Radio-opaque Material fro the Tibial and Soleal Veins.—This was measure in six groups of patients.

Group I: Leg Horizontal.—In 16 patients the low limb was kept horizontal and when the mid-thigh cu was released the contrast medium cleared first fro the tibial veins while it remained in the soleal vei for much longer (*Fig.* 1). The mean clearance time of contrast medium from the tibial veins was 1·1 minutes and from the soleal veins 9·6 minutes (*Fig.* 2). There was no correlation between the clearance times from the soleal veins and age (*Fig.* 3).

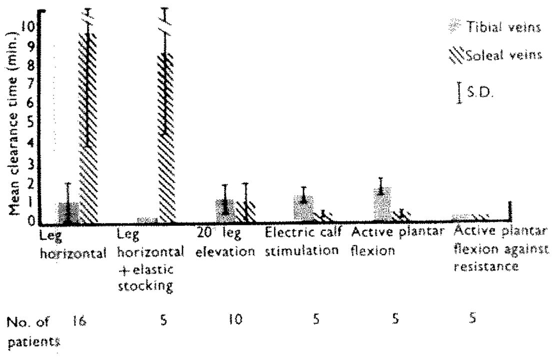

FIG. 2.—Clearance of sodium diatrizoate from the tibial and soleal veins.

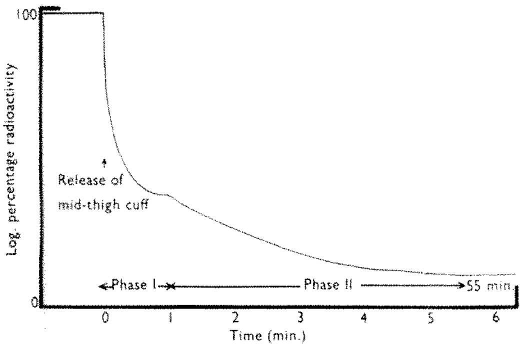

FIG. 4.—Clearance curve of ^{125}I-fibrinogen mixed with 45 per cent sodium diatrizoate from the tibial and soleal veins.

Group II: Leg Horizontal with Full-length Elastic Stocking on.—In 5 patients who were wearing full-length stockings the legs were also kept horizontal. The clearance rate from the soleal veins was similar to that in group I but the tibial veins emptied faster (*Fig.* 2).

Group III: 20° Leg Elevation.—In 10 patients whose legs were elevated 20° the tibial and soleal veins emptied simultaneously. The mean clearance time for the tibial veins was 1 minute and that for the soleal veins 1·1 minutes (*Fig.* 2).

Group IV: Active Plantar Flexion of the Foot.—Five patients were instructed to plantar flex the foot once every 4 seconds after the mid-thigh cuff was released while keeping the leg horizontal. The evidence at present indicates that the most effective rate of plantar flexion alternately to empty and refill the soleal veins is one every 4 seconds (Nicolaides, 1972). The contrast medium cleared from the soleal veins within 0·5 minute and from the tibial veins within 1·4 minutes (*Fig.* 2).

Group V: Electric Calf Stimulation.—In 5 patients the calf muscles were stimulated by electrodes to contract and produce a powerful but tolerable plantar flexion of the foot every 4 seconds after the mid-thigh cuff was removed. This rate is likely to be the most effective in preventing stasis (Nicolaides, 1972). The contrast medium cleared from the soleal veins within 0·2 minute and from the tibial veins within 1·4 minutes (*Fig.* 2).

Group VI: Plantar Flexion of the Foot against Resistance.—Five patients were asked to plantar flex the foot against resistance after the mid-thigh cuff was released. In these patients 2 plantar flexions were enough to empty both the soleal and tibial veins of contrast medium.

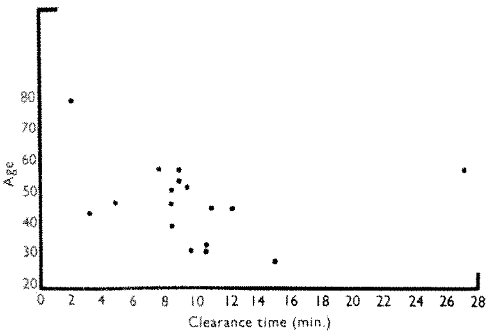

FIG. 3.—Correlation between age and clearance time from the soleal veins; $r = 0·22$, $P > 0·2$.

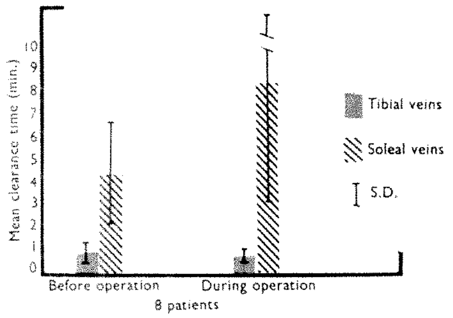

FIG. 5.—Clearance of ^{125}I-fibrinogen from the tibial and soleal veins before and during operation.

2. Simultaneous Clearance of Radio-opaque Material and ^{125}I-fibrinogen from the Tibial and Soleal Veins.—The clearance curves obtained were biphasic in all 8 patients who were investigated (*Fig.* 4). By intermittently screening and observing the clearance of sodium diatrizoate on the image intensifier it was noted that the clearance of the contrast medium from the tibial veins coincided with the end of phase I and from the soleal veins with the end of phase II (*Fig.* 4).

The mean clearance times obtained by the isotopic and radiographic method were in agreement (*Table I*). The final end-point of the isotopic method was defined as the point on the clearance curve after which the fall in radioactivity was less than 2 per cent of the initial count per minute. The final level of radioactivity was the same in both legs.

3. Clearance of ^{125}I-fibrinogen before and during Operation.—The mean clearance times of ^{125}I-fibrinogen from the tibial and soleal veins before and during operation are shown in *Table II* and *Fig.* 5. The mean clearance time of the ^{125}I-fibrinogen from the tibial veins was essentially the same before and during operation, but the mean clearance time from the soleal veins was twice as long during operation ($P < 0{\cdot}05$). In 1 patient (patient 6, *Table II*) the clearance of ^{125}I-fibrinogen from the soleal veins during operation was as long as 20 minutes.

Table I.—SIMULTANEOUS CLEARANCE OF HYPAQUE AND ^{125}I-FIBRINOGEN IN 8 PATIENTS (8 LIMBS)

PATIENT	CLEARANCE TIME OF HYPAQUE (min.)		CLEARANCE TIME OF ^{125}I-FIBRINOGEN (min.)	
	Tibial Veins (A)	Soleal Veins (B)	Tibial Veins (C)	Soleal Veins (D)
1	3·3	9·6	3·7	10·0
2	0·5	2·6	0·5	2·7
3	0·8	2·4	0·8	2·4
4	0·5	5·5	0·5	5·4
5	1·2	5·2	1·0	5·0
6	1·5	7·3	1·5	7·3
7	0·7	3·5	0·9	3·7
8	1·4	6·3	1·4	6·5

Correlation between A and C: $r = 0{\cdot}99$.
Correlation between B and D: $r = 0{\cdot}99$.

Table II.—CLEARANCE OF ^{125}I-FIBRINOGEN FROM THE SOLEAL AND TIBIAL VEINS IN 8 PATIENTS (8 LIMBS)

PATIENT	CLEARANCE TIME BEFORE OPERATION (min.)		CLEARANCE TIME DURING OPERATION (min.)	
	Tibial Veins (A)	Soleal Veins (B)	Tibial Veins (C)	Soleal Veins (D)
1	1·45	6·50	1·30	13·40
2	0·55	2·52	0·50	4·60
3	1·12	4·74	0·90	8·72
4	1·32	4·65	1·16	7·50
5	0·83	2·95	1·00	6·25
6	0·96	8·86	0·60	20·00
7	0·18	1·70	0·46	3·50
8	0·92	4·34	0·70	8·32
	Mean ± S.D. = 0·92 ± 0·41	Mean ± S.D. = 4·53 ± 2·31	Mean ± S.D. = 0·83 ± 0·30	Mean ± S.D. = 9·04 ± 5·35

B compared with D: $t = 2{\cdot}2$; $P < 0{\cdot}05$.

DISCUSSION

The present study supports the findings that deep-vein thrombosis usually commences in the soleal veins (Nicolaides, Kakkar, Field, and Renney, 1971) where there is undoubtedly the maximum degree of stasis. This is particularly so during operation and may well account for the fact that about 50 per cent of thromboses start at this time (Flanc and others, 1968) in the soleal veins (Nicolaides, Kakkar, Field, and Renney, 1971) as opposed to the tibial veins. However, it was interesting to find that there did not seem to be an increasing degree of stasis with age. This would suggest that the higher incidence of deep-vein thrombosis in the elderly may be related to factors other than stasis.

As regards the effectiveness of various methods of preventing stasis, the findings in conscious patients were interesting. Elastic stockings had a minimal effect on hastening the clearance of contrast medium from the tibial veins and this may well explain the findings that they do not prevent deep-vein thrombosis (Rosengarten and others, 1970). *Fig.* 2 demonstrates the efficacy of various other methods of preventing stasis, particularly in the soleal veins of conscious patients. Of the methods used, active plantar flexion against resistance was the most effective. Electrica stimulation of the calf and active plantar flexio were about equally effective; leg elevation to 20 was almost as effective. These findings provide guide to the value of physical methods employed b physiotherapists before and after operation to preven stasis in the deep veins of the leg.

It is particularly important to measure stasis durin operation since 50 per cent of thromboses occur a this time (Flanc and others, 1968). Radiographi techniques are inconvenient to use during operation A new technique involving the clearance of radioactive material from the deep veins of the leg has bee developed and found to be applicable withou difficulty during operation. The outstanding featur was that the duration of stasis in the soleal vein during operation was prolonged by a factor of abou 2 as compared with conscious patients. Investigations are now in progress to measure the effectivenes of various methods of preventing stasis during operation. It is not possible to give details of the results ye but there is good evidence that there are critica limits within which the stimuli are most effective i preventing stasis. It has become clear that wit electrical stimulation of calf muscles the mos important rate of stimulation alternately to empty an refill the soleal veins effectively is once every 4– seconds (Nicolaides, Kakkar, and Renney, 1971) With greater insight into the effects of these method of prophylaxis it is hoped that it will be possible t make them more effective.

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ANATOMY OF THE EXTERNAL ANAL SPHINCTER

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SUMMARY

1. The anatomy of the external anal sphincter has been studied in 48 adult cadaveric and surgical specimens by anatomical dissection and histological sections in three-dimensional planes.

2. The bilaminar and trilaminar concepts of external anal sphincteric anatomy are reviewed.

3. The significant anatomical differences in the anterior portion of the external sphincter compared with the lateral and posterior portion are emphasized.

4. The different configuration of the anterior part of the external sphincter in men and women is described.

5. A new terminology is proposed, 'superficial compartment' (subcutaneous and superficial) and 'deep compartment' (deep and puborectalis), on the basis of the close anatomical relationship between each of these two pairs of muscles.

THE external sphincter is made up of a group of muscles surrounding the anal canal and is continuous above with the fibres of the puborectalis. The descriptive subdivision of the external sphincter into three separate parts, i.e., subcutaneous, superficial, and deep, was first made by Santorini (1715), and later by von Holl (1897) and Thompson (1899). This trilaminar arrangement has been widely supported (Milligan and Morgan, 1934; Levy, 1936; Eaton, 1942; Wilde, 1948; Uhlenhuth, 1953; Gorsch, 1955, 1962; Morgan and Thompson, 1956; Stelzner, 1960; Stonesifer, Murphy, and Lombardo, 1960; Wilson, 1967. It has been adopted in texts by Gabriel (1945), Grant (1952), Last (1954), Buie (1960), Bacon and Recio (1962), and in *Gray's Anatomy* (1966).

However, other investigators have failed to distinguish three parts of the external sphincter and divide it into two parts—subcutaneous (or superficial) and deep (Courtney, 1950; Goligher, Leacock, and Brossy, 1955; Fowler, 1957; Walls, 1963; Goligher, 1967; Lawson, 1969). All observers agree that the subcutaneous portion is traversed by the terminal strands of the conjoined longitudinal coat, and that the deep fibres of the external sphincter blend with the puborectal muscle.

The external sphincter is usually described as a structure which encircles the anal canal uniformly in a laminated fashion. There have been few reports of differences between the anterior and the other parts of the sphincter and of variations between the male and female. The purpose of the present report is to record a detailed descriptive anatomy of the external sphincter with particular emphasis on the anterior portion and its composition in the male and female.

MATERIALS AND METHODS

Forty-eight adult specimens were studied—21 female and 27 male. The material consisted of 8 cadaveric kidney donors, 5 abdominoperineal resections, and the rest from necropsy specimens of patients dying of conditions unrelated to the anorectum. Anatomical dissection was performed in the various planes, and the difficult and complex areas such as the transverse perinei and the perineal body were studied by an under-water technique with the aid of a loop optic magnifier (Last, 1971). Histological sections were cut in the sagittal, coronal, and horizontal (cross) planes and stained with haematoxylin and eosin, Masson's stain, and Verhoeff's stain.

FINDINGS AND DISCUSSION

The anatomy of the trilaminar arrangement of the external sphincter described by most writers can be summarized as follows.

The *subcutaneous* part situated in the perineal space inferolateral to the internal sphincter is an annular muscle which is split by half a dozen or more of the conjoined longitudinal strands. A few fibres extend anteroposteriorly and are continuous with fibres of the superficial portion of the sphincter, with or without decussation. The *superficial* portion is an elliptical band of fibres lying slightly above and lateral to the subcutaneous sphincter and separated from the subcutaneous sphincter by the most superolateral fibres of the conjoined longitudinal coat. It consists mainly of anteroposterior fibres passing from the central tendinous point of the perineum to the anococcygeal raphe which is attached to the dorsal aspect of the coccyx. The anterior fibres decussate with few, if any, circular fibres while the posterior fibres are mainly circular with posterior extensions and some degree of decussation. The *deep* portion of the sphincter, for the most part an annular muscle, blends with the lowest fibres of the puborectalis. A posterior attachment is usually missing and only a few of its fibres extend to the anococcygeal raphe. Between the upper portion of the raphe of the levator ('coccygeal muscular raphe'; Courtney, 1949) and the lower part of the anococcygeal raphe formed by the subcutaneous, superficial, and deep sphincter there lies a space behind the anal canal filled with fibrofatty tissue—the 'sub-' or 'retro-sphincteric space' of Courtney (1949). Anteriorly, some of the fibres may decussate and extend to the transverse perineal muscle, and most of the lower fibres are circular (*Fig.* 1 A).

A somewhat different arrangement has been described by Courtney (1950); the sphincter is composed of two parts—subcutaneous and deep, the deep sphincter including the superficial and deep sphincters and the puborectalis. Goligher and others (1955) also failed to demonstrate three parts of the external sphincter and described the external sphincter as one continuous sheet which is fused with the puborectalis at its upper end. However, both Courtney and Goligher and others (1955) agree that the subcutaneous portion of the sphincter is distinct from the rest of the sphincter in that it is traversed by strands of the conjoined longitudinal fibres (*Fig.* 1 A).

The continuing dispute over the subdivisions of the external sphincter is based partly on disagreement over the arrangement of the fibres of the conjoined longitudinal muscle which bind together the external sphincter muscle; individual variation is not infrequent, and the complexity of the sphincteric musculature and adjacent tissue makes it mandator to dissect in a three-dimensional plane.

Present Study.—Because of its complexity we hav found that it is essential to study each aspect (posterior lateral, and anterior) by anatomical dissection (wit or without a loop magnifier) and by serial histologica sections in a three-dimensional plane.

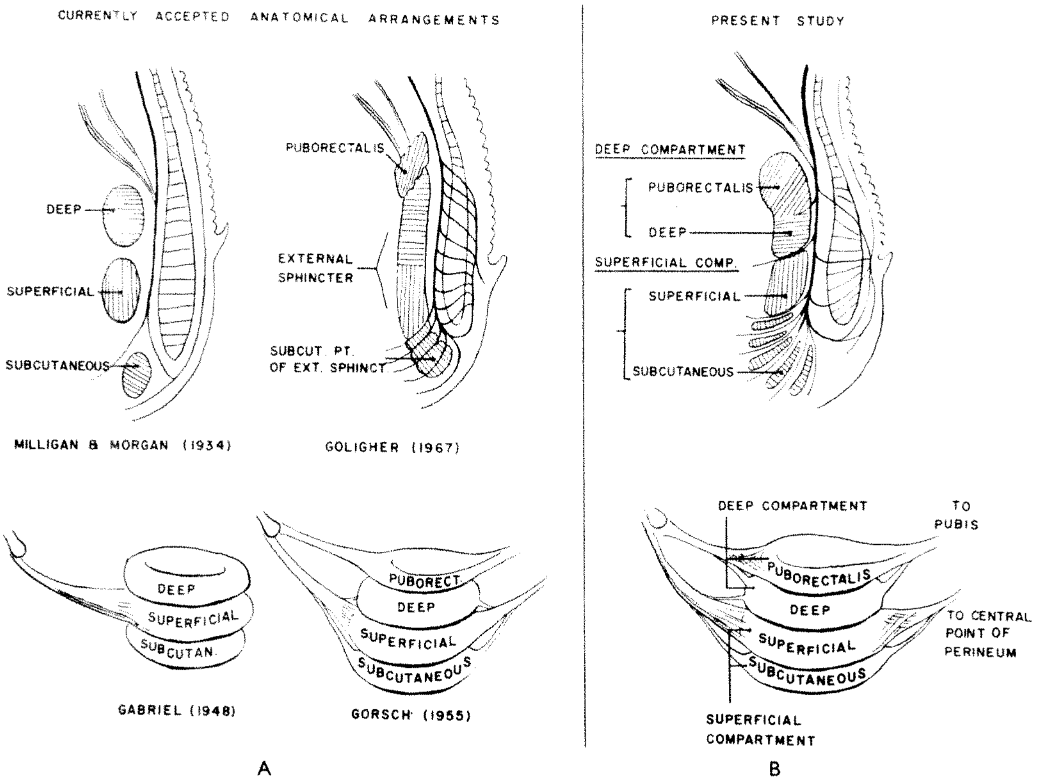


FIG. 1.—Diagram of the external anal sphincter comparing the current views (A) and the present authors' findings (B). A, Coronal sections of Milligan and Morgan (1934) and of Goligher (1967) present different views of the sphincteric arrangement—trilaminar and bilaminar patterns. The lateral views show the anteroposterior attachment of the external sphincter. Gabriel's (1948) view of the posterior attachment of the superficial sphincter differs from Gorsch's (1955) finding that all the components of the external sphincter attach anteroposteriorly. B, The deep compartment (puborectal muscle and deep sphincter) and the superficial compartment (superficial and subcutaneous sphincter) based on histological sections, and the pattern of anteroposterior attachment shown by gross dissection.

The configuration of the external sphincter show that there is a distinct difference in arrangement i the anterior aspect compared with the lateral an posterior aspects. These latter aspects also diffe in some degree from each other. Each of thes aspects will be discussed separately.

1. The structure of the posterior and latera aspects of the external sphincter conforms to th pattern described by others. However, there ar differences which need stressing.

The *lateral* portion of the external sphincte presents, on the one hand, a distinct subcutaneou component which is traversed by conjoined longitudinal fibres and, on the other hand, a deep externa sphincter which closely blends with the puborectalis Between these two muscle groups there is a stron and wide muscle sheath (superficial sphincter) close t the subcutaneous sphincter although not alway clearly distinguishable as such. This arrangement o the sphincter laterally can be clarified by histologica section rather than by anatomical dissection (*Fig.* 2 B)

Posteriorly, the subcutaneous sphincter is similarly easily recognizable with its traversing fibres of conjoined longitudinal muscle. However, the superficial and deep components are differently arranged. The superficial sphincter has the striking feature of a strong, tough, and triangular posterior extension to the back of the coccyx with some contribution by the subcutaneous sphincter. The deep sphincter, on the other hand, sends some fibres upwards and posteriorly which intermingle with the posterior

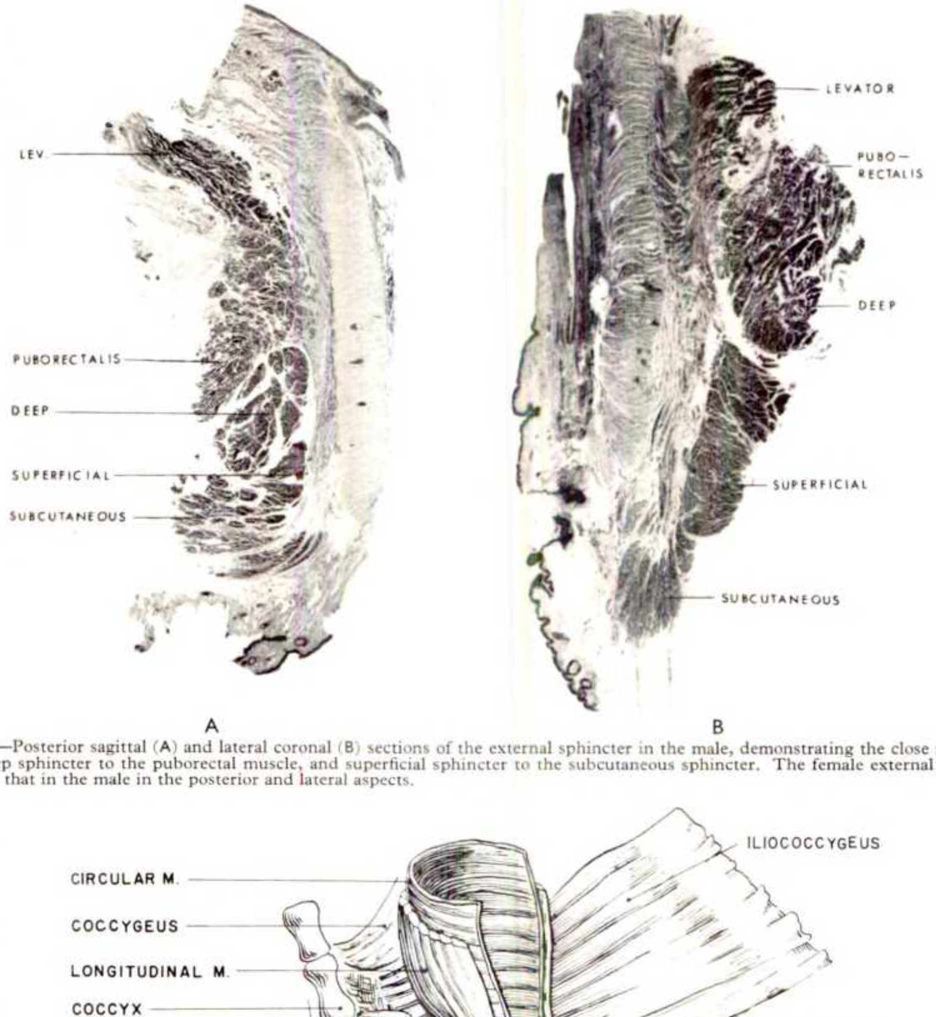


FIG. 2.—Posterior sagittal (A) and lateral coronal (B) sections of the external sphincter in the male, demonstrating the close relationship of the deep sphincter to the puborectal muscle, and superficial sphincter to the subcutaneous sphincter. The female external sphincter is similar to that in the male in the posterior and lateral aspects.

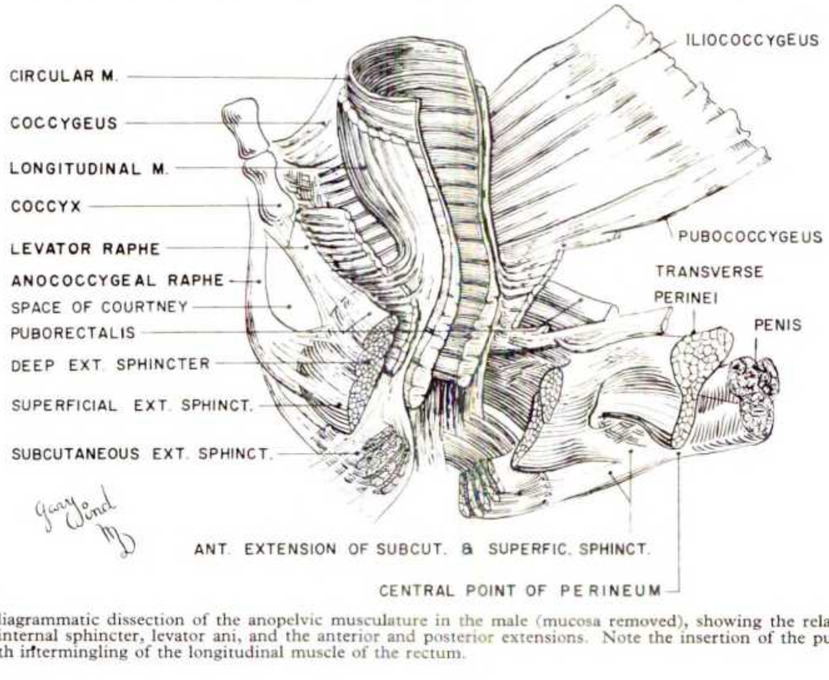
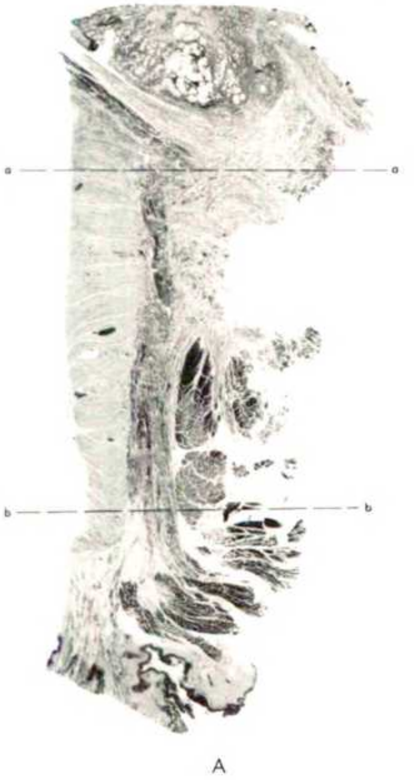


FIG. 3.—Semidiagrammatic dissection of the anopelvic musculature in the male (mucosa removed), showing the relationship between the external and internal sphincter, levator ani, and the anterior and posterior extensions. Note the insertion of the pubococcygeus into the rectal wall with intermingling of the longitudinal muscle of the rectum.



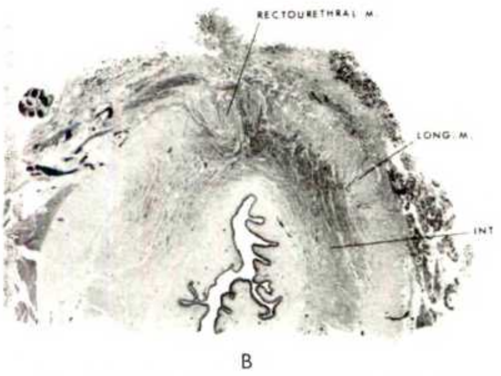


FIG. 4.—A, Anterior parasagittal section of the sphincter in the male, showing the internal sphincteric fibres projecting into the perineal body (inferior recto-urethral muscle). The conjoined longitudinal fibres envelop and bisect the deep part of the sphincter. B, Cross-section at the level of a—a in A, showing the insertion of the internal sphincter into the recto-urethral muscle.

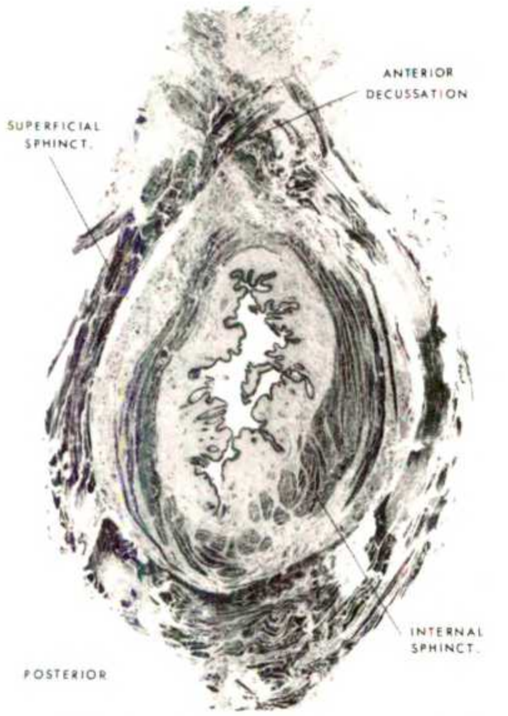


FIG. 5.—Cross-section of the superficial part of the anal sphincter in the male (at the level of b—b in *Fig.* 4 A), demonstrating the anterior decussation and its insertion into the bulbocavernosus and the central point of the perineum. No circular fibres can be seen anteriorly in the male.

puborectalis, and which then attach to the tip of the coccyx. A few fibres of the deep sphincter extend to the anococcygeal raphe. In other words, posteriorly the laminar pattern of the external sphincter can be identified by its manner of posterior extension but it is difficult to separate clearly the laminar structure by histological section (*Figs.* 2 A, 3).

Thus, a constant pattern is noted as follows:—

a. There is a close relationship between the deep sphincter and the puborectalis laterally (seen best on histological section; *Fig.* 2 B) and posteriorly (shown by their gross posterior extension to the tip of the coccyx; *Fig.* 3).

b. The subcutaneous and superficial portions of the external sphincter are also closely related by the common pattern of posterior extension to the anococcygeal raphe which inserts to the back of the coccyx, although laterally their proximity is subject to a wider variation than that of the deep sphincter and the puborectalis (*Fig.* 3).

Because there is a bilaminar arrangement in one plane whereas there is a trilaminar one in the other plane we feel that it is more accurate to describe the external anal sphincter as being composed of a *deep compartment* (deep sphincter and puborectalis) and a *superficial compartment* (subcutaneous and superficial sphincter) (*Fig.* 1 B).

2. Little attention has been paid to the marked dissimilarity of the anterior part of the external sphincter in men and women. Gorsch (1955) has noted the anterior part of the subcutaneous sphincter in women forming a prominent annular muscle lying directly below the perineal skin and bridging the interval between the diverging limbs of the superficial muscle; these limbs extend laterally, reach the pubic ramus, and fuse insensibly into the fibres of the lateral bulbocavernosus (vaginal sphincter); a few of the fibres may insert into the central tendinous point of the perineum. He did not mention any difference in the deep part of the male and female sphincters. However, on his schematic drawing of the sagittal section three distinct laminated muscles were illustrated. Fowler (1957) observed that some of the deep fibres in the female pass lateral to the perineal body to blend with the vaginal sphincter.

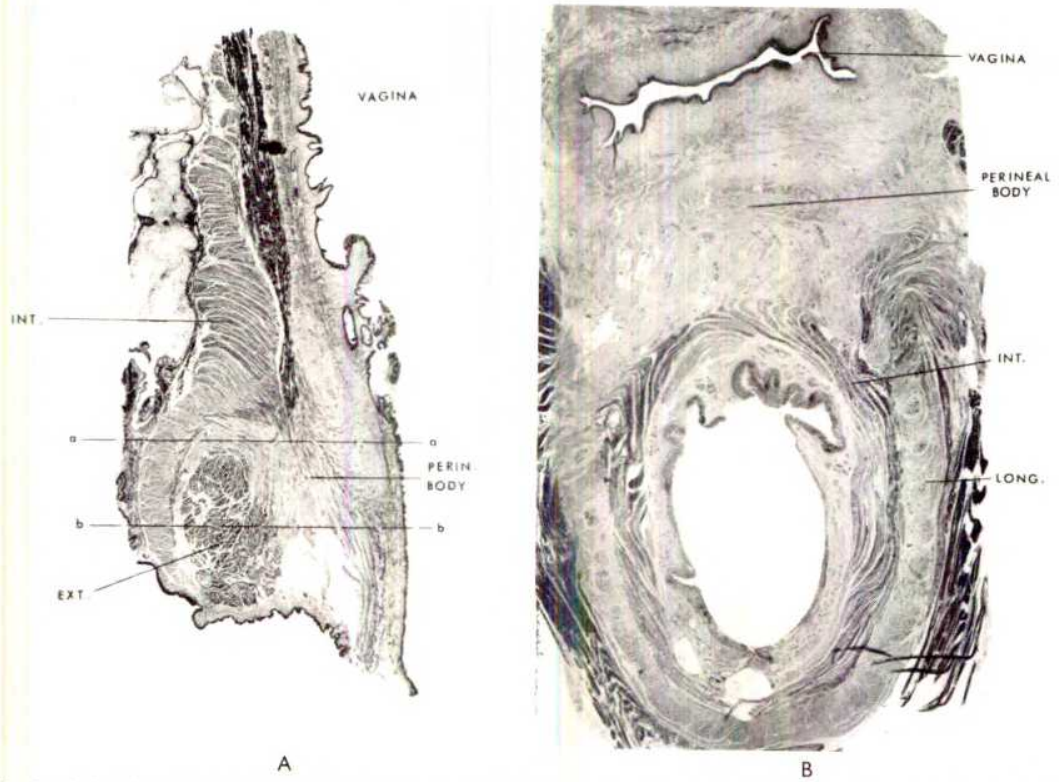


FIG. 6.—A, Anterior sagittal section of the sphincter in the female, demonstrating fibres from the internal sphincter mingling with longitudinal fibres. These fibres encapsulate the anterior muscle-bundle as a single mass. B, Cross-section of the sphincter in the female at the level of a—a in *Fig.* 4 A, showing the relationship of the projecting fibres of the internal sphincter, the longitudinal muscle, and the perineal body.

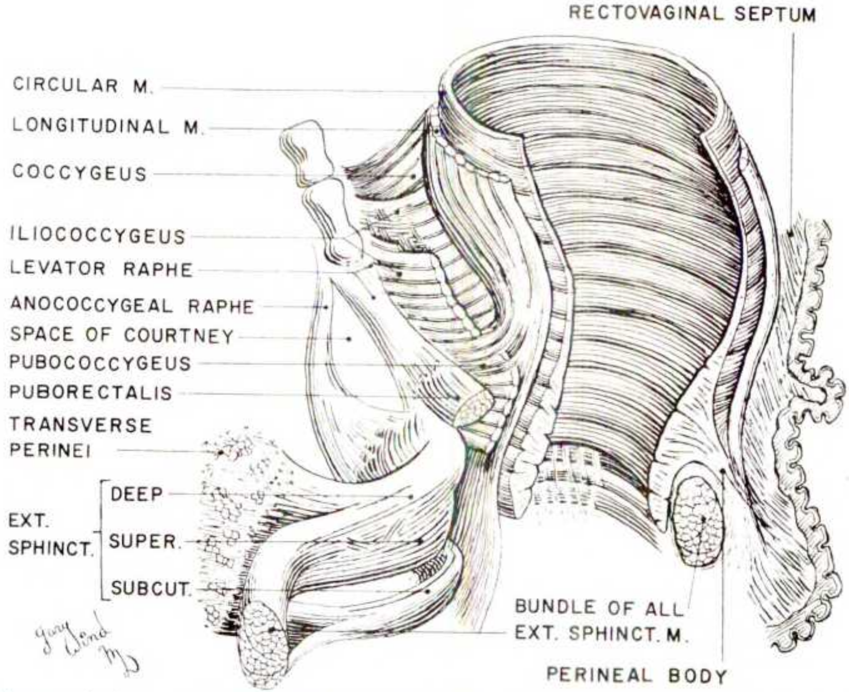


FIG. 7.—Semidigarammatic dissection of the anorectal region in the female with the external sphincter cut in the anterior mid-sagittal plane and reflected posteriorly (mucosa removed). The origin of the anterior muscle-bundle is clarified and the remaining anterolateral portions of the external sphincters are interdigitated into the transverse perinei.

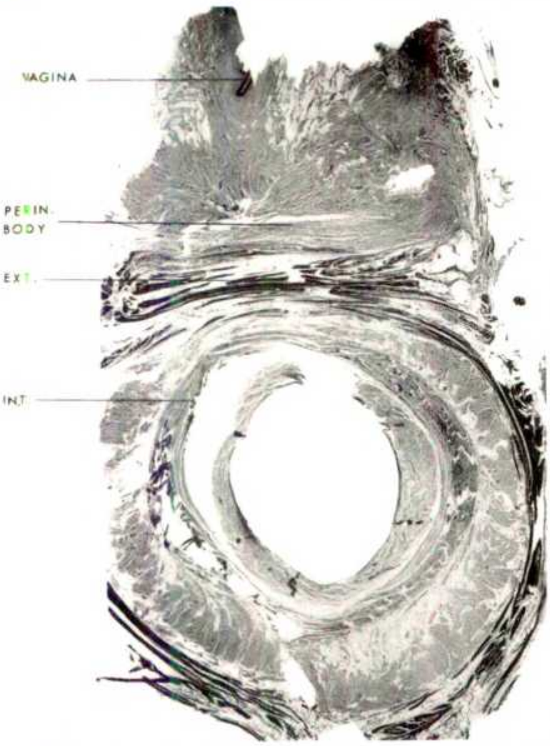


FIG. 8.—Cross-section of the sphincter in the female at the level of b—b in *Fig.* 4 A. A few decussating fibres are seen anteriorly; marked diminution of longitudinal muscle can be seen anteriorly.

The present study demonstrates that on sagittal section in the anterior midline there are specific features in each sex which differ also from those of the lateral or posterior part.

a. In the male the laminar pattern is well preserved. The lower half of the external sphincter muscles is traversed anteriorly by conjoined longitudinal fibres, and the upper half of the sphincter is enveloped (or occasionally bisected) by the conjoined longitudinal fibres in the longitudinal axis. The conjoined longitudinal fibres join with fibres of the internal sphincter which project anteriorly at the level of the perineal body (*Figs.* 4, 5). All the components of the external sphincter have anterior extensions with predominantly circular fibres, except for the superficial sphincter which has exclusively decussating fibres to the central point of the perineum, the superficial transverse perineal muscle, and the bulbocavernosus (*Fig.* 5).

The perineal body to which the external sphincter may relate is a complex structure in the male. The perineal body receives contributions from the longitudinal muscle, Denonvilliers' fascia, the transverse perineal and bulbocavernosus muscles, anteriorly projecting fibres of the internal sphincter, Colles' fascia, the urogenital diaphragm, and the recto-urethral muscle. A detailed description will be discussed elsewhere (Oh and Kark, 1972).

b. In the female the structure is very different anteriorly. On sagittal section in the anterior midline the whole sphincter appears as a single muscle-bundle which is grossly encapsulated by a mixture of longitudinal fibres and anteriorly projecting fibres of

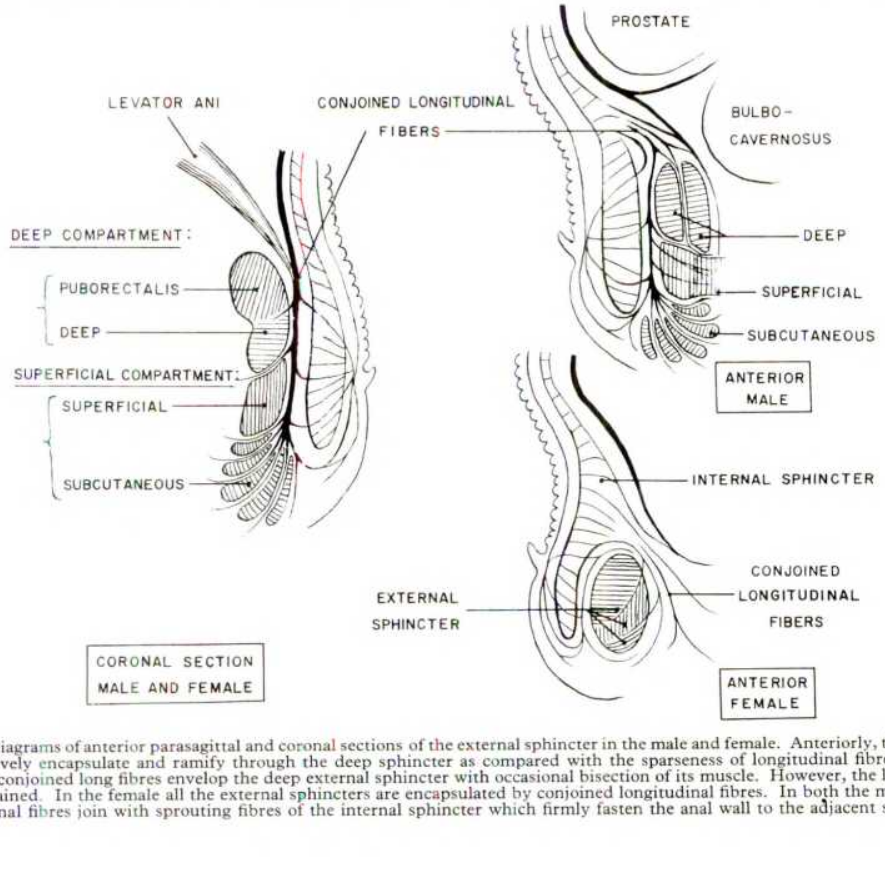


FIG. 9.—Diagrams of anterior parasagittal and coronal sections of the external sphincter in the male and female. Anteriorly, the longitudinal fibres extensively encapsulate and ramify through the deep sphincter as compared with the sparseness of longitudinal fibres laterally. In the male the conjoined long fibres envelop the deep external sphincter with occasional bisection of its muscle. However, the laminar pattern is well maintained. In the female all the external sphincters are encapsulated by conjoined longitudinal fibres. In both the male and female the longitudinal fibres join with sprouting fibres of the internal sphincter which firmly fasten the anal wall to the adjacent structures.

the internal sphincteric muscle (*Fig.* 6). In other words, on mid-sagittal section no muscular lamination can be identified anteriorly corresponding to the trilaminar sphincter of the lateral or posterior portion. However, dissection by an under-water technique and with the aid of a loop magnifier demonstrates that the origin of the fibres from each of the laminar fibres of the lateral part of the sphincter can be traced (*Fig.* 7). Only a few fibres of the lowermost part of the subcutaneous external sphincter are circular while the rest blend into the superficial external sphincter. The superficial sphincteric fibres are partly circular and may decussate and join the opposite side of the vaginal sphincter. These crossing fibres originate from the inferomedial portion of the superficial sphincter and form the antero-inferior portion of the anterior muscle-bundle. The rest of the fibres blend with the anterior median raphe and the superficial transverse perineal muscle. The deep sphincteric fibres are again partly circular in the inferomedial portion, and the superolateral portion of the sphincteric fibres fades out into the deep transverse perineal muscle and intermingles with the lower part of the puborectal muscle.

In general, all three parts of the external sphincter give circular fibres to the anterior single muscular bundle, with or without decussation (*Figs.* 8, 9). The lateral fibres of these muscles blend into the anterior median raphe or the transverse perineal muscle and puborectalis. Thus, the anterior sphincteric muscles can be distinguished from the lateral or posterior portion of the external sphincter by their appearance and in the pattern of the traversing conjoined longitudinal fibres (*Fig.* 9). These anatomical differences are probably derived from early developmental stages of evolution and integration of the anal tubercle from which the external sphincters originate (Tench, 1936; Gorsch, 1955; Wilson, 1967).

Acknowledgements.—We wish to extend thanks to Dr. G. Wind for his time and effort in preparing the anatomical illustrations; to Dr. G. Nirmul, who assisted in the dissections; and to Mrs. A. Acosta for the preparation of the histological sections.

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LONG-TERM REVIEW OF FUNCTION FOLLOWING PULL-THROUGH OPERATIONS OF THE RECTUM

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SUMMARY

1. Twenty patients previously reviewed from a functional standpoint following pull-through resection of the rectum have been reassessed 2 years or more following the initial review.

2. Fourteen of the 20 patients showed further improvement at the second examination, and half of these patients could be reclassified to indicate a significantly improved overall functional result.

3. It is clear that functional improvement may occur to a varying extent either gradually or at times rapidly even years after pull-through resection of the rectum.

IN an earlier report (Kennedy, McOmish, Bennett, Hughes, and Cuthbertson, 1970) it was suggested that functional results following pull-through operations of the rectum using the two-stage technique described by Turnbull and Cuthbertson (1961) eventually proved satisfactory in the majority of patients, though sometimes adequate function was delayed for many months. It was our belief that not infrequently a stable functional state was not reached for 12–18 months following operation, and that earlier unfavourable reports on postoperative continence (Goligher, Duthie, DeDombal, and Watts, 1965) might have been adversely influenced by the relatively short-term nature of the follow-up. To assess further the importance of time on the definitive degree of continence 20 of the original patients have been reviewed at least 2 years following the first assessment. The results of this survey confirm the original suggestion that continence frequently continues to improve for some time after operation but indicate that this period might be extended to several years in some patients. They also confirm that the majority of surviving patients will ultimately achieve quite reasonable function.

Table I.—RESULTS FOLLOWING PULL-THROUGH OPERATIONS ON THE RECTUM ASSESSED AT DIFFERENT TIMES AFTER OPERATION

CASE NO.	SEX	AGE AT OPERATION (years)	TIME OF ORIGINAL REVIEW (mth. after operation)	ORIGINAL CLASSIFICATION	TIME OF SECOND REVIEW (mth. after operation)	ADDITIONAL PERIOD OF FOLLOW-UP (mth.)	IMPROVEMENT	PRESENT CLASSIFICATION
1	M.	53	26	C	58	30	+ +	A*
2	F.	66	36	C	70	34	–	C
3	M.	49	54	B	87	33	+	A*
4	F.	57	72	B	105	33	+	B
5	F.	45	62	B	93	30	+	B
6	F.	46	60	B	93	33	+	B
7	F.	60	24	A	60	36	+	A
8	F.	42	84	B	112	28	±	B
9	M.	39	48	B	76	28	–	B
10	F.	40	40	A	72	32	–	A
11	M.	56	48	A	70	30	–	A
12	M.	62	7	B	28	25	+	B
13	M.	61	5	B	31	26	+	B
14	M.	62	6	C	32	26	+ +	B*
15	M.	59	47	B	72	25	+	A*
16	M.	50	10	B	36	26	–	A*
17	M.	63	30	B	58	28	±	B
18	M.	48	43	B	71	28	+	A*
19	M.	61	9	C	38	29	–	C
20	M.	51	39	B	68	29	+	A*

* = Reclassification.

MATERIALS AND METHODS

Twenty patients were selected at random from the original 79 who were interrogated and examined by us during the previous study (Kennedy and others, 1970). They included 13 males and 7 females with ages ranging from 39 to 66 years at the time of their original operations. The first review of postoperative function had been undertaken at varying intervals ranging from 5 months to 7 years following operation, and in each case the second review was undertaken at least 2 years later. In the majority of patients this interval actually ranged between 2½ and 3 years.

The patients were very carefully interrogated and examined by an independent observer (R. C. B.) according to the pattern previously described (Kennedy and others, 1970). In particular, special note was made of whether the patient wore a pad and if so to what extent and how frequently this was soiled. The ability of the patient to recognize and distinguish between flatus and solid or liquid faeces present within the rectum was recorded. Any lack of control in the passage of flatus or faeces was noted, including minor, though perhaps embarrassing, inadvertent errors. The regularity of the bowels, the ability of the patient to remain continent during attacks of diarrhoea, and also the possible necessity for the administration of enemas were recorded. Finally, any dietetic, domestic, social, or economic restrictions as a result of functional imperfections following the operation were documented. After all these parameters of bowel function had been considered the patients were classified according to an overall assessment of bowel function, as in the previous review. The results are considered in three groups.

Group A.—This included patients with function indistinguishable from normal or virtually so. By any standards these patients would be regarded as having achieved excellent postoperative results. They were able to differentiate between faeces and flatus and made no inadvertent errors in their passage. There were not required to wear perineal pads and their underclothes were not soiled. Their bowel habit was regular and they did not require enemas. Examination revealed normal sphincteric tone and no perianal excoriation.

Group C.—This included patients with unsatisfactory bowel function. They were unable to differentiate satisfactorily between flatus and faeces and made frequent errors in their passage. They wore perineal pads which were frequently soiled. They passed motions irregularly and often required enemas. Examination revealed anal sphincters with poor muscle tone and frequently there was evidence of perianal excoriation.

Group B.—This included patients whose postoperative function lay somewhere between that of the other two groups. Although they experienced mild to moderate imperfections with varying degrees of frequency, it was considered that the postoperative function was still sufficiently good to have made the operation worth while. Those who wore pads rarely soiled them to any extent, and errors in the passage of flatus or faeces were minor rather than major in degree. Their bowels were open regularly without enemas, and examination did not reveal excoriation though it frequently did demonstrate reduced sphincteric tone.

RESULTS

The results are set out in detail in *Table I* but some particular points should be emphasized. Of the 20 patients under review, none had deteriorated and 14 showed decided improvement in bowel function since the previous review. Half of the improved patients (7) were reclassified into a higher group. Special note should perhaps be made of *Case* 1 whose classification improved from group C to group A. A more detailed account of his postoperative function on the two occasions is as follows.

Case 1.—A male, aged 53 years, was operated upon for a carcinoma of the rectum on 24 Sept., 1965.

The original review on 17 Nov., 1967 (26 months after operation), indicated a poor functional result. He had worn a pad since the time of operation and he soiled it frequently. He was unable to recognize the presence of flatus in the rectum and claimed very little control over its passage. He was able to recognize the presence of faeces in the rectum, but his bowels acted very irregularly and sometimes as often as twenty times per day, indicating an almost constant dribbling of faeces from the back passage. He noted precipitancy and when his bowels were loose claimed reasonable control for only 50 per cent of the time. He was included in group C, indicating an unsatisfactory functional result.

At the time of the second postoperative review on 27 July, 1970, which was almost 5 years after operation, he claimed that he was very much better and had almost forgotten that he had had an operation. He no longer wore a pad and did not soil his underclothes. He could recognize the presence of both flatus and faeces in the rectum and claimed good control without the occurrence of minor errors. His bowels were then somewhat constipated and rarely, if ever, worked more than once per day. Examination revealed good sphincter tone with strong voluntary contraction of the external sphincter muscles and no evidence of perianal soiling or excoriation. He was reclassified at this time into group A.

One other group C case (*Case* 14, originally reviewed 6 months after operation) was reclassified as group B. In addition, 5 group B cases were reclassified as group A. It is important to note that while 2 of these cases were originally classified less than 1 year following operation, the remaining 5 were classified more than a year and in some instances as long as 4½ years after operation. This clearly shows that functional improvement, though usually maximal in the first 1–2 years following operation, can continue for some time thereafter and even occur to a significant extent 4 or 5 years later.

DISCUSSION

In our earlier publication (Kennedy and others, 1970) we emphasized that it often took many months before a definitive or stable state of bowel function was achieved following operation. The mean time required for this to occur was 13·3 months. We stressed that the impression which is gained of function following pull-through resection of the rectum might well be coloured by the time at which the review is undertaken. At that time we felt that little improvement was likely to take place beyond 12–18 months in the postoperative period. However, the current survey clearly shows this not to be so, and although subsequent improvement does not necessarily occur in each patient, it can and frequently does so, either gradually or at times quite quickly, as late as several years following operation. Although the most significant improvement apparently occurred in *Case* 1 at about the 3-year mark, appreciable though somewhat less impressive improvement also occurred in *Cases* 3, 15, 18, and 20, all at 3 years or more following operation. It is also clear from *Case* 1 that this late improvement can be quite considerable in extent; so much so that in this instance bowel function changed from an unsatisfactory status to one barely distinguishable from normal!

One might expect this improvement to be greatest and most noticeable in those with originally poor postoperative function, but it was also apparent from our interrogation of *Cases* 7 and 11 (both of whom we had originally considered to have excellent results) that marginal, though none the less worth-while, improvement had still occurred in these patients. Subsequent consideration of their original assessment did not provide grounds for reclassifying them at a less satisfactory level at that time.

It would seem therefore that patients with poor functional results following operation can, in all honesty, be given some hope that their function might still improve even some years after operation, and that in the final analysis very few surviving patients will be dissatisfied with their result. Admittedly, for the patients whose function improves most slowly this time can be a difficult and at times embarrassing period, though they are usually ultimately rewarded by satisfactory function and the retention of a natural sphincteric mechanism.

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THE FATE AND FUNCTION OF THE THYROID REMNANT

A SURGICAL AND RADIOACTIVE IODINE STUDY

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SUMMARY

Clinical, radioactive iodine uptake, and scan studies on a series of measured thyroid remnants indicate that after thyroidectomy one lobe only actively functions in a significant number of cases and that the subthyroid state only appears in toxic cases, usually those with certain pathological, familial, or therapeutically induced changes.

Remnant size did not appear to be critical, but under-function did not occur over 8 c.c. Above this size of residuum hypothyroidism does not appear to be directly due to the operation *per se* and should not therefore be called postoperative.

A fall in the assessment parameters after 6 months in a toxic case with a remnant measuring less than 8 c.c. and one or more of the associated features mentioned above would be an indication for commencing thyroxine.

Minor degrees of lymphocytic infiltration did not correlate directly with under-function.

There was a suggestion of right-sided dominance in the remnant as in normal and diseased glands.

THE key to the euthyroid state after thyroidectomy must lie in the size and/or function of the remnant. This has, as contrasted with the gland itself, three easily measured dimensions—length, breadth, and depth—which can be expressed as c.c. Taylor and Painter (1962) used this unit after the application of a stent mould. Murley and Rigg (1968) recorded the 'cuboid' volume as ml. Our measurements of the specific gravity of thyroid tissue (mean, 1·081) show that in figures of remnant size this is almost interchangeable with the grammes used by other authors. By relating this to the weight of the excised gland a non-visual percentage removal could be ascertained.

Table I.—DISTRIBUTION OF FUNCTION IN THE SCAN

TYPE OF GLAND	NO. OF CASES	TIME AFTER OPERATION (mth.)	RIGHT SIDE		LEFT SIDE		BOTH SIDES	NO OUTLINE
			Sole	>90 per cent	Sole	>90 per cent		
Toxic	46	1	6	4	4	2	29	1
		6	7	1	5	1	30	2
Non-toxic	32	1	12	1	2	1	14	2
		6	13	0	3	1	14	1

Function was measured by the scan outline and by 24-hour ^{131}I uptake. The scan outline and volume measurements were based on counts per second after a 50-μc. dose of ^{131}I. The 50 per cent line was taken as representing thyroid tissue within the limits of the collimated tube because:—

1. In several trial remnants this line corresponded well when the trachea was 2 cm. wide (in 18 out of 20 cases) (*Fig.* 1 B).
2. This corresponded well with the edge of a phantom with the same volume as a normal thyroid, although the scan edges fused if the containers were less than 2 cm. apart. The scan outline of any phantom could not be well delineated if the volume of radioactive material was less than 1 c.c.
3. The 50 per cent line corresponded in three freshly excised specimens after a preoperative dose of ^{131}I (*Fig.* 1 A).

AIMS AND PATIENTS STUDIED

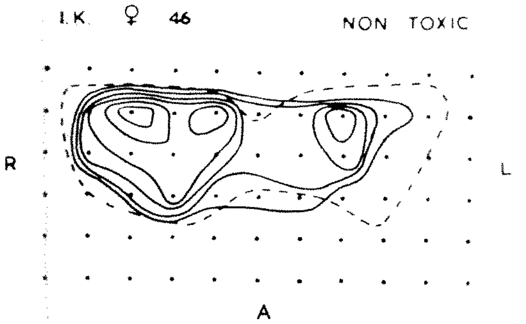
Our aims were:—

1. To measure the ^{131}I uptake and scan outline (including the lateral view) and hence the volume in each remnant about 1 month after operation when adjustment should have been made to the local effects of the operation, and to repeat these measurements in 6 months to see if any trend with regard to future function or mass of the remnant was developing.
2. To see if there was any direct relationship between the scan and remnant volumes with a view to assessing remnant size when this was not palpable in case of further trouble.
3. To see if any size was crucial to the development of the subthyroid state, which is still a matter of doubt.
4. To see if there was any evidence of right-sided dominance as in the intact gland.

The patients were operated upon between September, 1966, and September, 1969. Forty-six toxic and 32 non-toxic cases were able and interested enough to complete the assessment follow-up for periods of from 18 months to 4½ years. A further 12 (7 toxic, 5 non-toxic) did not attend at 6 months owing to pregnancy, distance, anaemia, psychological upsets, etc.

RESULTS

Table I shows the distribution of function in the scan. It was surprising to find that in more than 20 per cent of the toxic and 40 per cent of the non-toxic cases one lobe remnant only was functioning and that overall and especially in the non-toxic cases this was likely to be the right lobe (*Fig.* 1 C).



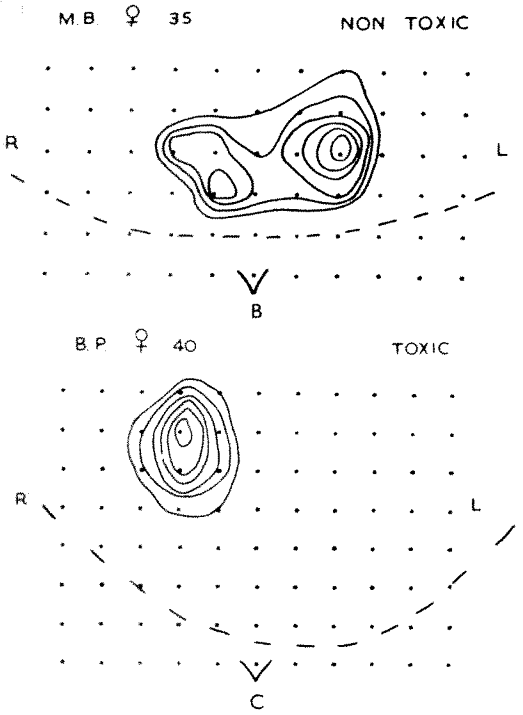


FIG. 1.—Diagrams of postoperative scans of the thyroid. A, Scan trace (50 per cent count line) (——) superimposed on the outline of the excised gland (– – –). B, A typical postoperative scan with both lobes functioning. C, A typical scan with one lobe only demonstrable.

Table II shows that no development of function was demonstrable after 6 months in the 24 remnants which did not function after operation, though in 1 toxic case a few tiny dots of function were picked up after this time. All but 1 of the cases with only one lobe functioning have remained euthyroid. *Table II* also shows that the size of the remnant that ceased to function varied from 0·125 to 8·0 c.c. in size.

Table II.—SIZE AND FATE OF NON-FUNCTIONING REMNANTS

NATURE OF CASE		SIZE OF REMNANT ON SIDE WITH ABSENT FUNCTION		APPEARANCE OF FUNCTION AT 6 MONTHS (Right and Left)
		Right	Left	
Toxic	No. Size (c.c.)	4 0·25–5·0 (average 2·2)	6 0·125–8·0 (average 4·2)	0
Non-toxic	No. Size (c.c.)	2 6·0–6·0 (average 6·0)	12 0·5–7·0 (averag 3·01)	0

All 24 cases with only one lobe functioning were euthyroid.

Table III.—RELATION BETWEEN SCAN AND REMNANT VOLUMES

NATURE OF CASE	SCAN LESS THAN REMNANT BY 1–3 TIMES (per cent)	GOOD CORRESPONDENCE ON ANTERIOR AND LATERAL SCANS (per cent)	SCAN GREATER THAN REMNANT BY 2–10 TIMES (per cent)
Toxic	10·2	38·5	51·3
Non-toxic	33·3	29·2	37·5

Table III shows that there was good correspondence between the scan and remnant volumes in nearly 40 per cent of the toxic and 30 per cent of the non-toxic cases. Where discrepancy was present, the scan was usually much larger in the toxic group than the actual stump size, perhaps owing to increased activity from continued stimulation by long-acting thyroid stimulator (LATS). Correspondence was greater in cases with only one lobe functioning, no doubt the result of lack of superimposition of one lateral lobe on the other. The lateral scan was the main variable owing to depth difficulties with the shoulder, though its actual measurement was fairly constant (0·75–1·0 c.c.). The chin occasionally caused similar difficulties with the upper part of the anterior scan.

Table IV indicates there is no relationship between the initial ^{131}I uptake and subsequent hypothyroidism, which only developed in the toxic group of cases. In the patients over 60 years of age 4 out of 5 had an initial uptake of less than 30 per cent, as did cases whose total remnant was less than 4 c.c. (*Table V*). If, however, the scan showed function on one side only and this residuum was below 0·4 c.c. the ^{131}I uptake tended to lie between 40 and 50 per cent, suggesting a contribution from the non-demonstrable remnant. *Table V* also shows that most small remnants were euthyroid.

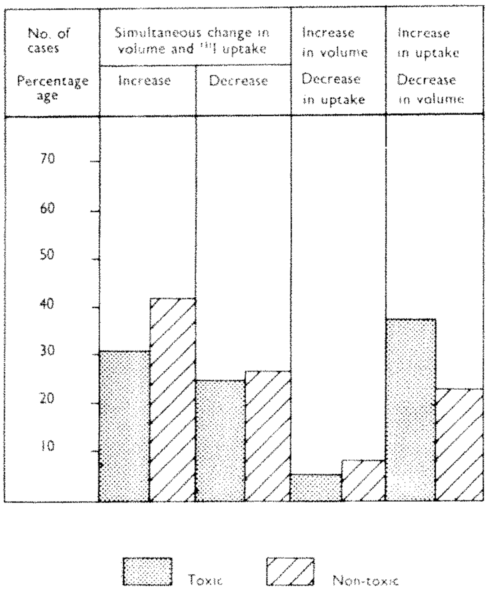


FIG. 2.—Changes in the volume of the remnant and ^{131}I uptake 6 months after the initial examination.

Table IV.—INITIAL ^{131}I UPTAKE AND SUBSEQUENT HYPOTHYROIDISM

NATURE OF CASE	NO. OF CASES	UPTAKE OF 0–30 PER CENT	UPTAKE OF 31–60 PER CENT	UPTAKE OF >60 PER CENT
Toxic	42	15	23	4
Subthyroid	8	5	3	0
Non-toxic	31	8	20	4
Subthyroid	0	0	0	0

No clear correlation could be found between the percentage of gland removed and the initial ^{131}I uptake, though high values tended to be found after 80 per cent removal while low values (under 30 per cent) occurred in two-thirds of those after 95 per cent removal. Of 2 cases with over 99 per cent removal, 1 non-toxic case had an uptake of 26 per cent while the other, a toxic gland, had no demonstrable function.

The histogram (*Fig.* 2) shows the several patterns of change after 6 months. Commonly there was a parallel increase or decrease in both parameters, but in 30–40 per cent the function increased though the volume decreased. The detailed figures from which this histogram was drawn show that one-half will show an increase of ^{131}I uptake (up to 600 per cent), one-quarter will show no change, and a smaller number a decrease. The volume most commonly remains the same or decreases, but there were wide individual variations.

Table V.—INITIAL ^{131}I UPTAKE IN PATIENTS WITH SMALL FUNCTIONING REMNANTS

NATURE OF CASE		SIZE OF REMNANT			AVERAGE INITIAL ^{131}I UPTAKE (per cent)
		1–2 c.c.	2–3 c.c.	3–4 c.c.	
Toxic	*a*	1	3	3	26
	b	1	2	0	41
Non-toxic	*a*	1	2	2	18
	b	1	0	1	49

a, Both lobes functioning; total thyroid tissue, 4 c.c.

b, One lobe functioning; lobal thyroid tissue on functioning side, 4 c.c.

The optimum size of remnant can be assessed by study of the fate of the average remnant, that of the small remnant, the histopathology present, and the clinical features associated with under-function of the residuum. In toxic cases the average size of the remnant was 6·5 c.c. (range 0·5–24·0 c.c.) and the average percentage removed, 84 (range, 71–96 per cent), with a 17·4 per cent incidence of subthyroidism and no recurrence.

In non-toxic cases the figures were 7·9 c.c. (range 2·0–18·5 c.c.), 85 per cent removal (range 42–99 per cent), and no case of hypothyroidism.

Small remnants (below 4·0 c.c.) were left in 8 toxic cases, with 1 subthyroid state, and in 5 non-toxic cases, with no under-function. In 5 cases in which the scan showed function on one side only the remnant was less than 4.0 c.c. and all were euthyroid.

In all the cases developing myxoedema the remnant was 8·0 c.c. or less, but certain other common factors were present. These are detailed in *Table VI*. All the cases were toxic; all had lost volume or even scan outline after 6 months; in most the function after this time had diminished even if originally adequate; in all these cases the pathological changes were degenerate (foci of calcification, lymphocytic infiltration, thyroiditis, or excess colloid). Usually other factors were present—a family history of goitre, severe or refractory disease, sensitivity to anti-thyroid drugs, or an odd psychology requiring continuous medication which was potentially goitrogenic.

No correlation was found in relation to age, moderate variations in toxicity, previous adiposity, menopause or diabetes, or blood group.

The time interval to the appearance of subthyroidism varied from 3 months to 3 years.

Some degree of lymphocytic infiltration was, however, not always ominous, and 10 toxic and 6 non-toxic cases (mean remnant size of 6·5 c.c. for toxic and 9·5 c.c. for non-toxic) were noted as showing minor degrees of lymphocytic infiltration without developing hypothyroidism at 3 years. In all except 1 either the ^{131}I uptake or volume had gone up markedly (over 40 per cent) at 6 months or both had gone up at this time. The exception was a woman of 57 years in whom the ^{131}I uptake fell from 26 to

Table VI.—DATA ON CASES DEVELOPING HYPOTHYROIDISM*

CASE NO.	AGE AND SEX	DESCRIPTION OF THYROID	P.B.I.	VOLUME OF REMNANT (c.c.)	PERCENTAGE OF THYROID REMOVED	POSTOPERATIVE ^{131}I UPTAKE	PERCENTAGE CHANGE AT 6 MONTHS		TIME OF ONSET OF MYXOEDEMA (mth.)	HISTOLOGY	ASSOCIATED FACTORS	BLOOD GROUP	RATIO OF PREOPERATIVE WEIGHT-LOSS TO POSTOPERATIVE WEIGHT-GAIN
							^{131}I Uptake	Volume					
2	48 F.	Nodular	19·4	4·0	91	Not done	Not done	−3	9	Hard calcified foci	Anxiety state	A, Rh +ve	2 : 2
9	63 F.	Nodular	10·2	3·0	97	29	−47	−19	9	Many calcified patches	Small, stout. Had ^{131}I previously	O, Rh −ve	1 : 2
13	37 F.	Smooth	16·1	5·5	85	55	+13	−2	15	Colloid markedly present	Odd psyche. On tablets. P.H. of asthma. Claustrophobia	A, Rh +ve	½ : 2
21	56 F.	Nodular	8·0	5·0	97	51	−23	−24	30	Nodular. No lymphoid tissue	Sister had had thyroidectomy	O, Rh −ve	1 : 2
25	46 F.	Smooth	14·8	8·0	84	23	−78	Too low to plot	6	Foci of lymphocytic infiltration	Sister had toxic goitre	A, Rh +ve	1 : 2
28	21 F.	Smooth	7·6	8·0	83	21	−75	−45	6	Lymphocytic infiltration	Joint pains on starting Neo-mercazole	A, Rh −ve	1 : 2
33	48 F.	Nodular	12·8	6·0	80	52	−37	−25	36	Areas of chronic thyroiditis	On tablets for nerves	A, Rh +ve	1 : 2
46	51 F.	Nodular	15·6	7·0	90	2	+50	Too low to plot	8	Hypercellular + degenerate pleomorphism	Severe myopathy. Pretibial myxoedema and fibrillation	A, Rh +ve	2 : 3

* All the cases were toxic.

16 per cent and in whom both scans were too low to plot. However, at 3 years she was clinically well and had a normal serum-cholesterol.

In a similar way the occurrence of one of the other adverse factors alone did not always presage underfunction. There were 3 cases who had had previous courses of drug treatment (remnant sizes 9·0, 7·0, and 4·75 c.c.—the last with some lymphocytic infiltration) and 3 with a family history of goitre (remnant sizes 6·0, 4·75, and 5·5 c.c.) who remained euthyroid. In 4 of these 6 cases both the ^{131}I uptake and the volume had gone up, but in 2 (remnant sizes 4·75 and 5·5 c.c.) they were down. These 2 patients will require careful observation or, better perhaps, prophylactic thyroxine.

These results indicate the following conclusions:—

1. It should be possible to predict many of those cases who would be likely to develop hypothyroidism after thyroidectomy if a ^{131}I uptake and scan outline were carried out 1 month after operation and 6 months later in any toxic case with degenerative histology, a family history, previous prolonged drug or irradiation therapy, or continued tablet taking; a falling uptake and volume would be a strong indication for prophylactic thyroxine administration.
2. Taking the 50 per cent count line there was a good correlation between the scan size and that of the remnant in 30–40 per cent of the cases, and more in the toxic group. In the others the ratio varied widely, the scan usually being the greater. This is not accurate enough to 'measure' the size of a 'non-palpable recurrence'.
3. A remnant size of just over 8 c.c. is likely to provide maximum protection against surgically induced myxoedema, with minimal recurrence of thyrotoxicosis, even in the presence of a single predisposing factor.
4. In remnants made similarly on each side often only one showed function on the scan and this was more likely to be the right side in the ratio of 3 : 1, suggesting that the remnant retains the dominance noted in normal scans.

DISCUSSION

It was surprising to find that in 24 cases (33·3 per cent)—mostly non-toxic glands—the postoperative scan showed function on one side only, though there was an apparently similarly treated and equally large and vascular remnant on the other side. The average size of the 'disappearing' stump was 4·1 c.c., though our studies indicated that 1 c.c. of active thyroid tissue should have been confidently demonstrable and separable from another of similar size 2 cm. apart.

Artagaveytia, De Grossi, Gotta, and Pecorini (1965), Thomson (1966), and Wiener and Roos (1968) have drawn attention to the fact that the normal scan is often asymmetrical, favouring the right side, and that most disease processes occur more frequently in the right lobe, while hemi-atrophy appears most often in the left lobe. Wiener and Roos (1968) state that the richer vascularization of the right lobe has been proposed as an explanation. We have often noted that the right inferior thyroid artery appeared larger than the left and that if there was any difficulty in finding an inferior thyroid artery it was usually the left one owing to its small size. The vascular insult of operation would thus be likely to affect the left remnant more severely. Such vascular factors would contri bute to the difficulties relating scan to actual volum measurements and would affect the less robustl bloody, non-toxic stump more than the toxic rem nant, accounting for the larger proportion of scan which were smaller than the remnants in this grou of cases.

The loss of function in a lobe did not lead to hypc thyroidism even when the remaining active remnar size was 4 c.c. or less. All were euthyroid except case with a 3-c.c. residuum which had had previou ^{131}I treatment and subsequently had become euthyroic

Our experience would suggest that in the nor degenerative, non-treated, non-familial gland a thy roid remnant of 4 c.c. would be unlikely to cause i effects or to allow recurrence.

However, the degree of lymphocytic or other de generation can only be clear after examining th postoperative histology and, as in our series, tox cases with such changes and a remnant of less tha 8 c.c. had an incidence of hypothyroidism of abou 18 per cent and it would seem wise to cover th possibility by leaving a remnant of more than th size.

Thus, leaving a residuum of just over 8 c.c. (i our cases tending to be 3 cm. long by 1·3 cm. wic by 1 cm. deep on each side) would probably be satisfactory standard remnant. Taylor (1966) recon mended this same size using a configuration of 4 2 × 0·5 cm. on each side. Taylor and Painter (196 found that in their cases of thyrotoxicosis who we euthyroid after operation the volume of the remna was 8 c.c. This corresponds with the lower end Murley and Rigg's (1968) measured thyroid remna range (6–15 ml.).

According to British experience, therefore, 8 c. would seem to be the optimum remnant. The use such an optimum remnant would not, howeve abolish completely hypothyroidism occurring aft operation, as this is well known to occur spo taneously in toxic and non-toxic goitres and certain minimum incidence of hypothyroidism wou be inevitable in any sizeable series from the progressi pathological changes involved.

Green (1950) found the correlation between th development of hypothyroidism and lymphocyt infiltration to be close and we found it to be sign ficant in those cases who became subthyroid.

Nevertheless, there was another group of 16 cas (10 toxic, 6 non-toxic) with a mean remnant size 6·5 c.c. and 9·5 c.c. respectively, in whom son degree of lymphocytic infiltration was noted, but myxoedema developed during up to 3 years of obse vation. In all the cases the ^{131}I uptake or volun had gone up markedly, viz. over 40 per cent, or bo had gone up significantly, with 1 exception.

In the main in both toxic and non-toxic cases fun tion tends to increase with the passage of time, b in 35 per cent it will diminish and it is in this grou especially if toxic and associated with one of th other factors outlined, that under-function will occ

Adequate remnant size covering degenerative hist logy will not alone prevent hypothyroidism and sm size alone will seldom cause it. Our own smalle remnant (500 mg.) gave a 55 per cent uptake at months. Szilagyi, Barrett, and Preuse (1955) fou the incidence of hypothyroidism was only significa below 150 mg., but the safety of operation was difficult to ensure below 800–1000 mg. Marchetta, Krause, and Sako (1963) noted that after 'total' thyroidectomy for carcinoma the postoperative scintigram after a few months showed a radioactive iodine uptake of 20–25 per cent.

Thus neither knowledge of the technique used by different authors, nor remnant size, nor operative histology, contains the whole secret of the development of hypothyroidism. In our series it only occurred in the toxic gland and in other series only significantly in the toxic gland.

Some other factor in addition, found for practical purposes only in the toxic group, must be necessary to produce this liability to myxoedema. Such a factor might be the continuation of the auto-immune process which caused the disease. While LATS is one of the few immunoglobulins to stimulate cells it might well later destroy or exhaust the gland. It appears to cause the type of thyrotoxicosis associated with focal thyroiditis (Mason, 1967) and with a tendency towards under-function without antibody formation—Category I of Hargreaves and Garner (1968). Anderson (1964) thought that this picture was in part due to a delayed hypersensitivity process. A genetic component in its aetiology is indicated by the high incidence of myxoedema and Hashimoto's disease in the relatives of those suffering from thyrotoxicosis. Spontaneous myxoedema can also develop.

There are thus many factors, other than operation, capable of producing hypothyroidism after operation. It is probable that if the remnant is above 8 c.c. hypothyroidism is not due to the operation *per se* and should not be labelled postoperative, as it is due to the nature of the disease or other iatrogenic intervention. Indeed, thyroidectomy can not only control thyrotoxicosis but even alter and improve the toxic histological appearances of the gland remnant, especially after the first year (Curran, Eckhert, and Wilson, 1958).

Recovery from any transient hypothyroidism following operation is generally thought to have taken place within 6 months. Therefore, whatever the individual cause in these high probability cases outlined above, the tendency towards under-function should be assessed by postoperative scan outline and ^{131}I uptake measurements after 1 and 6 months. If both are down or the ^{131}I uptake is markedly down thyroxine should be given to anticipate the appearance of myxoedema.

Neither a single postoperative ^{131}I uptake nor an assessment of the percentage uptake per c.c. of residual tissue gave any worth-while guide to subsequent thyroid status. However, a weight-gain of 6·35 kg. above that lost in the preoperative toxic phase in the presence of careful dietary habits might be considered a useful clinical hint of incipient hypothyroidism.

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EVALUATION OF BREAST TUMOUR SEX CHROMATIN (BARR BODY) AS AN INDEX OF SURVIVAL AND RESPONSE TO PITUITARY ABLATION

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SUMMARY

In a retrospective study of 36 patients with advanced breast cancer relationships were found between the tumour Barr body count and the response to pituitary ablation and the length of survival. High tumour Barr body counts were associated with long survival after treatment, and low counts with short survival $(P<0{\cdot}001)$. High counts were also associated with a good response to pituitary ablation, and low counts with a poor response $(P<0{\cdot}01)$. The tumour Barr body count gave possibly better prediction than urinary steroid measurement.

A BARR body is defined (*Fig.* 1) as a female cellular sex chromatin marker, 1 μ in diameter and located against the inner surface of the nuclear membrane envelope (Barr and Bertram, 1949). Any living nucleated cell may be used in the examination for sex chromatin, but in practice cells with clear nuclei obtained from easily accessible sites are used.

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Barr bodies may be identified in about 50 per cent of normal female cells. This is also the case for most tumours, in that the tumour Barr body count is equivalent to the normal count for that patient (Sohval and Gaines, 1955; Tavares, 1955). However, Kimel (1957) found that breast cancer was an exception to this rule. He studied 100 cells in a tumour and counted the number containing Barr bodies. In his study of 91 mammary cancers Kimel found that 66 per cent of the tumours had counts of less than 40 and that 53 per cent had counts of less than 30. In normal tissues, however, the lowest sex chromatin count observed was 40. Only 34 per cent of the tumours studied had counts in the normal range of 40 or more.

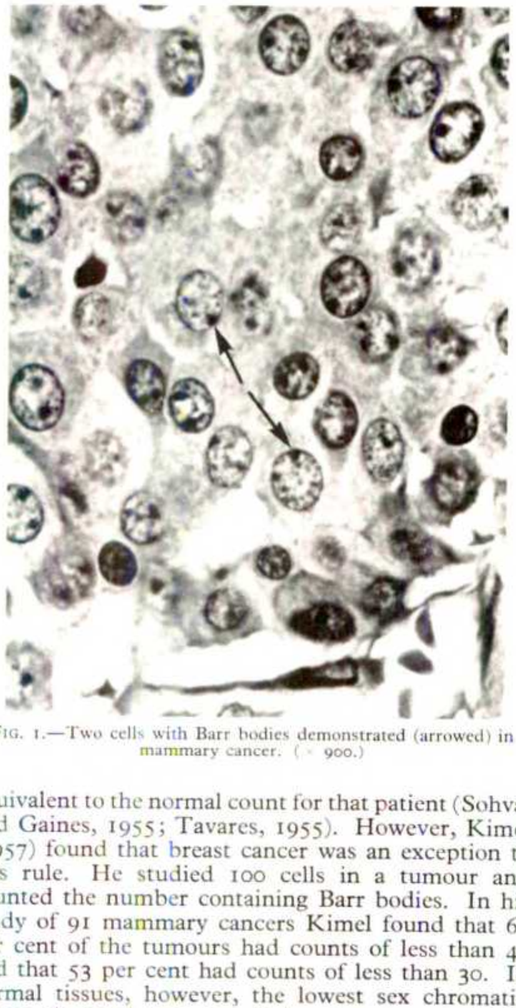

FIG. 1.—Two cells with Barr bodies demonstrated (arrowed) in mammary cancer. (× 900.)

Bohle, Burger, Fischbach, and Schooli-Tubingen (1965) summarized 10 reports from the German literature on studies of sex chromatin in cases of breast cancer. They concluded that low tumour sex chromatin counts were associated with lowered responsiveness to hormones and that these tumours were more malignant than those with high counts. Shirley (1967) confirmed these findings. In a retrospective study from the Massachusetts General Hospital he found that hormonal therapy was most likely to be successful in patients with normal sex chromatin in their tumours. In addition he found that the response to hormonal therapy was extremely poor in women under the age of 50 years with high sex chromatin counts and in older women with lo counts. These results do not confirm the hypothes that the sex chromatin complement of the tumo indicates oestrogen dependence. No comparison h been published of the value of the tumour Ba body with that of the urinary steroid estim tion in predicting survival or response to trea ment.

PATIENTS AND METHODS

Thirty-six mammary cancers were studied, select at random from routine surgical slides stained wi haematoxylin and eosin. Most of the sections we taken from drill biopsy specimens and thus we unsuitable for accurate interpretation of tiss differentiation. Approximately 100 cells were counte on each slide and the number of cells containing Ba bodies was expressed as a percentage of the tot number of cells counted. Slides were only include in the study if the sections were evenly stained an the cells clearly defined.

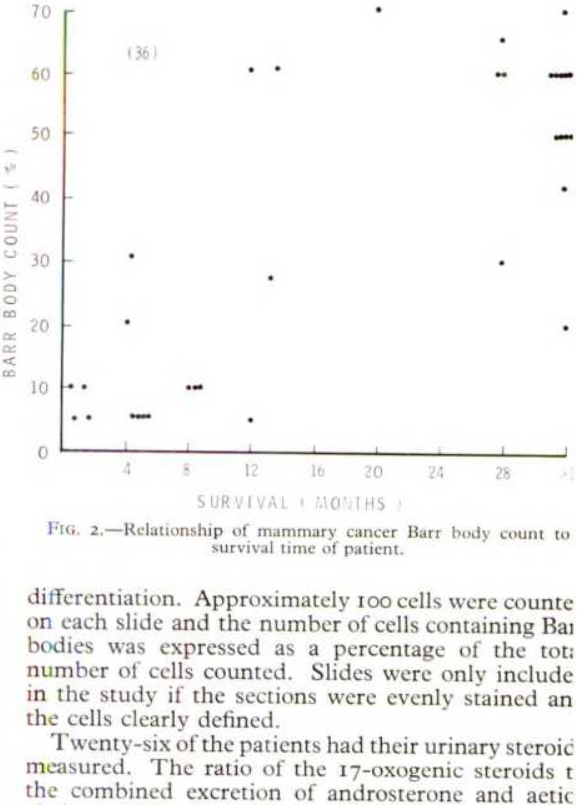

FIG. 2.—Relationship of mammary cancer Barr body count to survival time of patient.

Twenty-six of the patients had their urinary steroi measured. The ratio of the 17-oxogenic steroids t the combined excretion of androsterone and aetic cholone (11-deoxy-17-oxosteroids) has been foun to be a good index of response to endocrine therap (Fotherby, Sellwood, and Burn, 1970). A value of for the ratio provided a fair degree of discriminatio between those who responded and those who did no the proportion of responders being three times greate in those with a low ratio than in those with a hig one.

RESULTS

Relationship of Mammary Cancer Barr Bod Count to Survival Time of Patient.—In *Fig.* there appear to be two populations: one with lo counts and a short survival, and the other with hig counts and a longer survival. Many of the patient shown as having survived more than 30 months are in fact, still alive. All the patients in *Fig.* 2 an subsequent figures had advanced disease and were treated by endocrine therapy.

Comparison of Barr Body Count and Steroid Ratio in Relation to Response to Pituitary Ablation (*Fig.* 3).—The high tumour Barr body count was associated with a good response to pituitary ablation whereas the low count was not ($P < 0{\cdot}01$). Similarly, patients with low steroid ratios were found to respond to pituitary ablation significantly better than patients with higher ones ($P < 0{\cdot}05$).

Comparison of Barr Body Count and Steroid Ratio in Relation to Survival Time (*Fig.* 4).—Patients who survived up to 12 months after treatment have been compared with those who survived

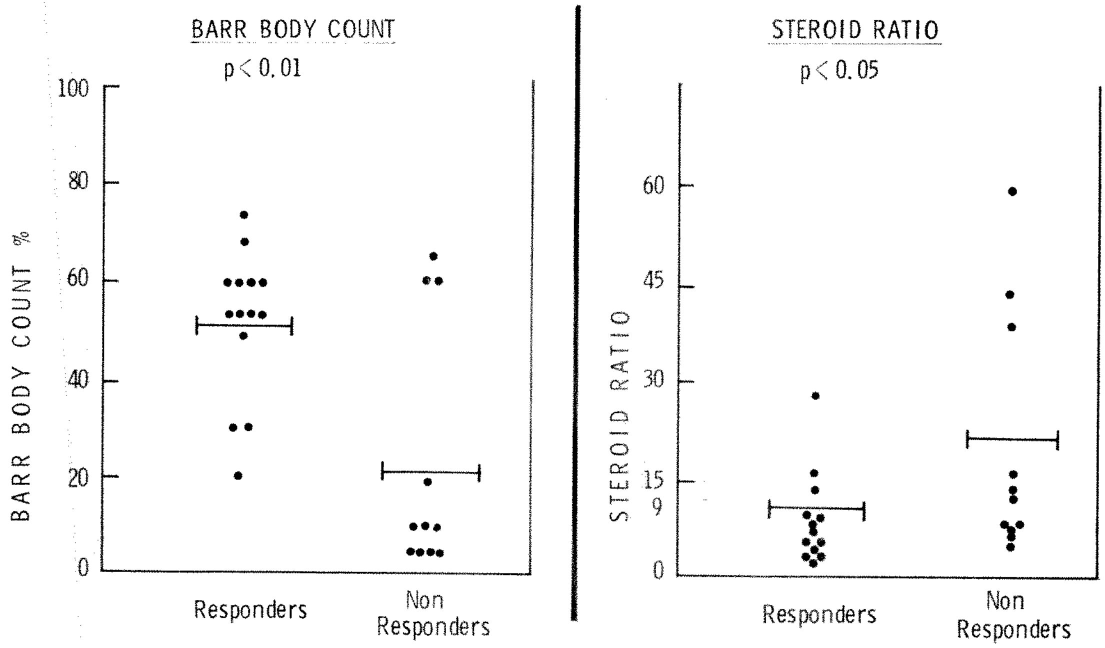

FIG. 3.—Comparison of Barr body count and steroid ratio in relation to response to pituitary ablation.

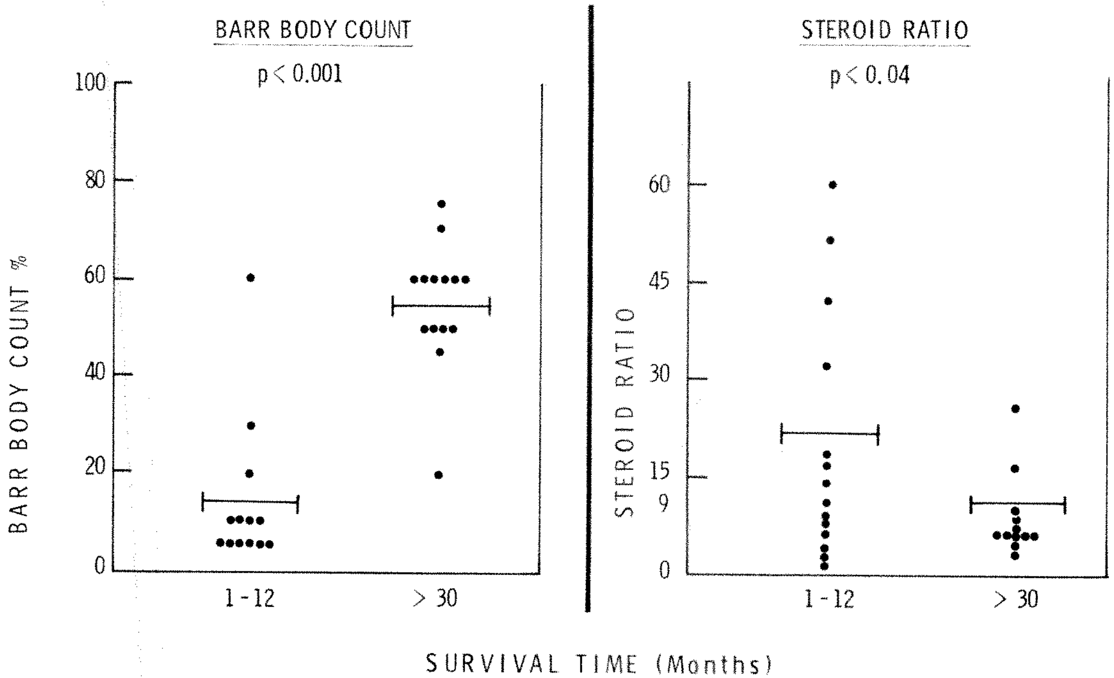

FIG. 4.—Comparison of Barr body count and steroid ratio in relation to survival time.

more than 30 months in respect of the Barr body count and of the steroid ratio. The mean Barr body count was higher ($P < 0.001$) and the mean ratio lower ($P < 0.04$) in those who survived the longer time.

Relationship between Barr Body Count and Steroid Ratio in Patients who underwent Pituitary Ablation.—Twenty-two of the patients who underwent pituitary ablation had both the tumour Barr body count and the urinary steroid ratio measured. Simple inspection of the data suggested that a level of 40 per cent for the Barr body count (like that of 9 for the steroid ratio) provided a fairly good discrimination between those who responded and those who did not. The relative values of these two factors in relation to response are shown in *Fig.* 5 and *Table I*. Although the numbers are small, the data suggest that the steroid ratio and the Barr body count together may provide a better prognostic index of the response to therapy than either alone.

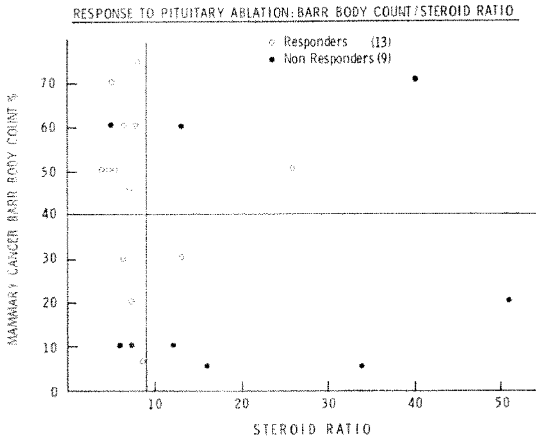

FIG. 5.—Relationship between Barr body count and steroid ratio in patients who underwent pituitary ablation.

Table I.—RELATION OF BARR BODY COUNT AND STEROID RATIO TO RESPONSE TO PITUITARY ABLATION (*see also Fig.* 5)

	RATIO OF RESPONDERS TO NON-RESPONDERS	PERCENTAGE
Steroid ratio alone		
<9	11 : 14	79
>9	2 : 8	25
Barr body count alone		
>40	9 : 12	75
<40	4 : 10	40
Steroid ratio and Barr body count		
<9 and >40	8 : 9	89
>9 and <40	1 : 5	20

DISCUSSION

This study suggests that the simple method of counting the numbers of cells containing Barr bodies in the mammary cancer is significantly related to both the length of survival of the patient and her response to pituitary ablation and that it may therefore be of prognostic value.

The tumour Barr body count has been criticized on the grounds that it is merely a reflection of the degree of differentiation of the tumour, normal counts being associated with well-differentiated tumours and low ones with poorly differentiated tumours. In the present study the pathologist was able to assess the degree of differentiation in only 14 of the 36 patients. All 14 patients had advanced disease of the breast and were not treated by mastectomy, the tumour material being taken by drill biopsy. However, it is interesting to note that in 9 out of the 14 specimens the count correlated well with the degree of differentiation of the tumour but that in 5 it did not. Conclusions cannot be drawn from such small numbers.

There is disagreement in the literature about the relationship of the tumour Barr body count and the degree of dissemination of the cancer. Kimel (1957) presented evidence that tumours with high counts were more likely to metastasize than those with low counts, whereas Bohle and others (1965) found that lower counts were associated with a shorter survival time—a finding in agreement with our results.

The comparison of the tumour Barr body count with the urinary steroid ratio is an interesting one. Both estimations agree with regard to prediction of survival and the response to pituitary ablation, but it may be that the tumour Barr body count provides better discrimination. When the two estimations are compared in *Figs.* 3 and 4 with respect to response to treatment and survival, the Barr body count shows a greater difference between the means and a higher level of statistical significance in both groups.

A good correlation might be expected between the tumour Barr body count and the urinary steroid ratio in view of their similar predictions concerning response to pituitary ablation and to survival of the patient. However, this is not the case (*Fig.* 5). It may be, as suggested already, that the two estimations together provide a better discriminant than either alone, but the attraction of the Barr body count is that it is simple and can be used in any hospital.

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AMPUTATION NEUROMA OF THE GREAT AURICULAR NERVE AFTER PAROTIDECTOMY

By MICHAEL HOBSLEY

DEPARTMENT OF SURGICAL STUDIES, THE MIDDLESEX HOSPITAL, LONDON

SUMMARY

Division of the great auricular nerve during the operation of parotidectomy sometimes results in an amputation neuroma. The condition can be diagnosed on clinical grounds, thus obviating the need for further surgical exploration.

THE finding of a subcutaneous nodule in or near he scar after parotidectomy for neoplastic disease naturally raises the strong possibility that the lump represents an implantation recurrence of the growth. The present article describes 2 patients in whom such nodule was found to be benign, namely, an amputation neuroma of the great auricular nerve, and another 2 in whom the same diagnosis seemed probable. Criteria are suggested by which the clinical diagnosis of this condition may be made.

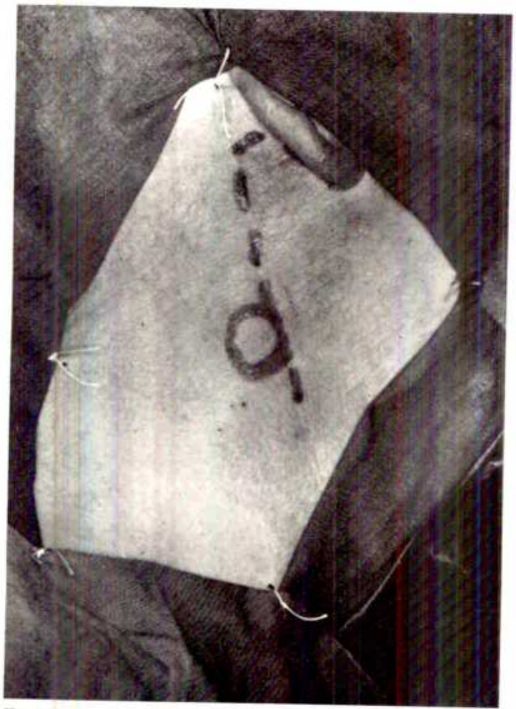

FIG. 1.—*Case* 1. The circular outline of the subcutaneous nodule has been marked and the position of the old parotidectomy scar indicated as a dotted line.

CASE REPORTS

Case 1.—E. H., a male aged 54 years, presented in 1964 with a 10-year history of a lump in the right parotid region. A total parotidectomy for a lesion in the deep part of the gland was performed on 20 March, 1964, with conservation of the facial nerve. The histological diagnosis was pleomorphic adenoma. The patient made a satisfactory recovery.

Follow-up was uneventful till 24 Nov., 1970, when the patient reported some discomfort in the lower third of the scar, radiating upwards and forwards into the face on movements of the neck. On examination there was a tender nodule in the region indicated in *Fig.* 1. Digital pressure on this nodule resulted in radiation of pain as the patient had described. On 12 March, 1971, the lump was excised with a wide margin of surrounding tissue; the proximal part of the great auricular nerve was found to run straight into the nodule, and 3 cm. of the nerve were excised with the nodule (*Fig.* 2). The histology of the excised mass (*Fig.* 3) was that of a typical amputation neuroma.

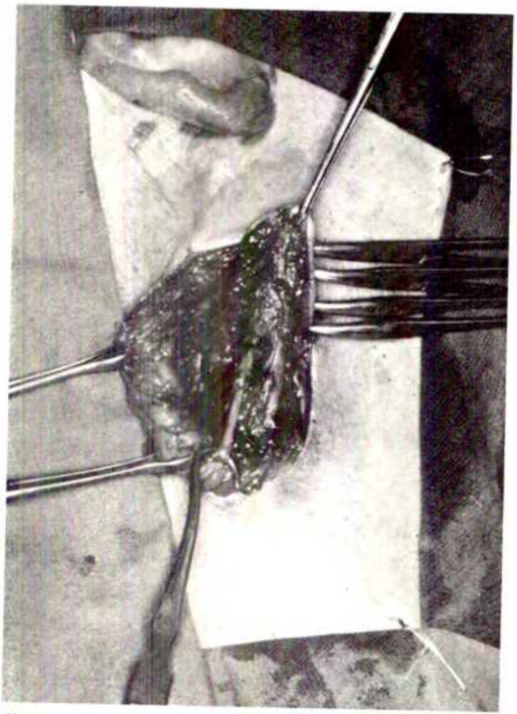

FIG. 2.—*Case* 1. The nodule is being explored. The stump of the great auricular nerve is stretched over the hook at the anterior border of the sternomastoid muscle and runs upwards and slightly forwards into the nodule. The latter was excised with a margin of normal subcutaneous tissue and the neighbouring part of the scar.

Case 2.—E. S., a female aged 42 years, presented in 1968 with a swelling in the right parotid region which had been slowly growing since she was a child. She was under treatment elsewhere for various symptoms and signs thought to be due to disseminated sclerosis. At operation on 8 Nov., 1968, a superficial parotidectomy was performed, with preservation of the facial nerve. Apart from a mild temporary paresis of the branches of the facial nerve to the right eye and lower lip recovery was uneventful. The histological diagnosis was pleomorphic adenoma. The facial weakness disappeared between 2 and 8 months later.

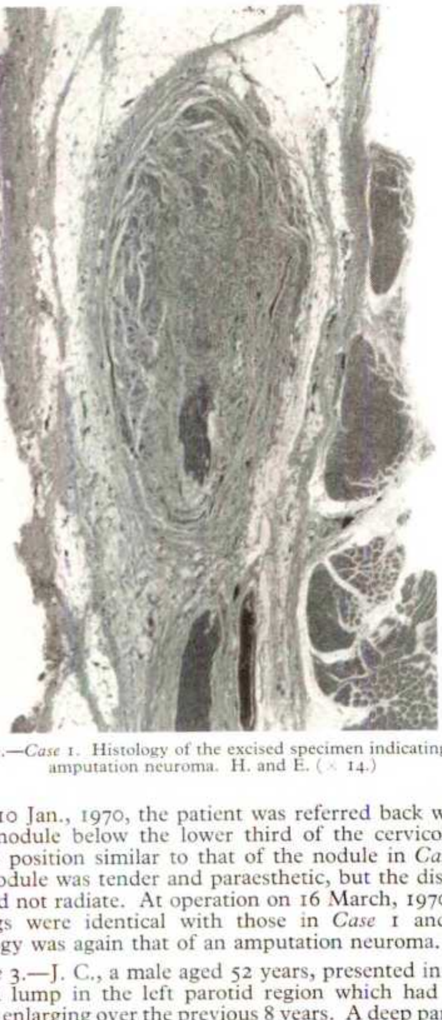

FIG. 3.—*Case* 1. Histology of the excised specimen indicating an amputation neuroma. H. and E. (× 14.)

On 10 Jan., 1970, the patient was referred back with a small nodule below the lower third of the cervicofacial scar (a position similar to that of the nodule in *Case* 1). The nodule was tender and paraesthetic, but the discomfort did not radiate. At operation on 16 March, 1970, the findings were identical with those in *Case* 1 and the histology was again that of an amputation neuroma.

Case 3.—J. C., a male aged 52 years, presented in 1968 with a lump in the left parotid region which had been slowly enlarging over the previous 8 years. A deep parotidectomy, i.e., removal of that part of the gland deep to the facial nerve with preservation of the nerve and the superficial part of the gland, was performed on 31 July, 1964. Recovery was uneventful. The histology of the excised gland showed a pleomorphic adenoma, with some areas suggesting a low-grade muco-epidermoid carcinoma.

On 9 May, 1967, mild gustatory sweating was noticed by the patient, and on 27 June a lump was noted in the subcutaneous tissue over the upper third of the anterior border of the sternomastoid. The lump was tender and the paraesthesiae produced by pressure radiated forwards and upwards into the face. No treatment was undertaken, and there has been no change in the size (1 cm. diameter) or tenderness of the lump during subsequent follow-up. The patient was last seen on 4 May, 1971.

Case 4.—T. D., a male aged 33 years, presented in 1968 with an 11-year history of recurrent right parotid swelling related at first to meals. Sialography showed a clinically dilated main parotid duct with a series of strictures and therefore parotidectomy was advised. Superficial parotidectomy was performed on 20 April, 1969, with conservation of the facial nerve. Recovery was uneventful. The histology of the excised gland showed non-specific chronic parotitis. Follow-up revealed no abnormality until 19 Jan., 1971, when a tender nodule was felt in a similar site as in the other 3 patients. There was no change in the findings on 4 May, 1971.

DISCUSSION

The great auricular nerve is usually one of the first landmarks to be encountered when the anterior border of the sternomastoid is defined during the operation of parotidectomy. It is standard practice that the nerve, which is usually present as two parallel branches, is divided at the muscle border. The theoretical possibility that the proximal cut end of the nerve might form an amputation neuroma was confirmed by the histological findings in *Cases* 1 and 2 The features of tenderness and paraesthesiae on pressure are similar to the clinical characteristics of amputation neuromata elsewhere and have been used to diagnose *Cases* 3 and 4 without recourse to excision biopsy.

A conservative policy seemed fully justifiable in *Case* 4 because the original operation was done for a non-neoplastic condition and in *Case* 3 such a policy has been vindicated by the lack of change in the nodule for 4 years.

It seems likely that the condition of amputation neuroma of the great auricular nerve is quite common. Knowledge of this possible diagnosis may save the patient and the surgeon needless worry, and in particularly characteristic cases may even obviate an unnecessary operation.

Recently it has been stated that the branches of th nerve running posteriorly (but not those anteriorly can be preserved in many parotidectomies (Patey 1969), and with this technique a palpable neurom has so far not been recognized (Patey, 1971).

Acknowledgement.—I am grateful to Mr. D. H Patey, who has seen several other examples of thi condition, for bringing it to my attention.

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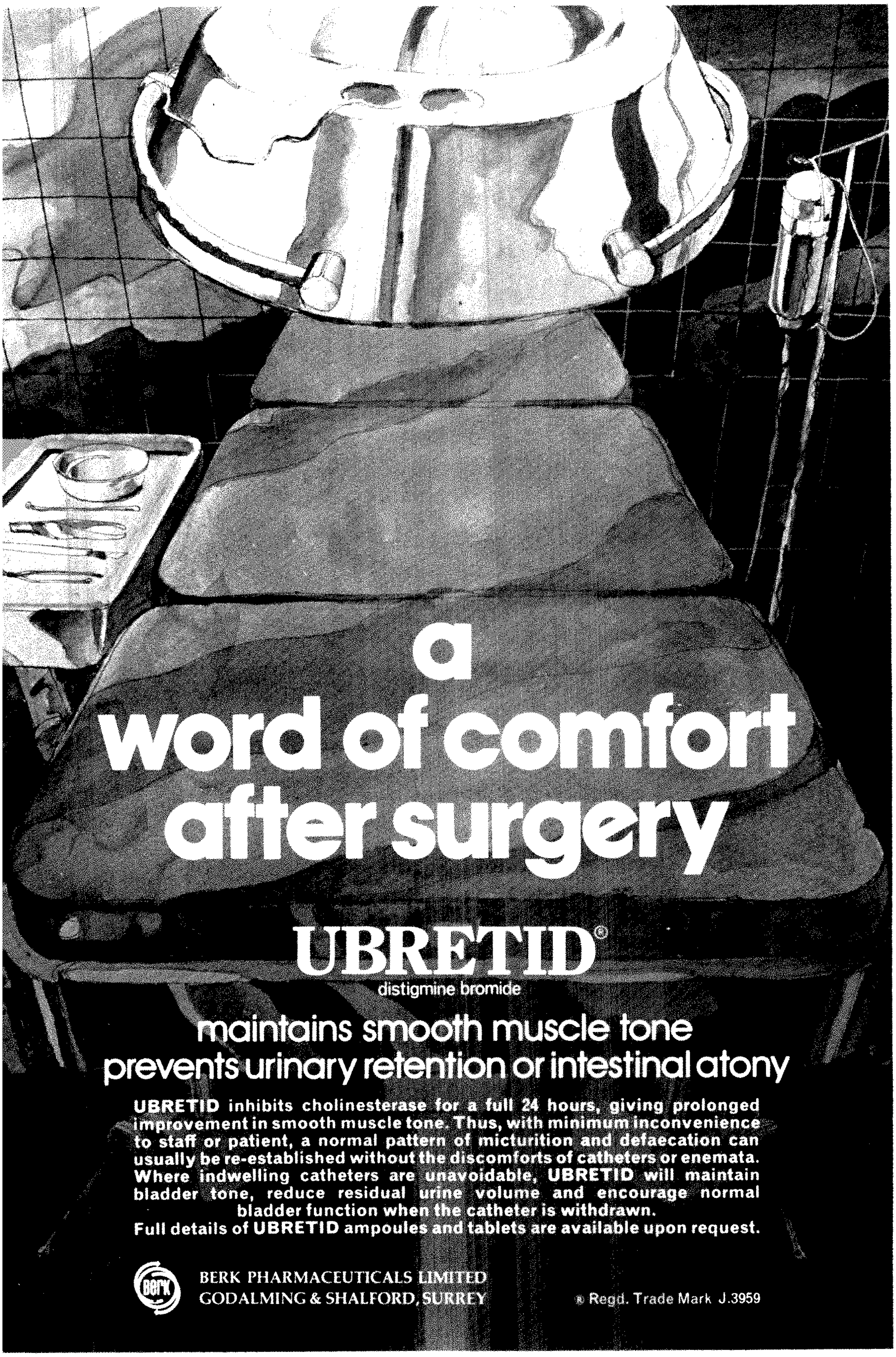
ADDENDUM

Since this article was written the author has seen more examples of the condition. The first patient, man of 31 years, had undergone elsewhere a super ficial parotidectomy for a pleomorphic adenoma i 1962, and on three occasions subsequently a nodul of similar tumour had been excised from the scar. fourth lump appeared in 1971 and had the feature of a neuroma as emphasized above, but because o the complicated history it was excised and the diag nosis of neuroma confirmed. In the other 2 patients a woman of 37 years whose parotidectomy for a pleo morphic adenoma had been performed 2 years prev ously, and a woman of 72 years whose parotidectom for an acinic-cell tumour had been performed 5 year previously, a clinical diagnosis of neuroma has bee made confidently and no excision performed.



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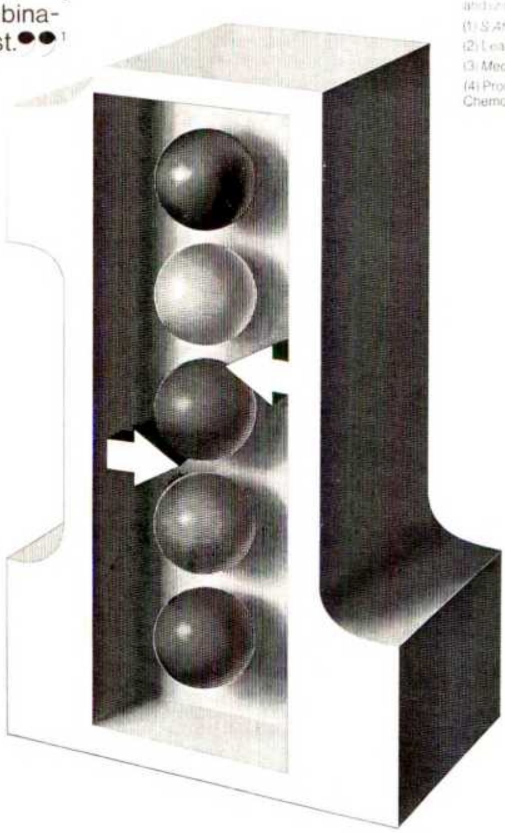

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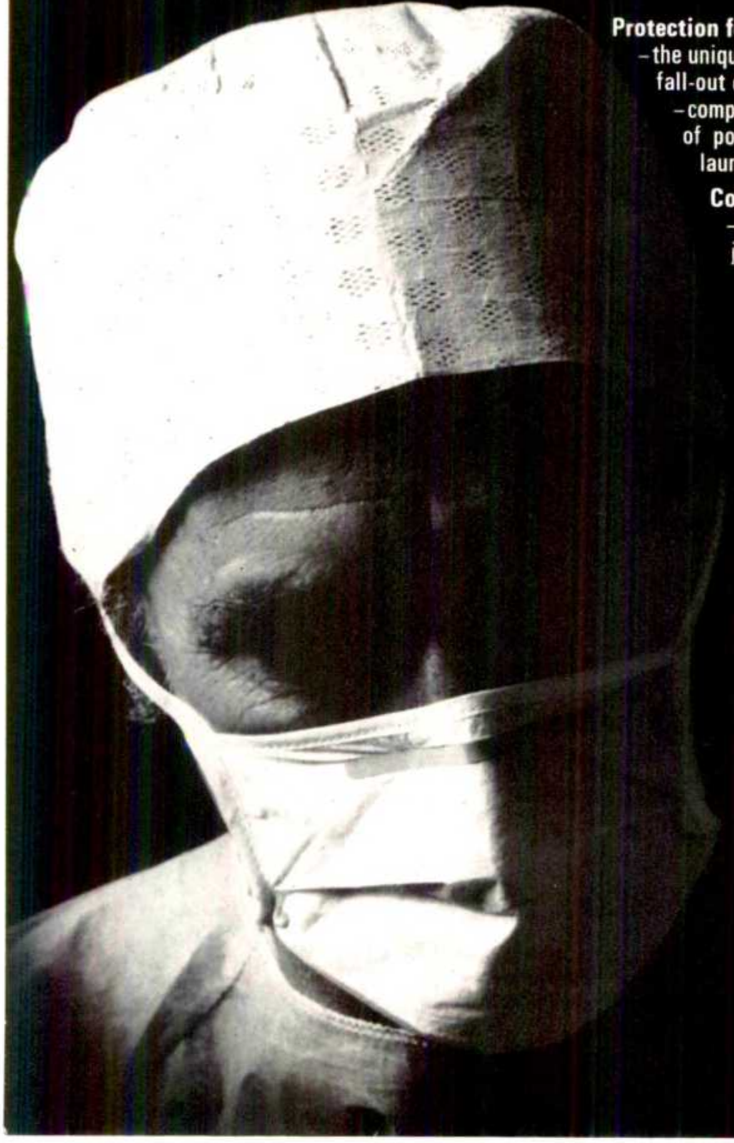

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SHORT NOTES OF RARE OR OBSCURE CASES

ANTEROPOSITION OF THE PORTAL VEIN AND SPONTANEOUS PASSAGE OF GALL-STONES

CASE REPORT AND EMBRYOLOGICAL HYPOTHESIS

BY WILFRID BROOK AND MICHAEL GARDNER
TORBAY HOSPITAL, TORQUAY

SUMMARY

A case of a woman who passed seven gall-stones 'per vias naturales' is presented. At subsequent operation for painful jaundice the portal vein was found to lie in front of the common bile-duct, although in its lower part it was retroduodenal.

A new embryological hypothesis to explain the preductal portal vein is presented.

THE spontaneous passage of gall-stones from the gall-bladder 'per vias naturales' has been regarded as an unusual happening, but in fact it is probably quite common and explains the rapid recovery observed in many cases of obstructive jaundice.

The case described here is 1 of the 20 cases which have been seen in the Torbay area during the past 8 years where the natural passage of stones has been proved (Gardner, Holden, and Monks, 1966). The second point worthy of record in this patient was the abnormal situation of the portal vein, which lay in a surgically hazardous position anterior to the common bile-duct.

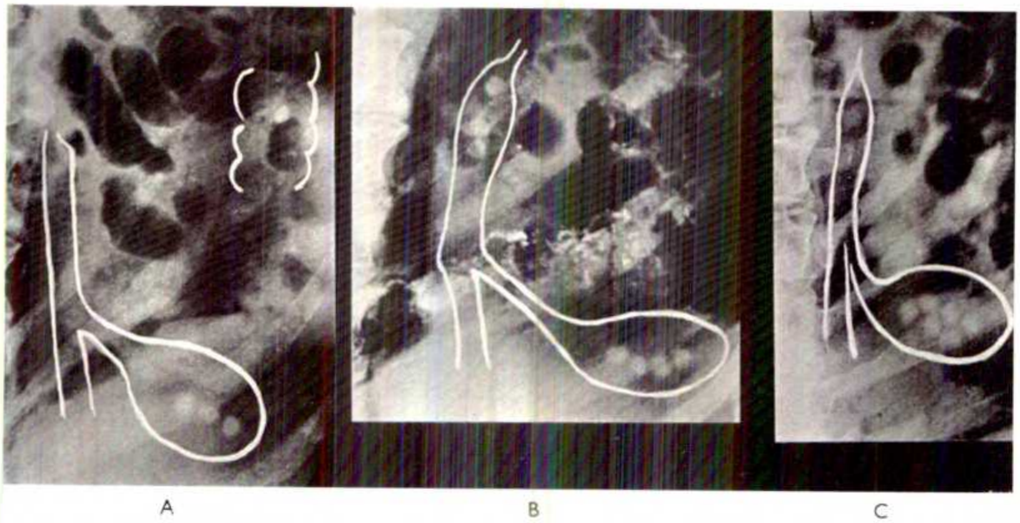

FIG. 1.—Serial straight radiographs showing the passage of seven radio-opaque gall-stones. For the sake of clarity the gall-bladder and main ducts have been outlined. A, Six stones are present in the gall-bladder and one in the common bile-duct (25 Jan., 1966). B, Four stones are present in the gall-bladder and three in the common duct (31 March, 1966). C, Three stones are present in the gall-bladder and one in the colon (9 April, 1966). A further radiograph on 15 April showed one stone in the common bile-duct, but none in the gall-bladder. At repeat examination 8 days later all the stones had disappeared.

CASE REPORT

L. B., a widow aged 84 years, had suffered attacks of biliary colic for 22 years following an attack of erysipelas complicated by pulmonary embolism, but jaundice had only been noticed during the past year. An especially severe attack necessitated her urgent hospital admission in January, 1966. Straight radiographs of the abdomen at this time showed seven radio-opaque stones (*Fig.* 1). A deep venous thrombosis in her leg dictated conservative treatment and during the next 4 months straight radiographs taken after further attacks of pain demonstrated the serial passage of all the stones (*Fig.* 1). Her symptoms then improved. Repeated cholecystograms during the subsequent 19 months failed to outline the gall-bladder, but 3 years later some return of function was demonstrated after a triple dose of contrast medium. However, she suffered recurrent attacks of painful jaundice and surgery became mandatory. At operation five black stones, 3 mm. in diameter, were found in an inflamed and partly disintegrated gall-bladder.

An attempt was made to locate the common bile-duct in the free edge of the lesser omentum in the usual way. Aspiration with a fine needle of the dark-coloured vessel that lay in the normal position of this duct produced only venous blood. In view of this the duct was explored by the transduodenal route. It soon became clear that the portal vein after emerging from behind the upper border of the duodenum came to lie anterior to the common bile-duct in its passage to the liver.

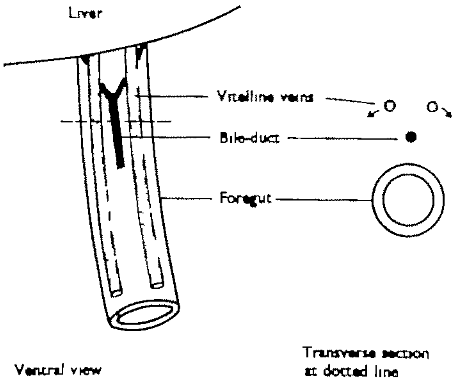

FIG. 2.—Vitelline veins in front of the foregut.

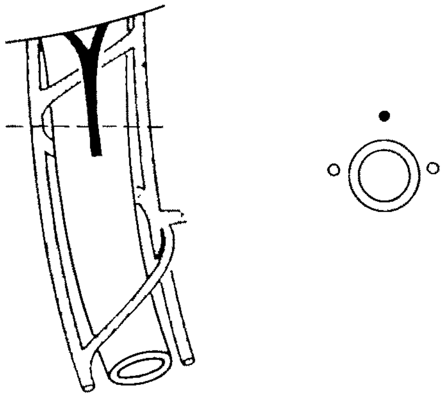

FIG. 3.—Cross-channels around the foregut. (*Modified from Last*, 1966.)

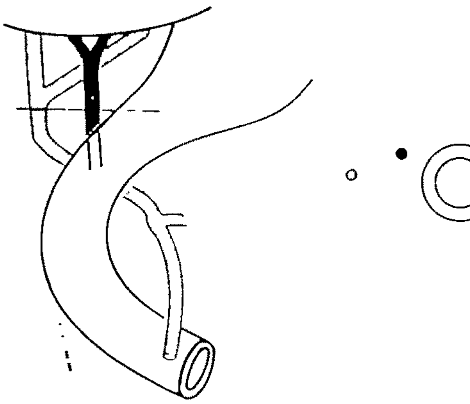

FIG. 4.—Development of the portal vein. (*Modified from Last*, 1966.)

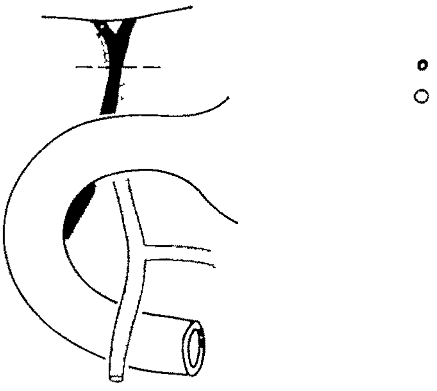

FIG. 5.—Final stage. (*Modified from Last*, 1966.)

Sphincterotomy of the ampulla of Vater was performed, and in view of the patient's past history of thrombo-embolism the inferior vena cava was narrowed by a silicone rubber clip to stop the upward passage of lethal-sized emboli to the lungs (Gardner, 1970).

Convalescence was uneventful apart from a further venous thrombosis in one leg and the patient has remained well during the past 2 years.

DISCUSSION

There is no reason in this case to postulate a connexion between the very rare condition of precholedochal portal vein and the relatively common phenomenon of spontaneous passage of gall-stones.

We have been able to find only 1 other recorded case where the portal vein passed up behind the duodenum and then continued upwards in front of the common bile-duct. This abnormality was discovered in a middle-aged woman during an operation for gall-stones (Greatrex, 1965). Other instances of anteroposition of the portal vein in the lesser omentum have been recorded, but in all of these the vein was anterior to the pancreas and duodenum in the lower part of its course. Indeed, in some instances this position had led to duodenal obstruction and to the discovery of the anomaly (Kakkar and Tompkin, 1968). A bleeding duodenal ulcer has been reported in association with an anteroposition of the portal vein (Bernard, Perry, and Walker, 1959) as have other developmental anomalies both local and distant, such as malrotation of the gut, biliary atresia (Renner and Child, 1963), cardiovascular defects, situs inversus, annular pancreas, and duodenal mucosal diaphragm (Boles and Smith, 1961).

Congenital Abnormalities of the Portal Vein.—In contrast to other veins anomalies of the portal vein are very rare, and they have been classified as follows (McGregor, 1963):—

1. The portal vein may empty directly into the inferior vena cava.
2. The vein, its formative vessels, and tributaries may lie anterior to the pancreas and duodenum.
3. The pulmonary veins may join the portal vein.
4. Congenital strictures of the vein may occur.

Embryology of the Portal Vein.—The normal ortal vein develops from the two vitelline veins and he anastomoses between them around the embryonal luodenum. Originally the paired vitelline veins eturn blood from the yolk sac to the heart. They un upwards, at first ventral (*Fig.* 2), and then later ne on each side of the gut (Davies and Davies, 962), the right and left veins communicating with ach other by cross-channels (*Fig.* 3). Parts of this enous system disappear and the portal vein develops rom the persistent caudal part of the left vitelline ein and the cranial segment of the right vitelline ein joined together by a persisting cross-channel hat passes behind the part of the foregut that ultimately becomes the first part of the duodenum. The S'-shaped vein so formed straightens out and with he rotation of the duodenum finally becomes the ortal vein (*Figs.* 4, 5).

To explain the abnormal retroduodenal-preductal osition of the portal vein Greatrex (1965) postulated he persistence of the cranial part of the left vitelline ein and the right caudal vitelline vein with development of a cross-anastomosis in an abnormally anterior lane (*Fig.* 6), as in his patient the portal vein crossed rom right to left in front of the common bile-duct. We suggest as an alternative explanation that the cranial segment of the right vitelline vein may fail to move from its original position in front of the gut to its normal embryonic position alongside it (*Fig.* 7).

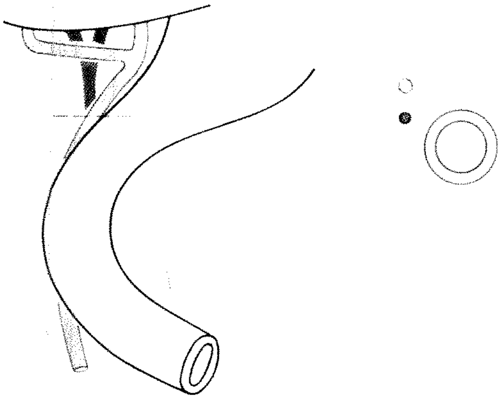

FIG. 6.—Greatrex's (1965) explanation of the development of a preductal portal vein.

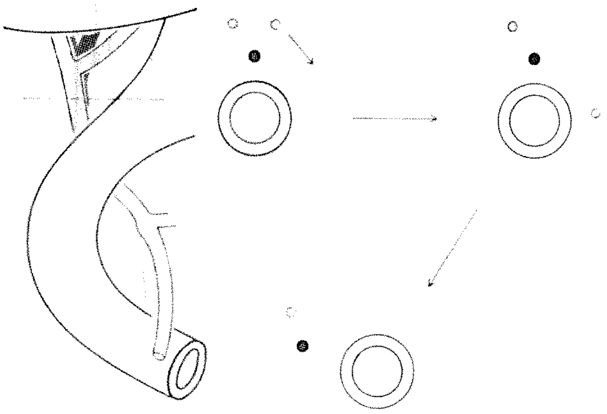

FIG. 7.—Development of a preductal portal vein. It is postulated that the cephalic portion of the right vitelline vein has remained in its original anterior plane.

Acknowledgement.—We are indebted to Dr. Gerald Crawford of the Department of Anatomy, Oxford University, for his help with our embryological problem.

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MESENTERIC NEUROFIBROMATOSIS IN CHILDHOOD

BY S. CYWES AND MARGARET J. MAYELL*

RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL, CAPE TOWN, SOUTH AFRICA

SUMMARY

A child is reported in whom severe malabsorptive ymptoms were present from a short time after birth ogether with increasing pseudo-obstructive episodes. Total neurofibromatous involvement of the small-owel mesentery was found at laparotomy at the age of 4½ years. The child survived a further 2¼ years. The relevant literature is discussed.

NEUROFIBROMATOSIS is a not-infrequent genetically determined disorder, the first clinical signs of which usually appear during late childhood or adolescence. As a mode of presentation malabsorption is rare at any age. The following case, for whom there appears

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* Present address: Consultant Paediatric Surgeon, The Children's Hospital, Nottingham.

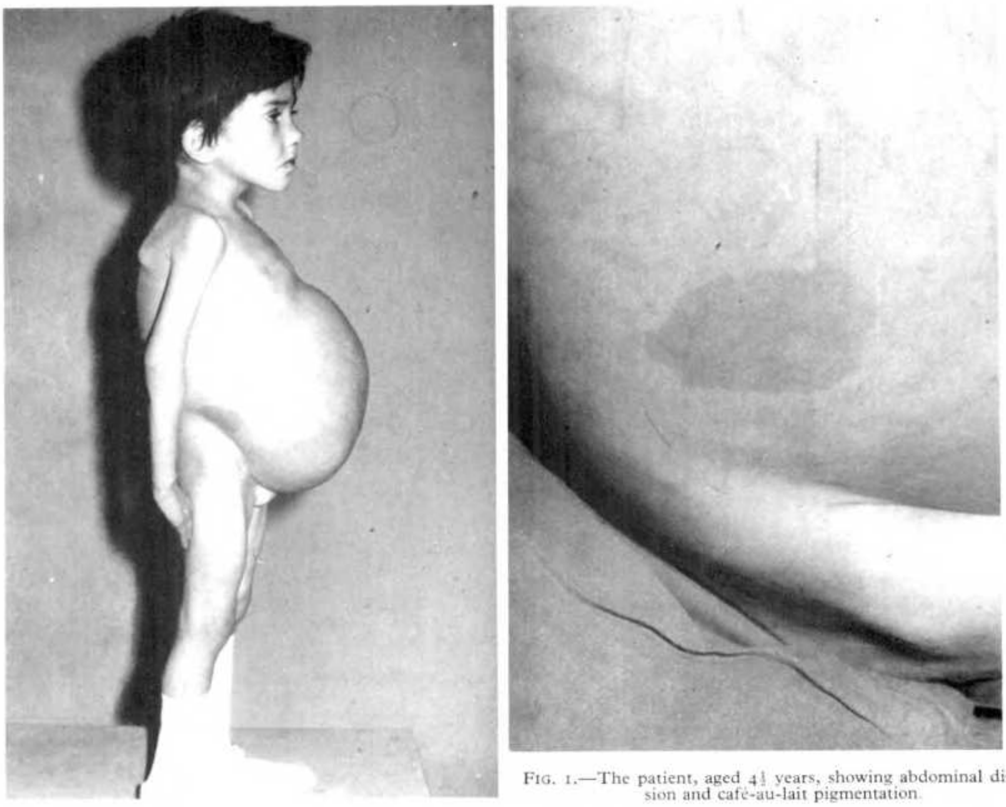

FIG. 1.—The patient, aged 4½ years, showing abdominal distension and café-au-lait pigmentation.

to be no parallel in the literature, showed the features of malabsorption and pseudo-obstruction from the first weeks of life, developed café-au-lait spots at 4½ years, and died from the effects of gastro-intestinal functional impairment 2 years later.

CASE REPORT

H. E., aged 1¾ years, was admitted to the Red Cross War Memorial Children's Hospital, Cape Town, in October, 1963, with a 7-day history of vomiting, diarrhoea, and abdominal distension. Further inquiry revealed, however, that although the recent episode was of 7 days' duration, with abdominal distension as a new feature, the patient had in fact been having episodes of vomiting with the passage of bulky, loose, offensive stools since birth, each episode lasting 5–7 days and recurring every 2 weeks. Initially the child had been fed on a powdered milk formula; since weaning her diet seemed perhaps to have been of a rather poor quality. She had been born on 15 Dec., 1961, by spontaneous vertex delivery to a healthy 36-year-old mother; the birth weight was 3 kg. There were 3 older siblings, 1 of whom had congenital heart disease.

Examination revealed a pale, undernourished, apathetic child, weighing 8·85 kg., with oedematous hands and feet, a generalized skin rash, and a very distended, tympanitic abdomen with visible loops of bowel.

Investigations showed a haemoglobin of 7·25 g. per cent, a reticulocyte count of 2·8 per cent (rising to 12 per cent during treatment), a reversed serum albumin/globulin ratio, a positive culture of *Salmonella* in the stool, and a megacolon on barium-enema examination. The megacolon was not thought typical of Hirschsprung's disease. Other investigations included a chest radiograph, blood-urea, cholesterol, calcium, phosphate, and alkaline

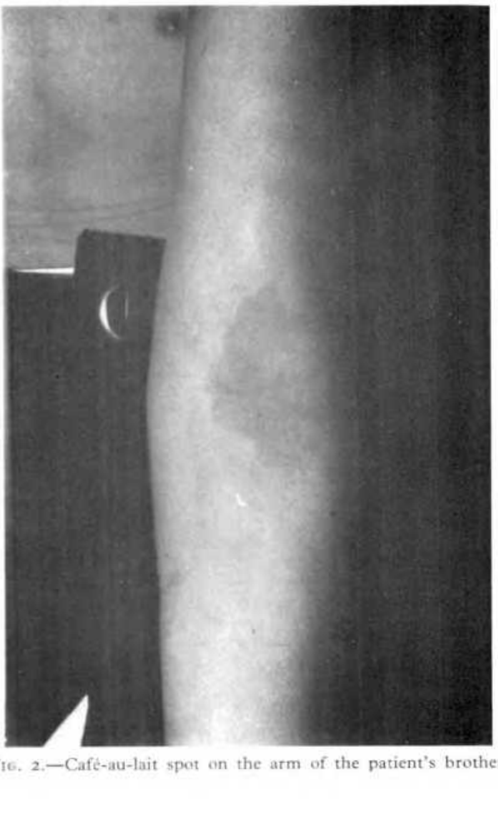

FIG. 2.—Café-au-lait spot on the arm of the patient's brother.

phosphatase estimations, and a sweat test. These showed no abnormality.

Treatment of the iron-deficiency anaemia and the *Salmonella* enteritis was given and the child improved to some extent. After 8 weeks her weight had risen to 10 kg. and she was discharged home on a toddler diet. She was still having several vomits and loose stools daily.

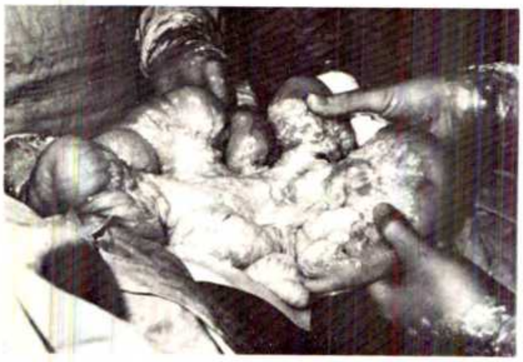

FIG. 3.—Operative findings in the small-bowel mesentery.

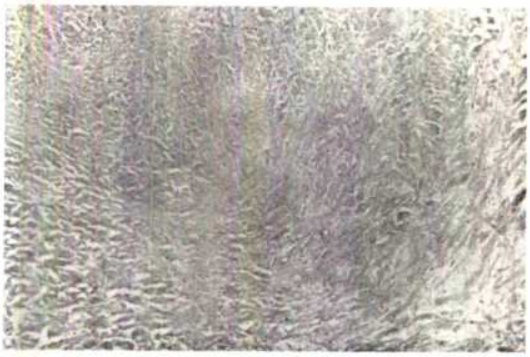

FIG. 4.—Histology of the biopsy specimen showing features of neurofibromatosis.

Her next admission, in August, 1965, was again for the nvestigation of recurrent episodes of vomiting and abdominal distension; diarrhoea had become less of a problem. She had been admitted twice to another hospital with the same symptoms earlier in 1965 but investigation had failed to reveal any obvious causative pathology. The episodes of vomiting and abdominal distension now lasted for 2–7 days and recurred every 4 weeks. Examination showed a similar picture to that on the previous admission —the child was grossly underweight at 11·8 kg., having gained only 1·8 kg. in the preceding 20 months, her abdomen was greatly distended, masses were palpable, and the liver was enlarged by two fingers' breadth. Rectal examination was thought suggestive of Hirschsprung's disease. A full investigation, including a rectal biopsy, failed to reveal any abnormality consistent with her clinical features. Symptomatic treatment, including a controlled diet, aperients, and rectal wash-outs, was carried out with some improvement.

Her symptoms continued unabated and in June, 1966, at the age of 4½ years, she was again transferred from another hospital where she had undergone further intensive investigation. On this occasion a family history of tuberculosis was obtained and both the patient and 2 of her siblings were found to have café-au-lait skin lesions *Figs.* 1, 2). Her weight had fallen to 11·47 kg. and her abdomen was tender and distended with palpable masses and free fluid present. Chest and abdominal radiographs showed features compatible with a diagnosis of tuberculosis, the Heaf test was positive, and the erythrocyte sedimentation rate was elevated.

Laparotomy on 4 July, 1966, showed, however, not tuberculosis but diffuse tumour infiltration of the whole depth of the mesentery of the entire small bowel from the posterior abdominal wall, where it measured 15 cm. in breadth, to the mesenteric border of the bowel (*Fig.* 3). There was no obvious abnormality of the bowel itself. Biopsy showed the tumour infiltration to be typical of neurofibromatosis (*Fig.* 4). Further surgery was not feasible.

The child made a good postoperative recovery and was discharged home. During the succeeding 2¼ years she became increasingly weak and ill as a result of recurring anaemia, hypoproteinaemia, and chest infections (*Fig.* 5); supportive therapy included blood and plasma transfusion, the use of intravenous fat and amino-acid solutions, and antibiotics. In addition she was admitted on six occasions with the features of acute intestinal obstruction, e.g., vomiting, abdominal pain, distension, hyperactive bowel sounds, and visible peristalsis. Although treated on each occasion by intravenous fluids, nasogastric aspiration, and low-bowel wash-outs these acute episodes usually seemed to settle spontaneously rather than as a result of therapy and the bowel would start to function again. A 24-hour stool-fat estimation during a functional period was 27·7 g. The child's condition deteriorated progressively, however, and she eventually died at home in October, 1968, at the age of 6¾ years.

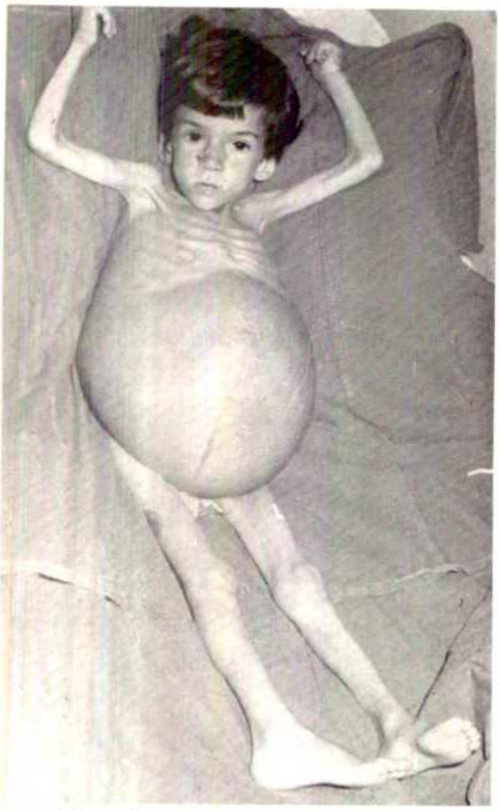

FIG. 5.—The patient, aged 6½ years, during the last hospital admission.

DISCUSSION

Neurofibromatosis, commonly named after von Recklinghausen who described it in its generalized form in 1882, is a hamartomatous disorder characterized principally by nerve-sheath tissue overgrowth but also by malformations of other tissues and secondary functional effects. It is genetically determined, the gene being an autosomal dominant with a variable degree of expression; this results in great variation in the clinical picture seen, from the full generalized syndrome through incomplete to monosymptomatic forms.

A family history is not obtained in all cases because (1) the relatives may only develop the clinical signs late in life, (2) the disorder in the relatives may be very mild and remain clinically unrecognized, and (3) a proportion of cases are the result of spontaneous gene mutation. The histogenesis is hard to understand and has been the subject of much debate. The hamartomatous nerve-sheath overgrowth contains both ectodermal (Schwann cell) and mesodermal (endo- and perineurial fibroblasts) derivatives in varying proportions. One possibility is that the endoneurial and perineurial fibroblasts are of Schwann-cell origin since Schwann cells have been shown to produce collagen in tissue culture and in neurolemmal tumours. The other possibility is that nerve sheaths may develop from a common blastema formed of both ecto- and mesodermal components, the ultimate cell differentiation being determined more by the proximity to the growing axon than by the cell of origin (Willis, 1962).

Reviews of the condition as it presents in childhood are few. Fienman and Yakovac (1970) report 46 cases collected over a 22-year period at the Children's Hospital of Philadelphia. They found a family history in 21 cases and clinical signs at birth in 20. The most common presenting sign was café-au-lait spots, or enlarging superficial tumours, or both. During the follow-up period serious central neural lesions occurred in 12 children, 19 cases had musculoskeletal pathology, and 4 had significant vascular pathology. In no case in this series did gastro-intestinal pathology feature at any stage.

A search of the literature for cases similar to the present one, with major gastro-intestinal involvement presenting in childhood, reveals 4 relevant publications. That of Chalkley and Bruce (1942) reports the case of an 8-year-old girl who presented with malnutrition and an abdominal mass. She was found to have neurofibromatous involvement of the mesentery of the terminal 80 cm. of ileum and of the whole colon to the sigmoid loop. She underwent excision with a good early result. There was no family history and the presence or absence of skin lesions is not recorded. Lane and Hooper (1964) report a fit, well-nourished, 8-year-old boy with café-au-lait pigmentation, who was found to have an abdominal mass at routine examination for another purpose. This proved to be neurofibromatous involvement of the mesentery supplying 35 cm. of ileum. Excision gave a good result. Contzen (1952) reported a 12-year-old girl who presented with a 4-year history of recurrent abdominal pain, an abdominal mass, café-au-lait spots, and other evidence of generalized neurofibromatosis. Laparotomy revealed neurofibromatous involvement of the ascending an transverse mesocolon which was amenable to excision The child subsequently died as a result of sarcomatou change in a cervical neurofibroma. The fourth case that of Ternberg and Winters (1965), is of interes because symptomatically it most closely resembles th present case although the mesentery was not primaril involved. The child, a boy, presented at 4½ years wit considerable emaciation, constipation, and café-au-lai pigmentation. A barium enema showed a megacolo but, on rectal biopsy, ganglion cells were present. Th patient's symptoms were severe and a Swenso procedure was carried out. His symptoms continue unchanged and at the age of 7½ years a further biops still showed ganglia to be present but also demonstrated replacement of the myenteric plexuses b neurofibromatous infiltration. A further excision o colon back to apparently normal bowel was done bu neurofibromatous tissue remained.

Two adults are reported with localized neurofibromatosis of the mesentery (Dudley, 1930; Barton an Inglis, 1931), and 1 case is recorded with simila involvement of the greater omentum (Thomas an Jelliffe, 1953). Two of these 3 patients had precedin café-au-lait pigmentation. The presenting symptom were, respectively, subacute obstruction due t kinking of the adjacent bowel, gastro-intestina haemorrhage, and an abdominal mass. Cases o mesenteric involvement secondary to a neurofibrom of the bowel wall are more numerous and no relevant to this discussion.

The case reported here differs from the case recorded in the literature in that the mesenteri involvement was very much more extensive an therefore quite unamenable to surgical resection. I seems possible, in the light of the case of Ternber and Winters (1965), that our patient may also hav had involvement of the myenteric plexuses of th colon.

Cytotoxic agents were not exhibited in this cas although both nitrogen mustard and cyclophosphamide have been tried in generalized neurofibromatosis (Hayes, Spurr, Felts, and Miller, 1961 Gulati, 1966).

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CHRONIC SCHISTOSOMAL APPENDICITIS

BY J. C. VOIGT* AND M. M. GREGORY
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SUMMARY

A case of schistosomiasis of the vermiform appendix in an immigrant patient is presented.

CASE REPORT

THE patient was a 29-year-old Nigerian woman who had been in England for 5 years. She had 1 child aged 3½ years, and the menstrual cycle was normal. On presentation at the Royal Free Hospital she complained of right-sided abdominal pain which had persisted for 1 year. There were no urinary or alimentary symptoms. On examination the only abnormality was an indefinite tender cystic swelling, possibly the caecum, felt in the right iliac fossa and also through the right vaginal fornix.

Investigations included the following: haemoglobin, 13·2 g. per 100 ml.; sickle test, positive (trait); white cell count, 6000 per c.mm., with 1260 eosinophils. A chest radiograph was normal. An intravenous pyelogram suggested slight medial displacement of the pelvic portion of the right ureter but showed no other abnormality.

The right-sided abdominal pain was of sufficient severity to interfere with the patient's daily activities, and she was admitted in due course for laparotomy. This was done through a right paramedian incision on 30 April, 1971. The liver and gall-bladder were seen and felt to be normal. The kidneys, spleen, stomach, duodenum, and pelvic organs also appeared normal. The caecum was not unusual, but the vermiform appendix had a yellowish colour and was tethered by several old inflammatory adhesions. Appendicectomy was carried out, and the postoperative progress was satisfactory.

Histological examination showed chronic inflammation and fibrosis of the appendix with many schistosome ova, some of which were calcified (*Figs.* 1, 2).

In the postoperative period further repeated urine and stool specimens were examined, but no ova or parasites were found and no blood was present. Liver-function tests were normal. Two weeks after operation a liver biopsy was obtained and the only abnormality was the presence of scanty, fine, dark-pigment granules of a schistosomal type lying in the portal tract phagocytes; no ova were seen and there was no fibrosis. Six days later *Schistosoma haematobium* ova were found in an unstained rectal biopsy. It was proposed to complete investigations with a cystoscopic examination, but the patient was now well and declined further investigation.

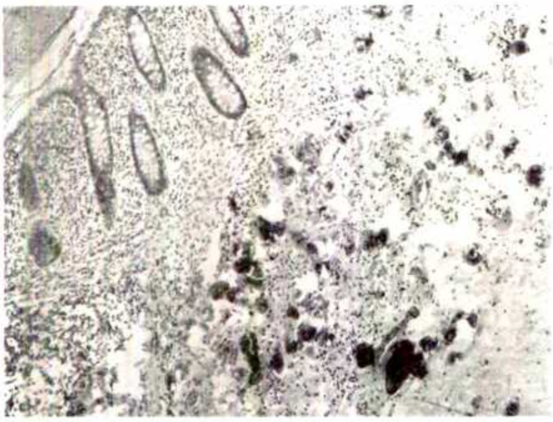

FIG. 1.—Section of the wall of the appendix showing many schistosome ova in the fibrotic and inflamed submucosa. H. and E. (× 40.)

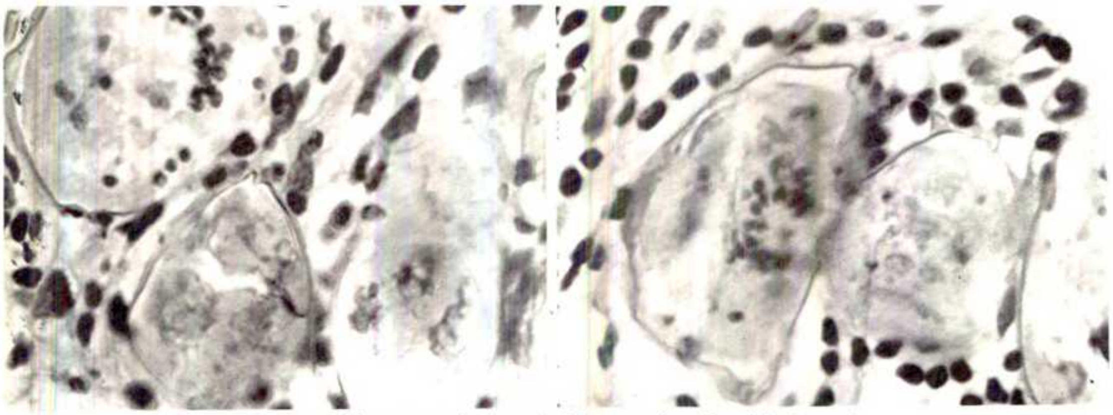

FIG. 2.—Schistosome ova in the wall of the appendix. H. and E. (× 550.)

DISCUSSION

Diagnosis in this case would not have been achieved without the histological examination of the appendix. The mild eosinophilia suggested a parasitic infection, but repeated stool and urine examinations were negative. Several rectal biopsies were needed before an ovum was found.

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Bowesman (1960) estimated that in West Africa about 20 per cent of cases of chronic appendicitis are due to schistosomiasis. These patients invariably have low-grade chronic discomfort, but the appendix is seldom acutely inflamed. A yellowish tingeing of the appendix owing to schistosomal pigment is sometimes seen at operation. No cases of post-appendicectomy faecal fistula have been noted in these patients.

Talib (1967) mentioned that recurrent appendicitis due to *S. haematobium* infection is common in Iraq. Ibrahim, El-Mazni, and Bahnassy (1968) described the disease in Egypt and stressed the frequency of mixed *S. mansoni* and *S. haematobium* involvement of the appendix, colon, and rectum. Mynors (1957) reported *S. mansoni* involvement of the distal small bowel in the Sudan, resembling a regional ileitis.

Gelfand (1967) made caustic potash digests of autopsy material in southern central Africa and counted the number of ova. In a series of 72 autopsies on subjects affected by bilharziasis 45 (62·5 per cent) appendices showed the presence of ova. All contained ova of *S. haematobium*, but, in addition, ova of *S. mansoni* were present in 6.

In conclusion, schistosomal infection of the vermiform appendix may be an incidental finding in endemic areas. It may, however, cause recurrent or chronic appendicitis and this possibility must be remembered in patients who have come from parts of the world where the schistosome is found.

Acknowledgements.—We are indebted to Dr P. J. Scheuer for the histology of the liver biopsy, to Dr. P. D. Marsden for the rectal biopsy, and to Dr I. A. D. Bouchier for permission to report this patient. We also thank Mr. C. Gilson for the photographs.

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FOREIGN-BODY PERFORATION OF A JEJUNAL DIVERTICULUM

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SUMMARY

Perforation of a jejunal diverticulum is usually the result of inflammation. A second example of a much rarer cause of perforation due to a foreign body is described together with a brief review of the literature.

The presence of jejunal diverticula is an infrequent radiological and operative finding, and such diverticula are present in only 0·2 per cent of autopsies (Browne and McHardy, 1940; Altemeier, Bryant, and Wulsin, 1963). Perforation is not rare but, to date, only 1 case of perforation by a foreign body has been reported (Navarre and Schmidt, 1958). A further case of foreign-body perforation is reported here, together with a review of the complications of jejunal diverticulosis and a discussion of the difficulties of diagnosis and treatment.

CASE REPORT

Mr. V. T., aged 64 years, was admitted as an emergency to University College Hospital, London, in November, 1969, with a 5-hour history of severe epigastric pain. The pain had begun suddenly and had been constant in nature, causing him to roll about. After about 15 minutes the pain had remitted, but had returned 30 minutes later and had remained constant since. The patient complained of nausea but had not vomited. There was no previous history of significant abdominal pain or indigestion. He had eaten fish on the previous day.

Examination.—The patient looked generally ill. He had false teeth and his tongue was dry; his temperature was 36·7° C. and his pulse was regular at 84 per minute Palpation of the abdomen revealed generalized tenderness rebound tenderness, and muscular rigidity, the signs being most marked in the epigastrium. A small, reducible right inguinal hernia and a small epigastric hernia were present. Rectal examination was normal.

Straight abdominal radiographs showed a little free gas under the left dome of the diaphragm and a few distended coils of jejunum.

A provisional diagnosis of perforated peptic ulcer was made and, following resuscitation, laparotomy was undertaken.

Operation.—The abdomen was opened through a right paramedian incision. There was copious free faeco-purulent fluid in the peritoneal cavity. As there was no obvious source of the fluid, the duodenum, stomach, large bowel, and appendix were examined and found to be normal Attention was then turned to the small intestine. The jejunum from 15 to 40 cm. distal to the duodenojejunal flexure was the site of numerous small diverticula on the mesenteric border. One of these, which was 2 cm. in diameter and larger than the others, had been perforated at its apex by a 2-cm.-long fish bone. As the patient's condition was satisfactory and only a short (25 cm.) length of bowel was involved with diverticula, it was decided to resect the whole affected segment to prevent future complications from any residual diverticula. Intestinal continuity was restored by an end-to-end anastomosis. The patient made a satisfactory recovery from the operation.

DISCUSSION

The first description of a false diverticulum of the intestine is usually attributed to Sömmering in 1794 (Fischer, 1900), and in 1807 Sir Astley Cooper included illustrations of jejunal diverticula in his monograph on hernia. In 1881 Osler described a patient with 55 diverticula of the jejunum demonstrated at autopsy. The first published account of an operation on jejunal diverticula was by Gordinier and Sampson (1906), who described a case where inflammation of a diverticulum in the lower jejunum or upper ileum had caused intestinal obstruction. Since then there have been several reports of jejunal diverticula and their complications which, according to Herrington (1962), occur in less than 10 per cent of cases. The complications have been summarized by MacGregor and Hamilton (1970) and the most important are, in order of frequency, malabsorption, haemorrhage, perforation (inflammatory or traumatic), diverticulitis without perforation, obstruction, volvulus, pneumoperitoneum, ectopic pancreatic tissue, and malignant disease.

Perforation of a jejunal diverticulum is most commonly the result of diverticulitis (Thorek and Manzonilla, 1954). Three cases of perforation following closed injury to the abdomen have been reported by Herrington (1962), and 1 case of perforation by a 3-cm.-long piece of bone in a patient who had had difficulty in chewing steak with his new false teeth (Navarre and Schmidt, 1958).

Probably the most important factor in arriving at a correct preoperative diagnosis is to bear the likelihood of this condition in mind, even though the previous history may not provide any indication as to the existence of these diverticula. In many cases, as in the patient reported here, the diagnosis will be thought to be perforated peptic ulcer and the true state of affairs will only be discovered at laparotomy. Even when the abdomen is open the diagnosis may not be obvious, and if a generalized peritonitis is found and the more common causes have been excluded the possibility of perforation of a jejunal diverticulum should be considered. That it may be difficult to demonstrate is shown by the fact that in some reported cases the diagnosis was only made at autopsy following an unproductive laparotomy. Welsh (1966) has described a technique of demonstrating diverticula, involving the distension of short lengths of the jejunum by 'milking' the bowel contents along.

Following the discovery of a perforated jejunal diverticulum, the treatment will differ according to circumstances and this may be summarized as follows:

1. Resect all the involved segment if the patient's age and condition permit this and not too much intestine is involved.
2. If much intestine is involved, resect the perforated segment and emphasize, for future reference, in the notes and to the patient that more diverticula remain. The procedure may be limited to excision only of the perforated diverticulum.
3. Invaginate the diverticulum.
4. Suture the perforation and cover with an omental patch in the old and very ill.

Acknowledgement.—I should like to thank Mr. David Bailey for his help and advice in the preparation of this article and for allowing me to publish details of the patient who was under his care.

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NICKEL SENSITIVITY TO SURGICAL SKIN CLIPS

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SUMMARY

1. A case of hitherto unrecorded skin sensitivity to surgical skin clips is reported.
2. A sensitivity test revealed that the sensitivity was to the nickel constituent of the copper/nickel alloy of which surgical clips are manufactured.
3. It is suggested that when the use of skin clips is anticipated inquiry should be made of the patient as to the previous experience of sensitivity to metal articles of attire and the use of skin clips consequently avoided if the reply is affirmative.

As there is no record of nickel sensitivity to surgical skin clips having previously been reported it is felt that the following case history will be of interest.

CASE REPORT

The patient, a male aged 57 years, presented with chronic intractable duodenal ulceration for which vagotomy and pyloroplasty was carried out in June, 1970. The midline upper abdominal incision was closed with metal skin clips.

The patient's postoperative recovery was complicated by pulmonary atelectasis superimposed upon his chronic bronchitis. On the eighth postoperative day a skin rash appeared surrounding the abdominal wound and which spread to involve a wider area of the abdominal wall, the elbow flexures, the area behind the knees, and the buttocks (*Figs.* 1, 2). The rash was initially erythematous, later becoming exudative with crusting and scaling. The patient was treated with Betnovate ointment and as the skin reaction was considered to be due to sensitivity to the skin clips—the rash first appearing in relation to the clips—these were promptly removed. Subsequently the rash in all the areas progressively faded and disappeared some 2 weeks after its initial appearance.

On detailed inquiry of the patient's past history it was revealed that some years previously he had noted a skin sensitivity to wrist watches, buckles, and collar studs. He had consequently discontinued wearing these articles.

A sensitivity patch test was carried out on the skin of the patient's back by fixing a sixpence in position with adhesive strapping. Within 48 hours the reaction shown in *Fig*. 3 resulted, evidently as a response to the nickel in the coin. A similar reaction was noted in relation to a skin clip applied to adjacent skin at the same time. Nickel sensitivity was further confirmed by a formal skin test using nickel sulphide (*Fig*. 4).

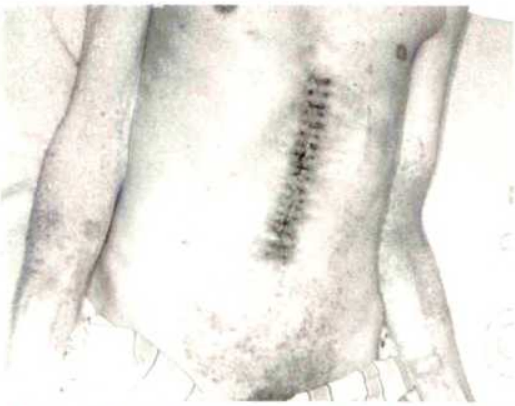

FIG. 1.—Skin-sensitivity reaction in relation to the site of the metal surgical skin clips and the metastatic rash on the abdominal wall and flexure aspect of the arms.

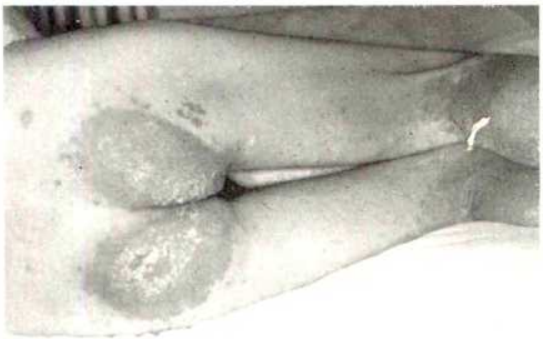

FIG. 2.—Metastatic skin sensitivity rash involving the buttocks and the flexure aspect of the legs.

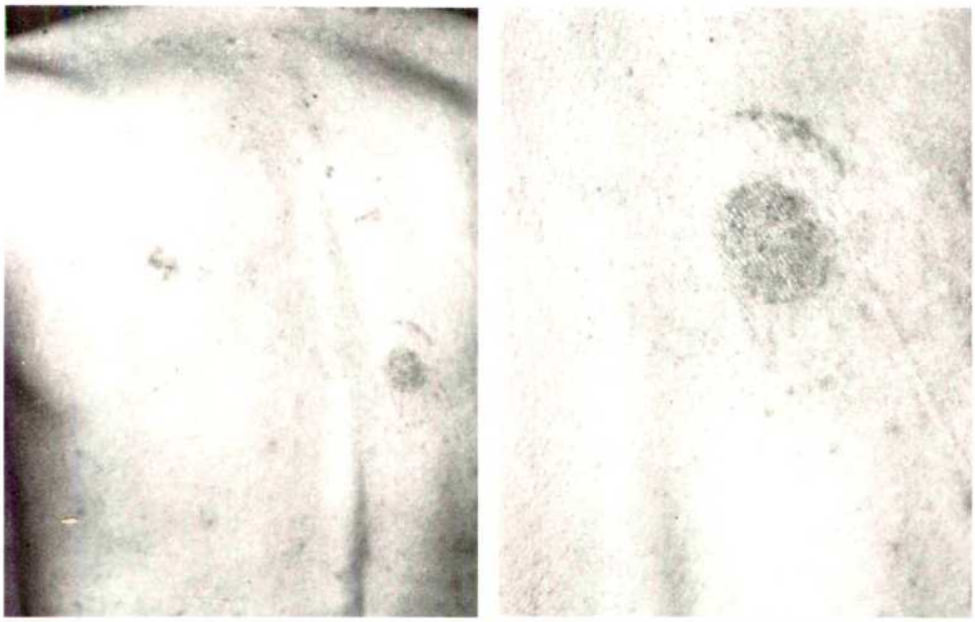

FIG. 3.—Skin reaction to a sixpence and a metal skin clip applied to the skin as a sensitivity test.

DISCUSSION

Nickel sensitivity is five to eight times more common in women than in men, and in the United Kingdom nickel is the single most common cause o contact dermatitis in women.

In 80–90 per cent of women with nickel sensitivity suspected dermatitis is the first manifestation women usually being sensitized by objects worn close to the skin such as suspenders, brassière fasteners ear-ring clips, necklace fasteners, and wrist watche and straps. Men, on the other hand, are more likely to develop nickel sensitivity by occupational exposure.

Secondary eruptions of the skin in areas other than those in direct contact with the nickel-containing articles are a characteristic feature of nickel dermatitis and occur in 80–90 per cent of patients. These secondary eruptions commonly start shortly after o at the same time as the primary eruption and in rare cases even precede it. Spread to other parts of th body may be caused by traces of nickel on th finger-tips but another possibility is that it is an autoimmune response. The elbow flexors and flexor surfaces of the arms and legs are the most common sites of the secondary eruptions (Rook, Wilkinson, and Ebling, 1968).

In men nickel dermatitis is predominantly of an occupational origin but some people are sensitized by the buckles of wrist watches, spectacle frames, collar studs, cuff links, and zip fasteners, as evidently was the present patient.

In the case reported here direct questioning of the patient revealed that many years previously he had abandoned wearing a wrist watch and the use of collar studs because he was aware that these articles provoked a rash involving the adjacent skin.

Although nickel sensitivity to surgical skin clips must be an uncommon occurrence, when a surgeon uses skin clips routinely for wound closure it is probably a wise precaution to ask the patient preoperatively about any previous experience of skin eruptions when in contact with metal objects. This question can be included in the inquiries routinely made into previous sensitivity to such agents as penicillin. If the patient gives a positive answer the use of skin clips should be avoided, closing the skin instead with suture material.

The rapidity of onset and the extent of the secondary eruption in the present case were probably related to the fact that the skin clips punctured the skin, thus increasing the opportunity for nickel to be absorbed and for a sensitivity reaction to develop.

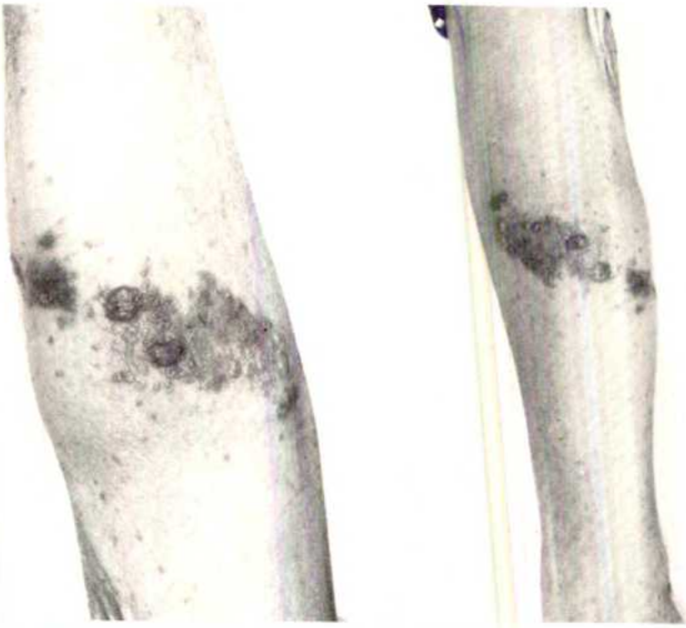

FIG. 4.—Result of a formal nickel sensitivity skin test carried out with the application of nickel sulphide.

An inquiry to the manufacturers of the surgical skin clips revealed that the clips are composed of cupronickel in the proportions of 80 per cent copper to 10 per cent nickel, the remainder being zinc with traces of lead as an impurity, and that the manufacturers were unaware of the possibility of sensitivity to their clips.

This case raises the question whether metal sensitivity to the staples used in stapling machines for intestinal anastomosis is a potential hazard. Staples should not perhaps be used indiscriminately but only after questioning the patient to eliminate the possibility of metal sensitivity.

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REVIEWS AND NOTICES OF BOOKS

Lumbar Disc Disease. Edited by Blaine S. Nashold, jun., M.D., Durham, N.C., and Zdenek Hrubec, Sc.D., Washington, D.C. 10 × 7 in. Pp. 139 + xiii. Illustrated. 1971. London: Henry Kimpton. £7·45.

This monograph gives the results of a 20-year clinical follow-up study from seventeen Veterans Administration Hospitals in the United States of America. The follow-up was the result of teamwork in which many orthopaedic surgeons, neurosurgeons, and radiologists took part.

Although the report raises more questions than it answers it does reveal certain facts.

Myelography is a safe procedure with few side-effects and the dye is not always absorbed as judged by the fact that it was still visable in some cases after 20 years. Radiographs may reveal degenerative changes in the disks although no clinical evidence may be found.

Pain was immediately relieved in a significant percentage of the patients by operation. It was noted that patients with intractable sciatica plus motor symptoms appear to be treated best by operation, but surgery may not relieve motor signs.

A large number of tables are included in this book, giving a detailed list of residual signs and symptoms. Goniometer readings of the spine movements are also included.

This investigation brings out the fact that we as yet know little about the final results of disk lesions in the lumbar region.

Ellison's Atlas of Surgery of the Stomach and Duodenum. By Larry C. Carey, M.D., Pittsburgh, Pennsylvania, and Robert H. Albertin, M.A., Milwaukee, Wisconsin. 12 × 9½ in. Pp. 165 + xii, with 349 illustrations. 1971. London: Henry Kimpton. £11.

This large atlas depicting various operative procedures on the stomach and duodenum will be of real value to all students and postgraduates who wish to have an accurate impression of these various techniques.

The wash illustrations show the various stages of the different operations. The drawings are excellent and very clear. This is by far the best illustrated atlas of the surgery of the stomach and duodenum that has so far been published.

Operations for splenectomy, distal pancreatectomy, and liver biopsy are also included.

An Introduction to Clinical Research. By W. P. Small, V.R.D., Ch.M., F.R.C.P.E., F.R.C.S.E., Edinburgh, and Urban Krause, M.D., Uppsala, Sweden. 8½ × 5½ in. Pp. 125 + ix, with 46 illustrations. 1972. Edinburgh: Churchill Livingstone. £1·50.

This is a useful and practical paperback which should be read by all clinicians who are interested in the long-term follow-up of their cases. It will appeal particularly to surgeons who wish to know the results of different forms of treatment.

It is interesting to compare and contrast the methods adopted in Edinburgh and Uppsala in Sweden. The problems of financing long-term follow-up are discusse at length.

It is pleasing to see reproduced part of one of Lor Lister's ward books from the Royal Infirmary Edinburgh in which the final result of treatment recorded.

Surgery Annual 1971. Edited by Philip Coope M.D., Florida, and Lloyd M. Nyhus, M.D Chicago. 9¼ × 6¼ in. Pp. 444 + xiv. Illustrated. 197 London: The Butterworth Group. £7.

This book with its numerous contributors, mainly fro American medical centres, deals with important surgic topics. Such subjects as post-traumatic pulmonar insufficiency and progress in clinical organ transplantatio are discussed in great detail. Burn therapy is considere and it is surprising to read that in a large series of bur Curling's ulcer occurred in 11·7 per cent.

Other subjects, such as urodynamics and urete surgery, spasms of the oesophagus, primary brea cancer, the ischaemic limb, and cardiac pacing, are dea with in an interesting and practical manner.

At the end of each chapter there is a representative li of references culled from the international medic literature. Senior graduates who are working for high surgical degrees or diplomas will find this book a gre help in their studies.

This is a book for the library of the modern surgeon.

Questions and Answers in Orthopaedics. Secon edition. By Floyd G. Goodman, B.S., M.D., Michiga and George R. Schoedinger, III, B.S., M.D., S Louis. 9¼ × 6¼ in. Pp. 264 + vii. 1971. Londo Henry Kimpton. £5 60.

The fact that a second edition was necessary proves th value and popularity of this book, which contains 159 review questions covering the whole field of orthopaedic including pathology, physical medicine, and rehabilitatio The answers and references are given at the end of th book.

This book will be very useful to students and hospit residents as it acts as a quick revision of the whole fiel of orthopaedics.

Non-specific Mesenteric Lymphadenitis. By V Tuchel, Bucharest. 9¼ × 7 in. Pp. 139 + viii, with 4 illustrations. 1972. Basel: S. Kargar. £7·05.

This monograph on non-specific mesenteric lympha denitis, or lymphadenopathy as we term it in this country gives a very comprehensive survey of this condition. I contains the author's personal experience, the results o many years of study, in addition to a rich bibliography Every facet of this clinical condition is discussed a length and clinical cases are recorded.

The physiology and physiopathology of the conditio are considered at length. Terminal ileitis and Crohn' disease are contrasted with this condition.

Surgery is indicated if abscess formation or obstructio of the bowel occurs. The author has published numerou papers in Romania, France, Germany, Belgium, and Switzerland.

This is a useful reference work on non-specific mesenteric lymphadenitis.

Instructional Course Lectures, Vol. XX. THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS. 11 × 8¼ in. Pp. 244 + x. Illustrated. 1971. London: Henry Kimpton. £9.

THIS volume XX of *Instructional Course Lectures* represents selective lectures given at the Annual Meeting of the American Academy of Orthopaedic Surgeons held in Chicago in January, 1970. It contains articles on the orthopaedic management of haemophilia, deformities due to cerebral palsy, the painful shoulder, osteotomies of the hip, and osteo-arthritis of the knee and its early arrest.

These various articles are stimulating and instructive and reveal the trend of American orthopaedic surgery and the treatment of some interesting conditions.

Physics applied to Anaesthesia. Second edition. By D. W. HILL, M.Sc., Ph.D., F.Inst., F.I.E.E. 8½ × 5½ in. Pp. 304 + xvii. Illustrated. 1972. London: The Butterworth Group. £4·60.

THE second edition of this important book appears 4 years after the first and it has been thoroughly revised and brought up to date. It is an important contribution to anaesthetic literature and it will be a valuable addition to the library of all anaesthetists. All those junior anaesthetists, and they are many, who are working for the F.F.A. R.C.S. will find this book invaluable.

New illustrations have been added, and there are extensive references for the reader who wishes to explore a particular topic.

Pathology of Tumours of the Oral Tissues. Second edition. By R. B. LUCAS, M.D., M.R.C.P., F.R.C. Path., Professor of Oral Pathology, University of London. 9¼ × 7¼ in. Pp. 386 + x. Illustrated. 1972. Edinburgh: Churchill Livingstone. £7.

PATHOLOGY is an important branch of medicine and it is of interest to all clinicians.

Tumours of the oral tissues are of interest, not only to dental surgeons, but also to all surgeons who operate on the mouth and adjoining tissues.

The numerous illustrations throughout this book are superb and could not be bettered; the photomicrographs are outstanding. An excellent short account of the normal histology and development of the oral tissues has been included.

A first-rate reference volume on the pathology of tumours of the oral tissues.

Postoperative Cardiac Intensive Care. Second edition. By M. V. BRAIMBRIDGE, M.A., M.B., B.Chir. (Cantab.), F.R.C.S. (Eng.), Consultant, St. Thomas's Hospital, London. 9¼ × 6¼ in. Pp. 176 + x. Illustrated. 1972. Oxford: Blackwell Scientific Publications. £2·50.

THE second edition of this very practical book has been very extensively revised and brought up to date.

The emphasis is on an accurate assessment of the haemodynamic situation so that appropriate measures can be taken to prevent cardiac deterioration.

The various chapters deal with water, electrolyte, and energy requirements, the management of a low cardiac output, respiratory failure, cerebral damage, renal failure, hepatic damage, and infection, and the diagnosis and management of the complications affecting each of these systems are considered in detail.

The chapter dealing with cardiac arrest is excellent and the clear pictures depicting the treatment of this condition are admirable.

This is a book that should be in every intensive care unit for the use of resident medical officers, students, and nurses.

Surgical Disorders of the Peripheral Nerves. By SIR HERBERT SEDDON, C.M.G., F.R.C.S., London. 9¾ × 7¼ in. Pp. 332 + xi. Illustrated. 1972. Edinburgh: Churchill Livingstone. £8.

THIS is one of the most important works that has been published since the end of the Second World War. Injuries of nerves are common in wartime, but they are also common in road accidents today. It is the clinical experience of wartime nerve injuries that is being used to deal with civil injuries.

Sir Herbert Seddon has long been dedicated to the treatment of peripheral nerve injuries and it is pleasing to find that he has dedicated his work to the memory of Hugh Cairns and George Riddoch, with whom he worked during the Second World War.

This book is a classic and will remain one for a very long time to come, for the author presents his subject in a masterly way.

The structure of a peripheral nerve is discussed in detail and illustrated with excellent photomicrographs, including some electron photomicrographs. The degeneration and regeneration of an injured nerve are considered in a practical and lucid way. The clinical picture and methods of examination are portrayed in a very clear fashion. The operative treatment is discussed at great length and the factors influencing indications for operation are stressed to the full.

The results of repair of nerves are given. There is a full list of references and an author and subject index.

A great feature of this work is the excellence of the illustrations. The line drawings, the clinical photographs, the X-ray pictures, and the photomicrographs are all of a very high order.

This is a book of which the medical profession of Great Britain may well be proud.

A great credit to British surgery.

Management of Arterial Occlusive Disease. Edited by W. ANDREW DALE, M.D., Nashville. 8¾ × 5¾ in. Pp. 506 + xiii. Illustrated. 1972. London: Lloyd-Luke (Medical Books) Ltd. £11·70.

THIS book is the outcome of the National Conference on Management of Arterial Occlusive Disease which was held at Nashville, Tennessee, in November, 1970.

The many contributors from various centres and clinics from all over America have covered the subject of arterial occlusive disease in a very comprehensive manner. It may be said that during the past three decades much progress has been made in the treatment of this condition.

The twenty-eight chapters contained in this book deal with the effect of diet and exercise on arterial disease, angiography in arteriosclerosis, vein-grafts, bovine arterial grafts, thrombo-endarterectomy, transluminal angioplasty, and sympathectomy.

The illustrations throughout the book are good, especially the arteriograms. Transluminal dilatation of an atheromatous core seems to give better results than one would expect.

Dr. Dale, who has devoted the greater part of his surgical career to the study of vascular disease, must be pleased with the production of this book. It is a useful reference volume dealing with an all-too-common disease.

Fundamental Physics of Radiology. Second edition. By W. J. MEREDITH, O.B.E., D.Sc., F.Inst.P., and J. B. MASSEY, B.Sc., F.Inst.P., Manchester. 9½ × 6½ in. Pp. 666 + viii, with 460 illustrations. 1972. Bristol: John Wright & Sons Ltd. £6·25.

THE second edition of this very practical and useful book on the fundamental physics of radiology has been very thoroughly revised, and the chapter on radioactive isotopes and the section on radiation protection have been enlarged.

Although this book has been written for students who are preparing for the various examinations of the Society of Radiographers and Radiotherapists, it will be useful to all those who wish to know more about the physics of isotopes, radium, and cobalt.

Physics continue to play an important part in the clinical medicine and surgery of today and all branches of medicine will find this book a very useful reference volume.

Every medical school library should have this book on its shelves.

A Manual of Respiratory Failure. Tracheostomy, Endotracheal Intubation and Mechanical Ventilation. By ELI RUSH CREWS, M.D., and LEOPOLDO LAPUERTA, M.D., Texas. 9¼ × 6 in. Pp. 198 + xiii. Illustrated. 1972. Springfield, Ill.: Charles C. Thomas. $11.75.

THIS is a practical and useful manual, for it describes and discusses the many and varied causes of respiratory failure and then proceeds to give the necessary treatment. With the ever-increasing multiple accidents on the roads of Great Britain and America the necessity for emergency tracheostomy and endotracheal intubation is increasing daily.

It is true that tracheostomy has been used for centuries for laryngeal obstruction. At the turn of the century it was used in the treatment of laryngeal diphtheria, a disease rarely seen today. Tracheostomy is a life-saving procedure in certain cases of brain injury and upper-airway obstruction but its use is now being replaced by endotracheal intubation.

The authors of this book have described the physiopathology of respiratory failure in an excellent fashion and have given the treatment which is required.

Numerous illustrations and tables are used to clarify and enhance the text. Special attention is given to respiratory nursing care and respiratory care units.

A book which students and nurses will find of real value.

Examination of the Hand. By GEORGE L. LUCAS, M.D., Madison, Wisconsin. 9 × 6 in. Pp. 232 + xiv. Illustrated. 1972. Springfield, Ill.: Charles C. Thomas. $14.

ALTHOUGH there are many books devoted to the surgery of the hand, there is still room for this one which is devoted to the examination of the hand and the diagnosis of various conditions which may affect this part of the upper extremity. The hand is frequently injured in the ever-increasing number of road-traffic accidents. Treatment of an injured hand begins with an accurate diagnosis.

This book is divided into three convenient sections: acute injury, evaluation of reconstructive problems, and disability evaluation.

The section on disability evaluation is concerned largely with a description of the measurement and methods of arriving at a permanent partial disability estimate. Several tables relating to amputation and disability formulae are included at the end of the book.

The illustrations throughout the book, especially the line drawings, are excellent. This is a book for students, house-officers, and casualty residents.

Surgeon to Soldiers. By EDWARD D. CHURCHILL, M.D., Boston. 9 × 6 in. Pp. 490 + xiii. 1972. Oxford: Blackwell Scientific Publications. £6.

THIS interesting and informative book is culled from the diary and records of a very distinguished surgical consultant who served on many fronts during the Second World War. Although this book is packed with surgical information concerning every aspect of modern warfare, Professor Churchill has a lucid style of writing and his book has the warmth of a novel.

The book is divided into five parts. Part 1 deals with medical mobilization and all that this entails. Wound shock and blood transfusion are considered at length. Thermal burns and new sulpha drugs are discussed. Part 2 is devoted to North Africa, the various hospitals, prisoners of war, and war wounds, and there is an important chapter on prostitution and venereal disease. Part 3 is concerned with the Sicilian campaign. Part 4 describes the war in Italy and the treatment of gas gangrene and mustard-gas casualties. Part 5 deals with the last phase of the war, and the invasion of Southern France is described and various congresses of army surgeons are detailed.

The author discusses some of the medical controversies and the drama behind them that polarized many physicians into separate factions and, at times, posed a threat to the best possible care for the wounded.

Professor Churchill makes liberal use of case histories, official medical reports, and the experience of other combat surgeons, which add a further dimension to this informal, first-hand account of surgery and surgeons in just about every type of hospital in an overseas theatre, from surgical field tents to rear echelon installations.

There can be no doubt whatever that this volume is a major contribution to medical military literature. This book will make a strong appeal to all surgeons the world over.

Der Vena Cava-Katheter. By C. BURRI, Ulm, and D. GASSER, Basel. 9 × 6 in. Pp. 126, with 29 illustrations. 1971. Berlin: Springer Verlag. DM.42.

THIS book is an excellent review of 3241 patients treated in nine different centres in Germany, Austria, and Switzerland during a 1-year period with caval catheters used either for infusion or for the measurement of central venous pressure. The different sites of insertion of the catheter are discussed, and jugular and subclavian catheters are preferred, while femoral catheters are condemned because of their high complication rate. Venepuncture is preferred to the cut-down technique. The various complications encountered are discussed in detail and as a result of large experience the authors draw logical and sensible conclusions. The detailed summary is given in English, and this little book should be consulted by anyone using caval catheters in the management of the seriously ill patient. The printing and paper are excellent, but for what it is the book is expensive at about £5.

1971 Year Book of Surgery. Edited by SEYMOUR I. SCHWARTZ, M.D., Rochester. 9 × 6 in. Pp. 516. Illustrated. 1972. London: Lloyd-Luke (Medical Books) Ltd. £6·55.

MOST surgeons will agree that the *Year Book of Surgery* is a 'must' for their library, for this book enables them to keep up to date with all that is new in surgery in every part of the world.

Today it is hard to believe that it was at the turn of the century that the *Year Book of Surgery* first appeared and has continued ever since.

As one would expect, the present volume covers a mass of different subjects, including fluids and electrolytes, shock, trauma, burns, wound healing, transplantation, tumour immunology, the liver, congenital heart disease, and the peripheral arteries.

The illustrations throughout the book have been well chosen and are well produced. Experimental surgery receives full coverage.

This is a desk book for the surgeon of today; it can be read at odd times between seeing patients.

Sectional Anatomy and Tomography of the Head. By GUY D. POTTER, M.D., New York. 11 × 7½ in. Pp. 334 + xi. Illustrated. 1972. London: William Heinemann Medical Books Ltd. £13·50.

THIS is a useful and practical atlas comprising 145 radiographs of anatomical sections 1 mm. thick of the human head. A line drawing of each section is shown so that the reader can pick out easily the various relations of the different structures of the head. These sections were made in the coronal, lateral, axial, and oblique directions.

When all the sections are added together one has a detailed three-dimensional concept of the anatomical formation of the structures of the head and their relationships to one another.

This atlas will be of real value to the radiologist who can compare his radiographs with those in this volume. Any abnormality in the body structure can be seen.

Anatomists will find this atlas useful in teaching students the outline of the skull at various levels, and nasal surgeons will find this volume invaluable as a reference work.

The author is to be congratulated on a great piece of work.

Modern Trends in Diseases of the Ear, Nose and Throat—2. Edited by P. MAXWELL ELLIS, M.S., F.R.C.S., London. 8½ × 5½ in. Pp. 401 + ix. Illustrated. 1972. London: The Butterworth Group. £8.

THIS book is badly published and is certainly not in line with the Butterworths tradition. The review copy contains no title page, only 1 page of the list of contents, and an incomplete preface. Pages 16 and 17 are blank. For a book costing £8 net these omissions show grave lack of supervision as far as the publishers are concerned.

The subject-matter contained in this book is of real interest to all those who are concerned with the treatment of diseases of the ear, nose, and throat. Some of the contributions are outstanding, namely, laryngeal paralysis, cancer of the larynx, and the surgery of the salivary glands.

The illustrations throughout the book are good and well produced.

Progress in Surgery, Volume 10. Edited by M. ALLGÖWER, Basel, S. E. BERGENTZ, Malmo, R. Y. CALNE, Cambridge, and U. F. GRUBER, Basel. 9½ × 7 in. Pp. 132, with 55 illustrations. 1972. Basel: S. Karger. £6·05.

THIS book is volume 10 of a popular series which was begun in 1961.

In this present volume there are some outstanding articles. J. C. Goligher and his colleagues at the Department of Surgery at Leeds contribute an interesting article on Crohn's disease, with special reference to surgical management. This article reviews new information of importance concerning this complicated field. Peter Lord of London reveals his originality in his articles on the treatment of hydrocele and haemorrhoids.

Another article of interest is that by Morgan and Fleisch in which these authors explain the remarkable progress which has been made during the past years regarding calcium and phosphate metabolism, an area of interest even for those not directly involved in bone surgery.

This is a book that all practical surgeons will wish to possess.

Surgery of the Oesophagus. The Coventry Conference. Edited by R. ABBEY SMITH, Ch.M., F.R.C.S., F.R.C.S. (Edin.), and R. E. SMITH, M.A., M.B., B.Ch., F.R.C.P., Coventry. 8½ × 5½ in. Pp. 240 + xvii. Illustrated. 1972. London: The Butterworth Group. £6.

THIS volume contains the proceedings of the conference held at the Postgraduate Medical Centre, Coventry, in July, 1971. After reading this book, which covers every aspect of the surgery of the oesophagus, the reader must be convinced that the conference was a great success. Not only are the proceedings of real interest and importance, but the discussions which followed reveal a great interest in this type of surgery.

Up to the beginning of the Second World War carcinoma of the oesophagus was for the most part treated by palliative gastrostomy, although Grey Turner struggled on with his 'pull-through' operation.

Today resection of the oesophagus is an everyday procedure and this very practical book records how replacement of the oesophagus may be achieved both in the infant and in the adult.

The consultants at Coventry are to be congratulated in producing such an interesting volume.

Handbuch der Kinderheilkunde, Volume VIII, Part 2. Edited by H. OPITZ, and F. SCHMID, Heidelberg. 10½ × 7½ in. Pp. 770 + xvii. Illustrated. 1972. Berlin: Springer Verlag. DM.236.

THIS volume on tumours in childhood is the last one in a series on paediatrics. The authors of the various chapters are paediatricians from West and East Germany and the total omission of a paediatric surgeon or a radiotherapist from the list of authors is remarkable. The volume covers all conceivable tumours in childhood including benign lesions such as haemangiomas and lymphangiomas as well as neurofibromatosis. The book contains a vast amount of statistical information collected from the world literature but, on the other hand, it is of little help to the clinician in relation to diagnosis, and it is certainly of no use to the surgeon or radiotherapist wanting advice about the treatment and management of a particular patient.

However, this volume is a superb summary of the world literature on malignant disease in children even if the summary appears to be totally uncritical. All the chapters have extensive lists of references and undoubtedly this book will be a great help to anybody wishing to publish a paper on any aspect of malignant disease in childhood. This volume should therefore find its place in the libraries of units dealing either with children or with malignant disease but it is expensive at £30 and it is unlikely to be of practical help to the practising paediatrician or paediatric surgeon.

Testicular Tumours. Edited by DOUGLAS E. JOHNSON, M.D., Texas. 10 × 7 in. Pp. 296. Illustrated. 1972. London: Henry Kimpton. £9.

THIS monograph written by a team of urologists, pathologists, and radiotherapists from various medical centres in the United States of America presents a comprehensive survey of the whole problem of cancer of the testicle.

Few medical practitioners realize that cancer of the testicle ranks second only to reticulo-endothelial neoplasms as a cause of death from cancer in young men. Although primary tumours of the testicle are common, secondary or metastatic tumours are rare.

In this book the surgical management of testicular tumours is discussed at length, and the part played by radiation therapy and chemotherapy is well presented.

The actual operation of radical orchidectomy with high ligation of the spermatic cord at the internal abdominal ring is described and illustrated.

Throughout the book the numerous illustrations are of a high order and are quite a feature of the book.

An excellent reference volume on an important subject.

Radiology of the Skull and Brain, Volumes 1 and 2. Edited by T. H. NEWTON, M.D., San Francisco, and D. GORDON POTTS, M.D., New York. 11 × 8¼ in. Pp. 869 + xxiv. Illustrated. 1971. London: Henry Kimpton. £35·35.

THESE two large books with numerous illustrations constitute the most up-to-date and comprehensive work on the radiology of the skull and brain. The numerous contributors, all masters in their own particular field, come from various centres in America, Canada, Great Britain, and Italy.

Volume 1 is divided into four parts. Part 1 deals with the technical aspects of skull roentgenography, which includes film analysis and tomography of the skull. Part II is concerned with skull maturation, the foetal skull, and the changes in the skull during childhood. In Part III the size and shape of the skull vault are discussed in some detail. The thickness of the skull is considered as well as the cranial sutures and the fontanelles. Part IV deals with the skull base, and the basal foramina and canals and the sella turcica are dealt with in detail. This is really a radiographic atlas as the vast majority of the illustrations are skiagrams. These pictures—often ten to a page—are excellent and well produced.

Volume 2 is also divided into four parts which are a continuation of Volume 1. Part V is concerned with the orbit, including the optic canal and superior orbital fissure. Orbital calcification also comes under review. Part VI deals with the congenital abnormalities of the skull. This is an excellent account and is illustrated with a profusion of first-class clinical photographs. Part VII presents a series of metabolic diseases involving the skull, while Part VIII is devoted to other diseases of the skull including acromegaly and Paget's disease.

This is a most comprehensive reference work and it should be found in every medical library.

An excellent production.

Frontobasale Verletzungen. By C. PROBST. 9 × 6 in. Pp. 285. Illustrated. 1971. Bern: Verlag Hans Huber. DM.56.

THIS is a monograph on injuries to the anterior cranial fossa. The book reports in detail the author's experience of 28 patients and this is compared with the large published series available. Active and early surgical intervention is advocated and the various methods of dealing with cerebrospinal rhinorrhoea are described. Both synthetic materials and cartilage grafts are used to close defects in the base of the skull.

Some experimental work on sheep relating to surgical techniques is also described.

The most impressive part of the book is the list of references, totalling almost 700. This volume should be of interest and use to neurosurgeons who have to deal with trauma. It is, however, very expensive.

Neoplasms of the Gastrointestinal Tract. By WILLIAM C. LOWE, M.D., M.Sc., New Jersey. 10 × 7 in. Pp. 347, with 64 illustrations. 1972. London: Henry Kimpton. £9.

THIS book although written for students will prove of interest and value to surgeons, gastro-enterologists, and nurses.

The vast amount of clinical material which has been portrayed in this volume came from the Veterans Administration Hospital in New Jersey.

The long-term follow-up of cases of gastro-intestinal cancer produces some interesting figures. Cancer of the stomach still remains a killer, but cases in which complete gastrectomy is performed have the best prognosis. Cancer of the colon because of its early obstructive symptoms and consequent resection has a high percentage of cures.

In this book a very extensive survey of gastro-intestinal cancer is presented and the pathology, prognosis, and treatment are discussed in detail.

A useful contribution to our knowledge of cancer of the alimentary canal.

Prosthetic Replacement of the Aortic Valve. By LESTER R. SAUVAGE, M.D., Washington, ROBERT F. VIGGERS, M.S., Washington, KNUTE BERGER, M.D., Washington, STEPHEN B. ROBEL, M.S., Washington, PHILIP N. SAWYER, M.D., New York, and STEPHEN J. WOOD, M.D., Washington. 9 × 6 in. Pp. 217 + xiv. Illustrated. 1972. Springfield, Ill.: Charles C. Thomas. $18.

SINCE the termination of the Second World War surgery of the heart has progressed by leaps and bounds and the latest achievement is the replacement of the human heart valves by various and ingenious prostheses. In this monograph which is truly comprehensive the emphasis is on the replacement of the aortic valve. The book begins with an account of the structural mechanics of the aortic valve and then the hydraulics of the valve are considered. The healing of the encapsulable parts of the aortic valve prosthesis is discussed at some length.

Aortic valve design resolves itself into the application of principles of healing and hydraulics to the specific geometry of the aortic root. While many factors remain to be clarified, the basis for continued progress has been established. It may well be that within a few years the aortic valve prosthesis will be sufficiently safe to be implanted early in the course of the patient's illness before significant structural damage has occurred to the myocardium or to the lungs.

This is a book that all cardiologists and heart surgeons should read, for it is full of useful clinical information.

Emergency Room Care. Second edition. Edited by CHARLES ECKERT, M.D., New York. 9 × 6 in. Pp. 423 + xv. Illustrated. 1971. Edinburgh: Churchill Livingstone. £4·50.

THE second edition of this useful students' book has twenty-six contributors, all of whom are affiliated with the Albany Medical College of Union University, Albany. They cover this important subject in a very practical and comprehensive way.

Today when intensive-care units are common to most hospitals both at home and abroad this book will be found invaluable to both students and nurses. The price of the book is quite moderate.

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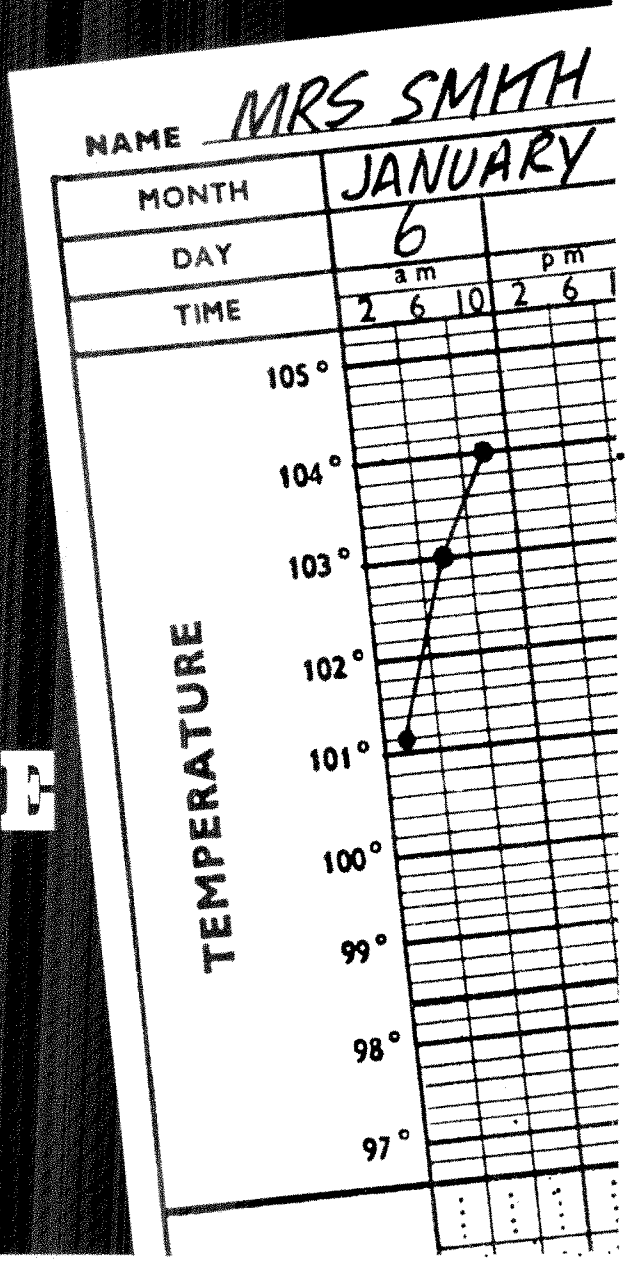

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Selection of Chirurgical Books

Die Hämodynamik während des extrakorporalen Kreislaufs

Of. Doz. Dr. G. BAUST, Halle/S. 1971. 88 *pages, with* 32 *illustrations and* 1 *table, gr.* 8⁰. *Cloth binding.* **13,50M**

Stiellappenplastik bei chronischen Unterschenkelwunden

Of. Prof. Dr. H. BRÜCKNER, Rostock, with contributions of Dr. P. Pietsch, Rostock. 1970. 150 *pages, with* 174 *illustrations and* 19 *tables, gr.* 8⁰. *Cloth binding.* **31,20M**

Neurochirurgie kurzgefasst

Of. Doz. Dr. W.-E. GOLDHAHN, Leipzig. 1970. 268 *pages, with* 105 *illustrations.* 8⁰. *Cloth binding.* **31,20M**

Chirurgie des Kehlkopfkrebses

Of. Doz. Dr. H. GOLLMITZ, Halle/S. 1965. 100 *pages, with* 63 *illustrations, gr.* 8⁰. **10,50M**

Das Schädelhirntrauma im Kindesalter

Of. Doz. Dr. S. KIENE, Rostock, und Doz. Dr. J. KÜLZ, Rostock. 1968. *VIII*, 162 *pages, with* 75 *illustrations and* 17 *tables, gr.* 8⁰. **22,90M**

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Of. Prof. Dr. K. PITZLER, Jena. 1972. 58 *pages, with* 50 *illustrations, gr.* 8⁰. **10,20M**

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☐ **THE SPINAL CORD: Basic Aspects and Surgical Considerations (2nd Ed.)** *by* **George Austin,** *Editor-in-Chief, Loma Linda Univ. School of Medicine, California. [16 Contributors]* '72, 780 pp. (7 × 10), 486 il., 31 tables, $48.50

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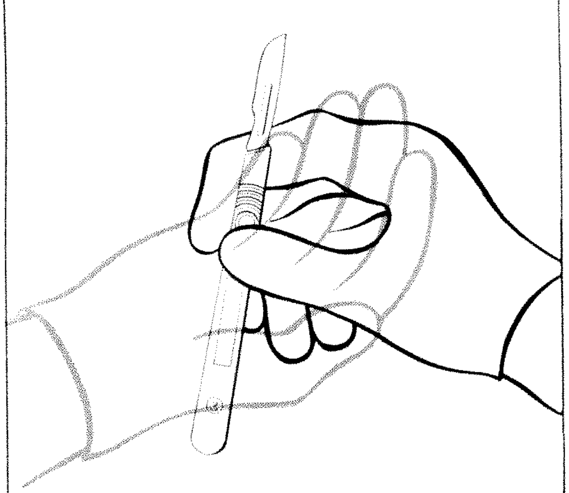

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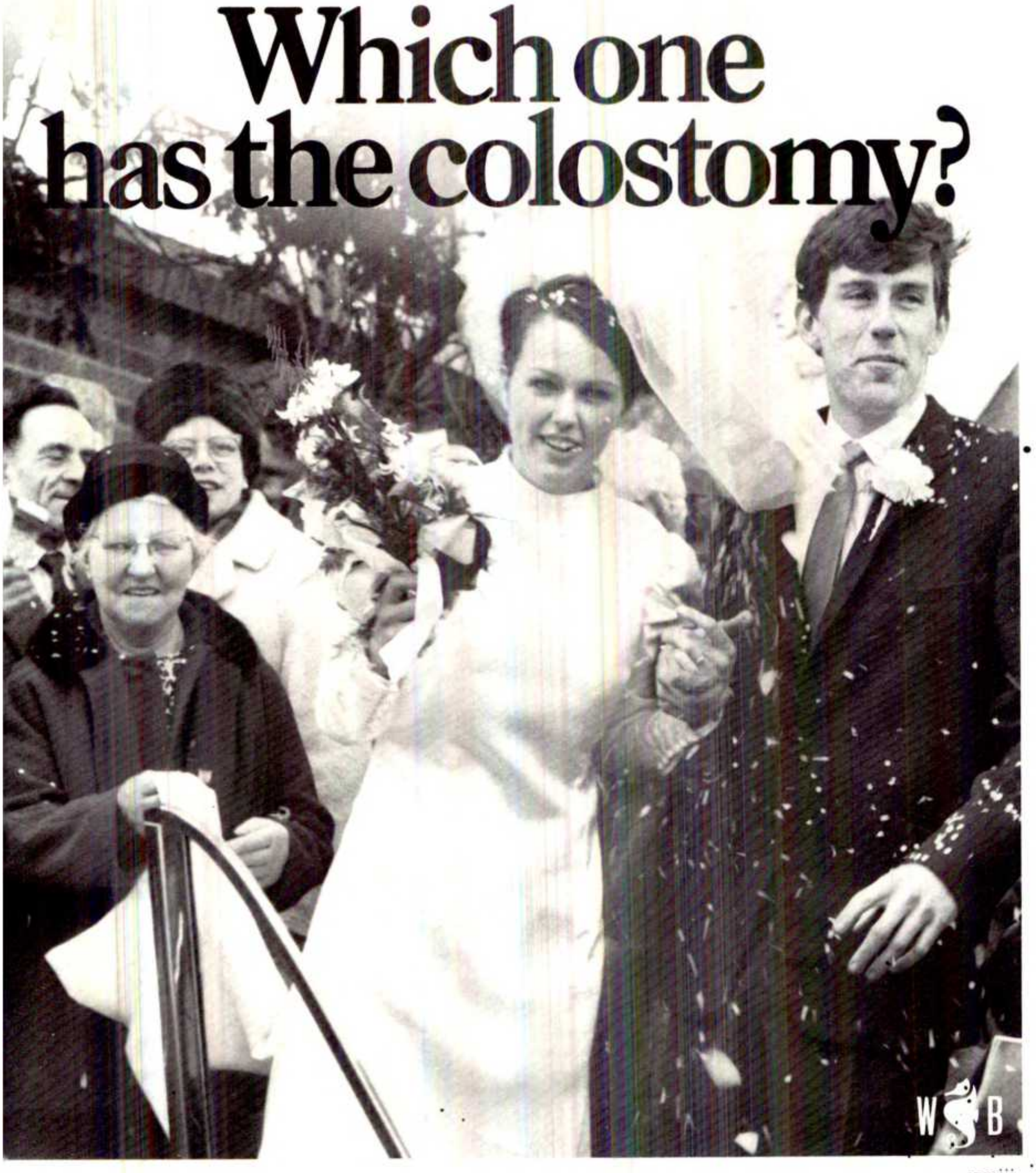

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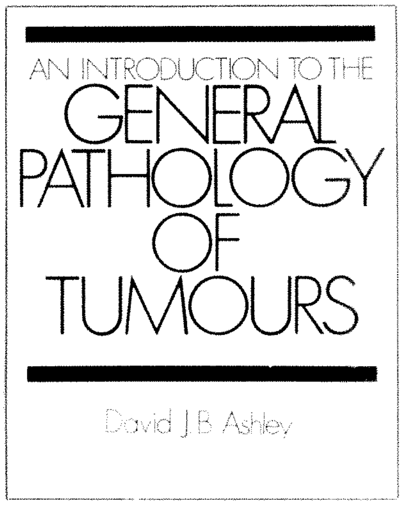

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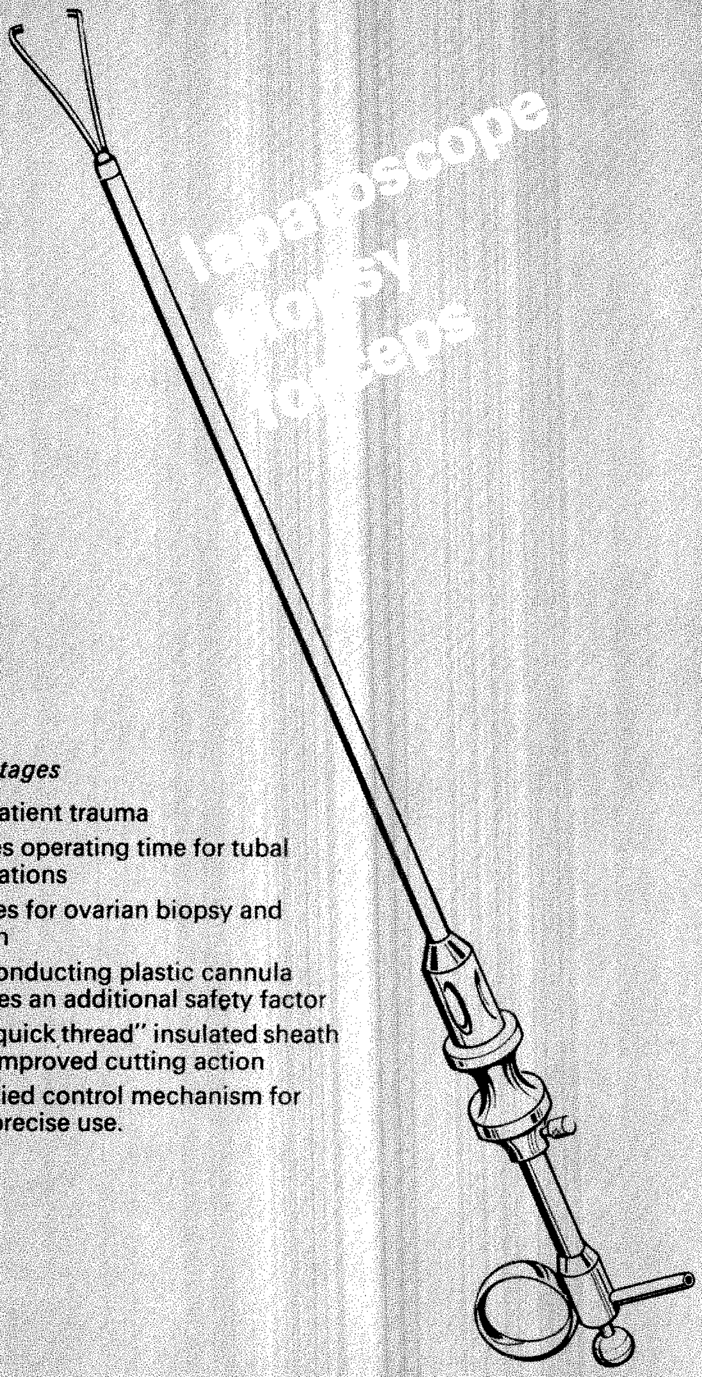

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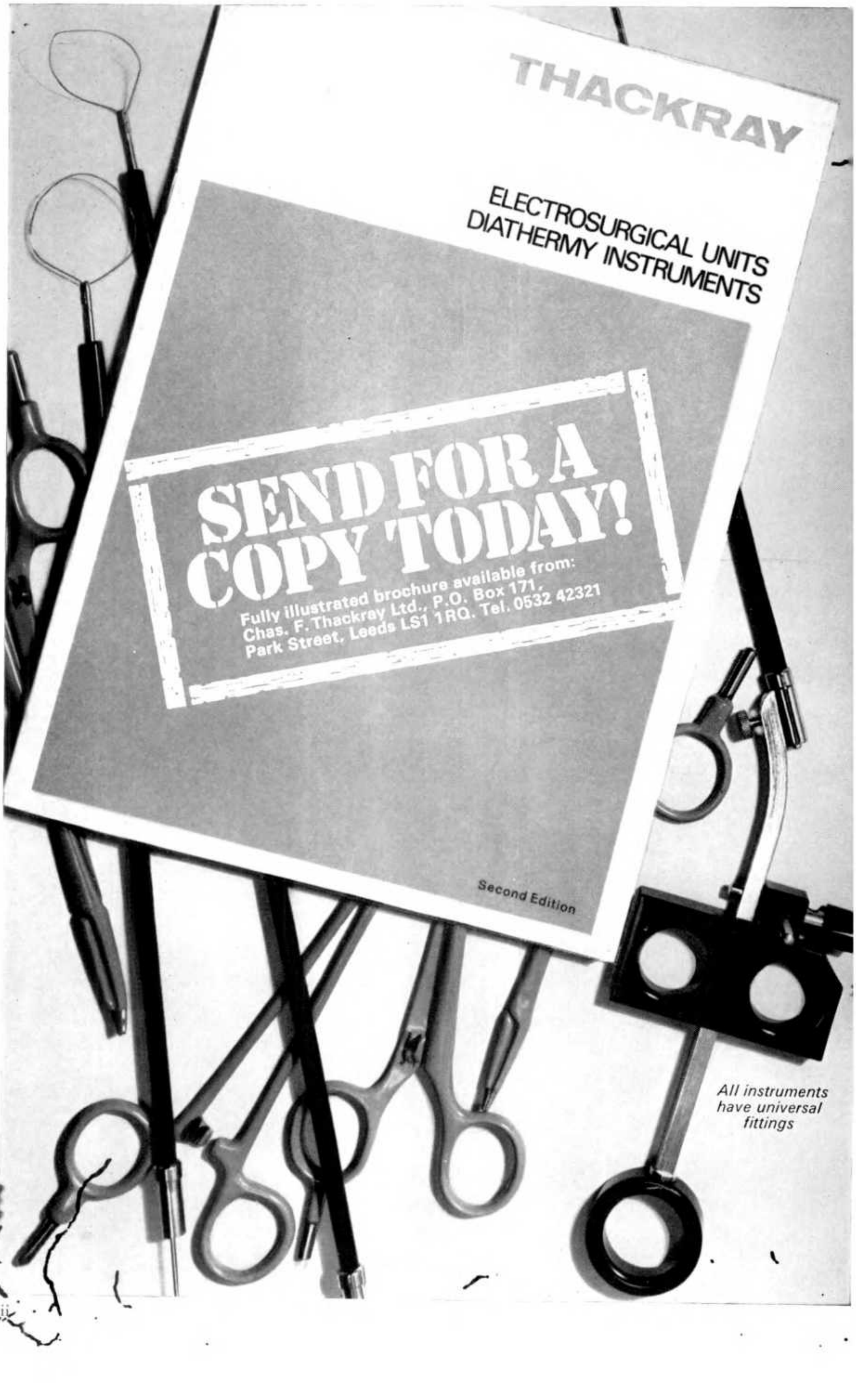

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CONTENTS

PAGE

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SHORT PAPERS FOR THE MOYNIHAN PRIZE

IE NATURAL HISTORY OF VENOUS THROMBO-EMBOLISM - - - - - - *M. G. Walker* 753
TERATION IN FIBRINOLYSIS ASSOCIATED WITH SURGERY AND VENOUS THROMBOSIS - *Averil O. Mansfield* 754
PERIMENTAL ORGAN PRESERVATION - - - - - - *K. C. Calman and P. R. F. Bell* 758
IE EFFECT OF ISCHAEMIC INJURY ON KIDNEYS PRESERVED FOR 24 HOURS BEFORE TRANSPLANTATION *R. W. G. Johnson* 765
MODEL WHICH CAN BE USED TO IMPROVE THE TREATMENT OF ACUTE HEPATIC FAILURE - *John Winch* 771
GRESSION OF AXILLARY LYMPH-NODES IN CANCER OF THE BREAST *M. H. Edwards, M. Baum, and C. J. Magarey* 776
IE VALUE OF PRESERVING THE PYLORUS IN THE SURGERY OF DUODENAL ULCER *C. S. Humphrey and A. R. Wilkinson* 779

SHORT PAPERS

LOROPLASTY ALONE IN THE MANAGEMENT OF PATIENTS WITH A NEGATIVE EXPLORATION FOR DUODENAL ULCER *M. Douglas and H. L. Duthie* 783
REATMENT OF GASTRIC ULCER BY HIGHLY SELECTIVE VAGOTOMY WITHOUT A DRAINAGE PROCEDURE: AN INTERIM REPORT - - - - *D. Johnston, C. S. Humphrey, R. B. Smith, and A. R. Wilkinson* 787
IE VALUE OF UPPER GASTRO-INTESTINAL GASTROSCOPY - - - - - - *Ian McColl* 793
IE IMPORTANCE OF BILE IN REFLUX OESOPHAGITIS AND THE SUCCESS IN ITS PREVENTION BY SURGICAL MEANS *E. W. Gillison, K. Kusakari, C. T. Bombeck, and L. M. Nyhus* 794
HE CAUSE OF VARICOSITY IN SUPERFICIAL VEINS OF THE LOWER LIMB *W. G. Fegan and A. L. Kline* 798
RGERY FOR CORONARY ARTERY DISEASE *D. C. Bouch, D. J. Julian, A. H. Kitchin, M. F. Oliver, and J. D. Wade* 801

SYMPOSIUM ON CROHN'S DISEASE

HE VALUE FOR DIAGNOSIS AND RESEARCH OF SPECIAL INVESTIGATION ON RECTAL BIOPSIES IN CROHN'S DISEASE *I. M. P. Dawson* 806
OME ASPECTS OF THE RADIOLOGY OF CROHN'S DISEASE - - - - *K. C. Simpkins* 810
UTRITIONAL DISTURBANCES IN CROHN'S DISEASE - - - - - *A. M. Dawson* 817
ZATHIOPRINE IN THE TREATMENT OF CROHN'S DISEASE - - - - - *J. Rhodes* 819
URGICAL TREATMENT OF CROHN'S DISEASE OF THE SMALL INTESTINE - - - - *James Kyle* 821
ROHN'S DISEASE OF THE LARGE BOWEL - - - - - *H. E. Lockhart-Mummery* 823
HE RESULTS OF SURGICAL TREATMENT FOR CROHN'S DISEASE - - - - *F. T. de Dombal* 826

SYMPOSIUM ON THROMBO-EMBOLISM—CURRENT MANAGEMENT

HE DIAGNOSIS OF DEEP-VEIN THROMBOSIS - - - - - - - *David Negus* 830
ONSERVATIVE MANAGEMENT OF THROMBO-EMBOLISM - - - - - - *P. T. Flute* 834
HE DIAGNOSIS AND MANAGEMENT OF MASSIVE PULMONARY EMBOLISM - - *G. A. H. Miller* 837

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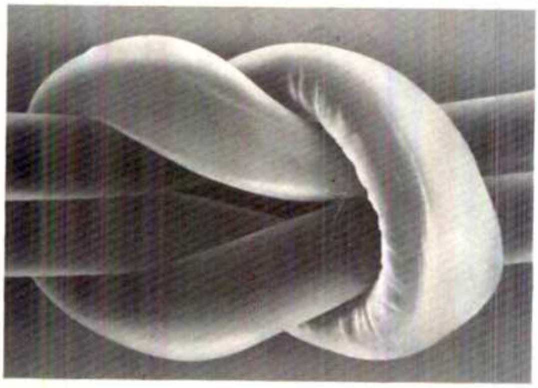

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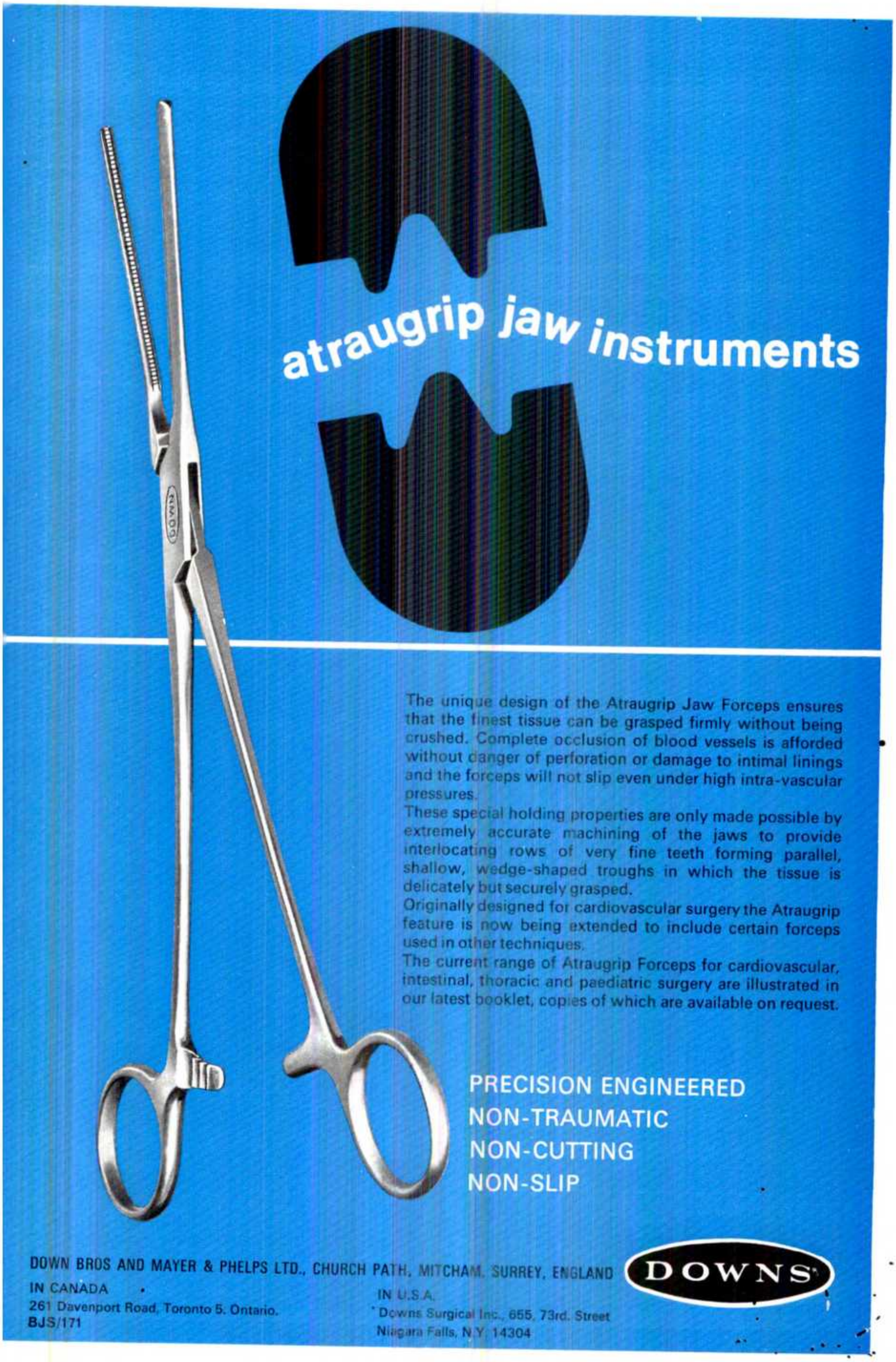

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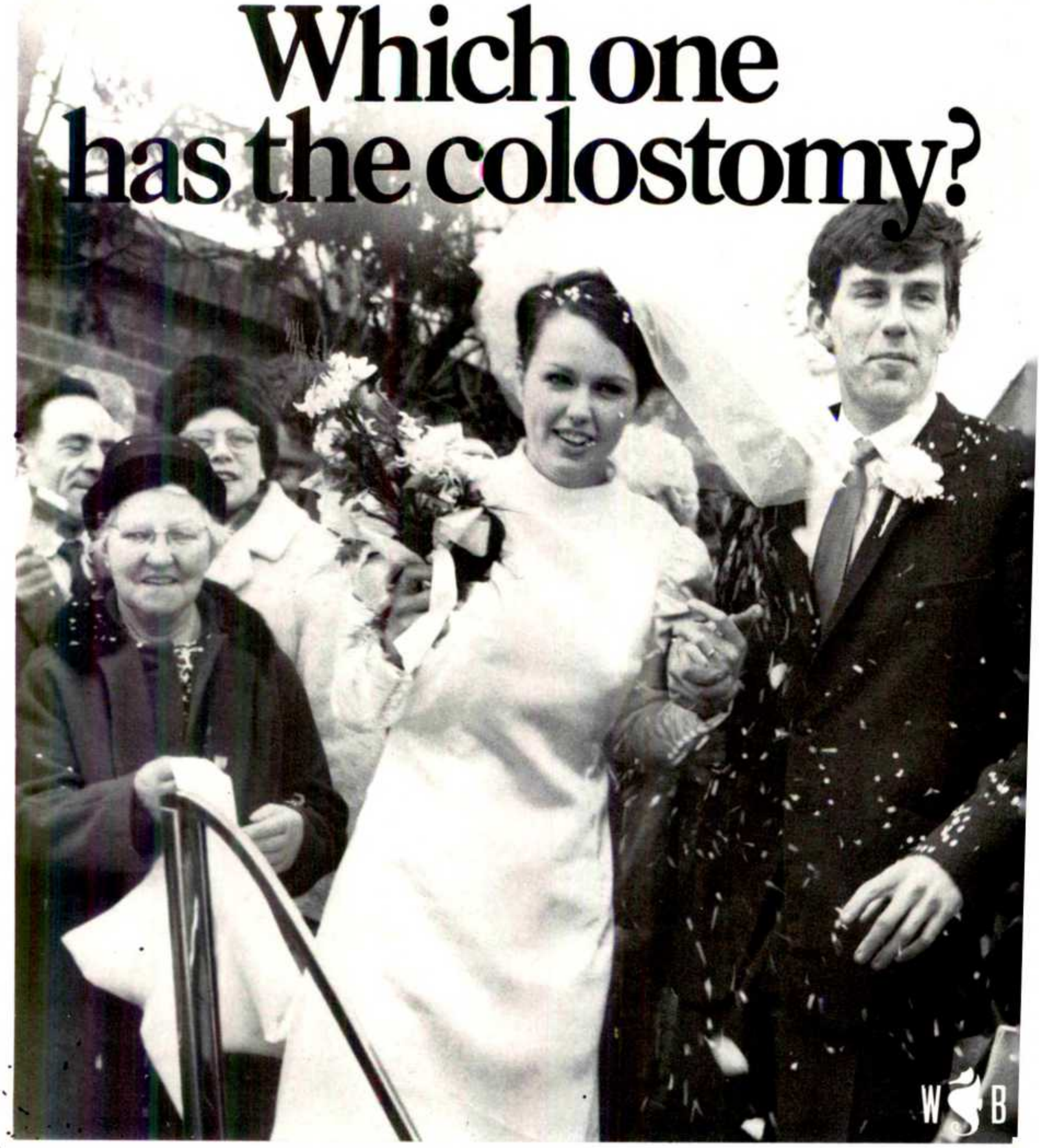
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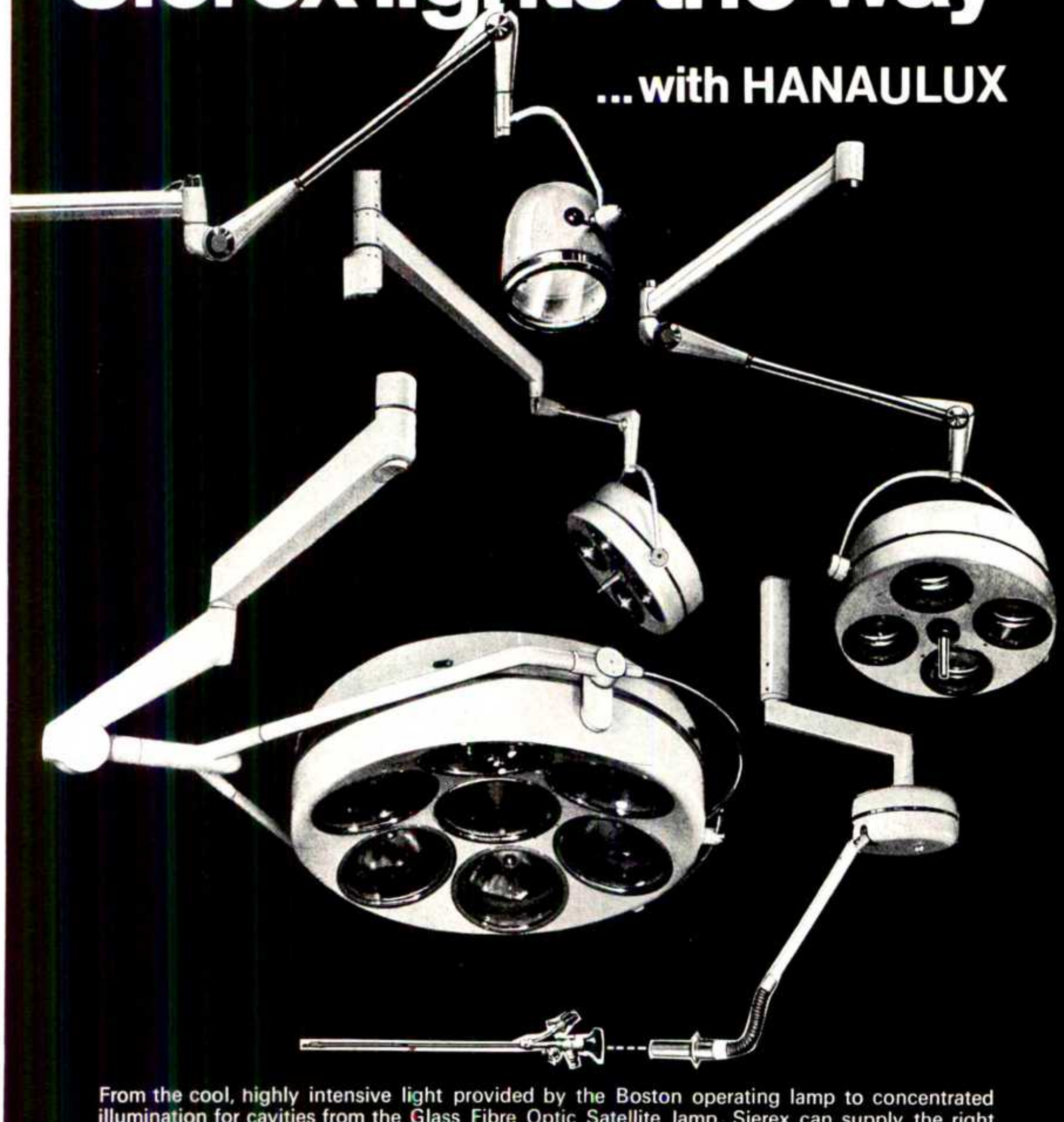

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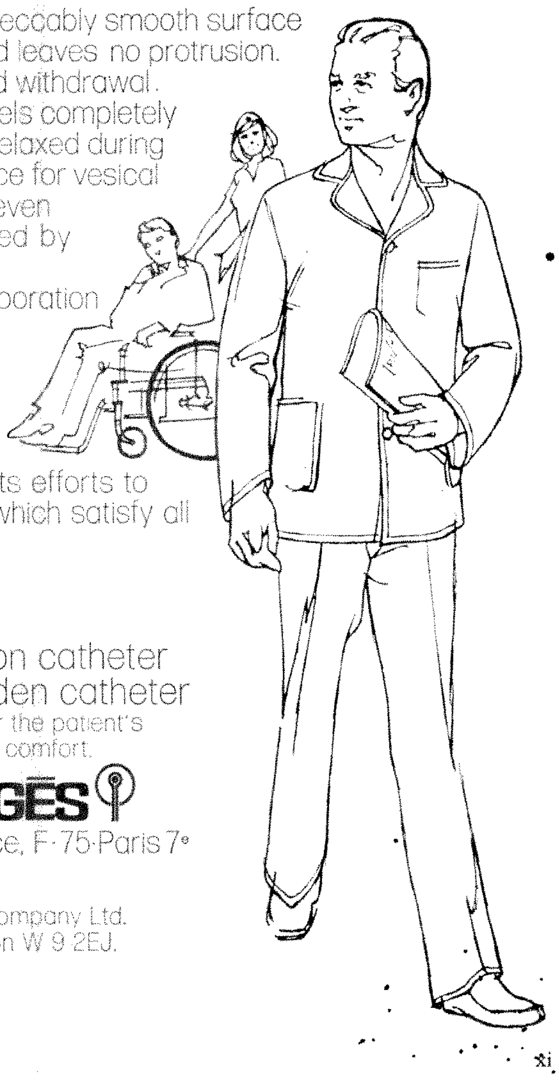

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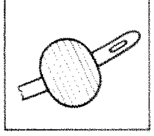

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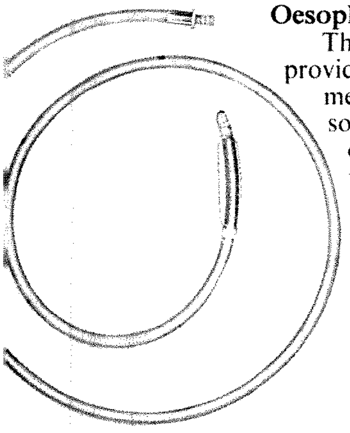

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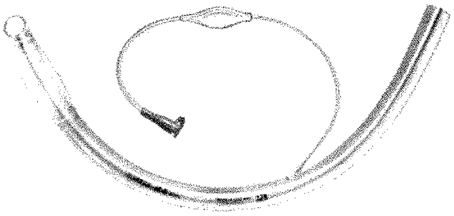

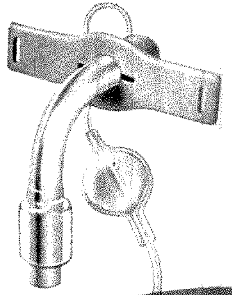

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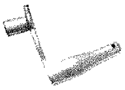

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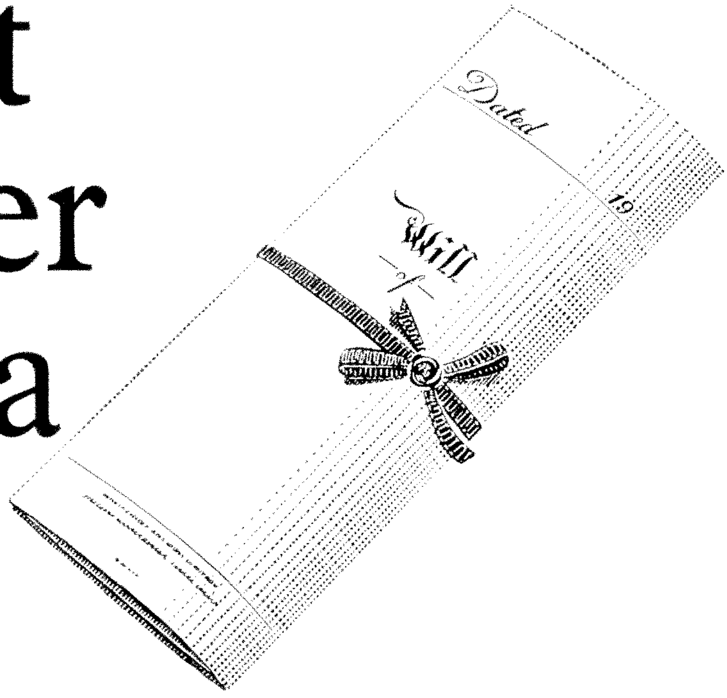

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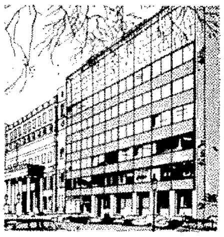
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Vol. 59 OCTOBER, 1972 No. 10

ASSOCIATION OF SURGEONS OF GREAT BRITAIN AND IRELAND

The Annual Meeting of the Association took place in Harrogate and Leeds on 6, 7, and 8 April, 1972, with the President, Professor J. C. Goligher, in the Chair.

After the Business Meeting there was a Symposium on Crohn's disease at which the President acted as Chairman. On the following day there were several sessions of Short Papers, some of which were entered for the Moynihan Prize. The second Symposium, at which Professor G. W. Taylor was the Chairman, was entitled 'Thrombo-embolism—Current Management'.

SHORT PAPERS FOR THE MOYNIHAN PRIZE

[The prize was won by Messrs. C. S. Humphrey and A. R. Wilkinson (Leeds)]

THE NATURAL HISTORY OF VENOUS THROMBO-EMBOLISM*

By M. G. WALKER
ABERDEEN ROYAL INFIRMARY

INFORMATION not hitherto available can be obtained in relation to the site and extent of thrombus formation in early cases of venous thrombo-embolism using three diagnostic tools:—

1. Lung scanning with ^{131}I macro-aggregated human albumin.
2. Bilateral percutaneous femoral phlebography to visualize the iliofemoral segments.
3. Peripheral leg scanning using ^{125}I-tagged fibrinogen.

Two groups of patients were investigated. Group I consisted of a series of 84 patients with iliofemoral venous thrombosis, both non-occlusive and occlusive, confirmed by iliofemoral phlebography in which peripheral scanning was carried out. In 34 cases (40 per cent) non-occlusive thrombus was demonstrated in the iliofemoral segment and in only 3 cases was the peripheral leg scan positive. In 50 cases the iliofemoral segment was totally occluded and in only 16 cases (32 per cent) was the peripheral leg scan positive.

Group II consisted of a series of 86 cases presenting with pulmonary embolism as the initial sign of venous thrombo-embolism; all the patients were without signs or symptoms referable to the legs. Thirty-one patients showed non-occlusive thrombus in the iliofemoral segment and the peripheral scan was negative. In only 3 cases where the iliofemoral phlebogram was positive for non-occlusive thrombus was the peripheral scan positive. Eight cases had a positive peripheral scan and a negative phlebogram, the source of embolus possibly being in the peripheral segment. In 46 cases both the iliofemoral phlebogram and peripheral leg scan were negative, no source of thrombus being demonstrated by these techniques. Follow-up phlebography and peripheral scanning studies were undertaken in these 46 cases where no source of thrombus could be demonstrated. Subsequently in 8 cases non-occlusive thrombus was demonstrated in the iliofemoral segment, the peripheral leg scan again being negative. In each of these cases a further pulmonary embolism had occurred. Corrected figures for iliofemoral involvement are therefore $34+8=42$ (49 per cent).

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* This article is a summary of the paper which was presented at the meeting of the Association of Surgeons.

CONCLUSIONS

1. In 49 per cent of the cases presenting with pulmonary embolism where the legs were clinically silent the source of emboli was in the iliofemoral segment, the right side being involved more frequently than the left in the ratio of 2 : 1.

2. Peripheral leg scanning gave a positive result in 27 (19 per cent) cases.

3. Cases in which thrombus formed in the peripheral venous segment seldom presented with pulmonary embolism.

4. Thrombus developing in the iliofemoral segment became occlusive without, in the majority of instances, thrombus forming in the peripheral venous segment.

As regards the investigation and treatment of deep-vein thrombosis, therefore, considerable emphasis should be placed on the iliofemoral segment, and visualization of these segments by phlebography is always an essential aspect of management. Peripheral scanning is of value in screening the peripheral venous segment, and is useful, as shown here, in helping to elucidate features of the natural history of venous thrombo-embolism. It is not, however, superior to ascending phlebography which gives a clearer picture of events, nor does it represent an 'early-warning system' for significant clinical venous thrombo-embolism. If diagnostic efforts are to be concentrated on the peripheral segment the more important, more insidious, and much more dangerous involvement of the iliofemoral segment is likely to be overlooked.

Acknowledgement.—I am deeply indebted to Mr G. E. Mavor for his advice, help, and encouragement in the preparation of this paper.

ALTERATION IN FIBRINOLYSIS ASSOCIATED WITH SURGERY AND VENOUS THROMBOSIS

By AVERIL O. MANSFIELD*
DEPARTMENT OF SURGERY, UNIVERSITY OF LIVERPOOL

SUMMARY

1. A marked increase in fibrinolytic activity occurs during surgical operations, especially major surgery.

2. This increase sometimes begins prior to the induction of anaesthesia.

3. There is reduced fibrinolytic activity during the postoperative period and this occurs earlier and to a greater degree in those patients who develop a venous thrombosis as shown by the ^{125}I-fibrinogen test.

THE term 'fibrinolysis' means the enzymatic liquefaction of blood or fibrin clot and it can be regarded as the physiological antithesis of coagulation. It is known that increased coagulability of the blood is a feature of surgical operations. It is also known that an alteration in fibrinolysis occurs during an operation. A haemostatic balance has been postulated between clotting and fibrinolysis. Although this is an oversimplified concept it is not unreasonable to suppose that some relationship probably exists between these two factors. Consequently an investigation has been undertaken to determine, in detail, the changes occuring in fibrinolysis in the peripheral blood during and after surgical operations. In addition, a further investigation has been undertaken to assess whether these differences are in any way related to the onset of venous thrombosis.

REVIEW OF THE LITERATURE

In 1937 MacFarlane made a chance observation that blood removed from a patient immediately following cholecystectomy clotted normally but was 'quite fluid' when inspected the following day. This was probably the earliest observation of fibrinolysis in relation to surgery.

In a later series of 34 patients MacFarlane and Biggs (1948) employed dilution of blood to demonstrate fibrinolysis, and in 50 per cent of cases after operation a positive result was obtained, even in some cases where only a minor procedure had been undertaken. The methods which they used failed to demonstrate fibrinolysis in the normal patient and so there was no way of obtaining a quantitative estimate of the change.

These findings were confirmed by Truelove (1952, 1953). Further investigation by Andersson, Nilsson, and Olow (1962) showed increased fibrinolytic activity during operation.

Several investigations were undertaken by Innes and Sevitt (1964) in patients who had recently been injured. One of these studies included the measurement of the fibrinolytic activity, which was found to be increased soon after injury, but because of the nature of the investigation base-line measurements were, of course, impossible.

Chakrabarti, Hocking, and Fearnley (1969) showed that there was prolongation of lysis time following surgical operations and that this prolongation was maximal on the fifth postoperative day. The authors referred to this period of reduced fibrinolytic activity as the 'fibrinolytic shut-down'. In the same investigation they showed a temporary increase in fibrinolysis shortly after electroconvulsive therapy. A previous investigation by the present author (Mansfield, 1970) demonstrated that the period of fibrinolytic shut-down was in fact preceded by a marked increase in fibrinolytic activity during and shortly after the operation. In summary, lysis time was shortened during the surgical operation and remained so in the immediate postoperative period.

---

* Present address: Consultant Surgeon, United Liverpool Hospital.

METHODS

1. **The Dilute Blood-clot Lysis Time.**—The method described by Fearnley (1964) depends on the differential reduction of inhibition as compared with fibrinolytic activity when blood is diluted. A photographically determined end-point has been employed in the present study.

2. **Euglobulin Lysis Time.**—The euglobulin fraction is obtained by dilution and acidification of plasma and the inhibitors are largely removed (von Kaulla, 1963). It is generally regarded as a measure of activator activity.

3. **Detection of Venous Thrombosis.**—^{125}I-fibrinogen was administered intravenously in a dose of 100 µc. at the termination of the operation. Employing a portable scintillation counter, counts were made at 8-cm. intervals from the groin to the ankle. The method employed has been fully described by Flanc, Kakkar, and Clarke (1968), Negus, Pinto, Le Quesne, Brown, and Chapman (1968), and Kakkar, Nicolaides, Renney, Friend, and Clarke (1970). Using this method, venous thrombosis can be accurately determined from the ankle to the groin but not in the pelvic vessels. *Fig.* 1 demonstrates thrombus formation in the calf.

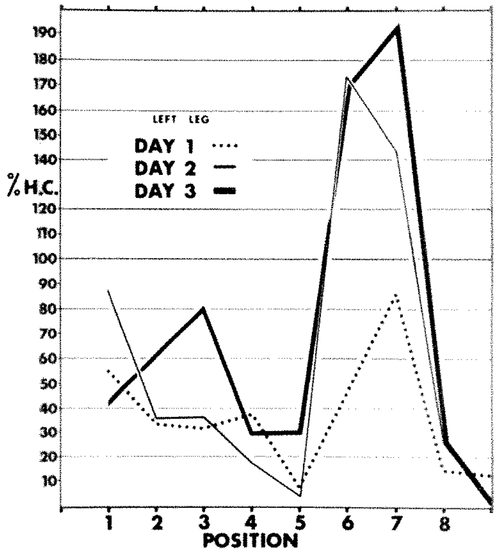

FIG. 1.—^{125}I-fibrinogen test demonstrating thrombus in the calf.

PATIENTS INVESTIGATED

A group of unselected patients undergoing routine general surgery was investigated. All the blood-samples were obtained with the patients fasting and resting in bed. A tourniquet was not applied because this increases fibrinolytic activity. The samples were placed directly in ice after their removal.

Timing of Blood-samples.—Two preoperative blood-samples were obtained on consecutive days. On the day of the operation blood was obtained in the anaesthetic room before the induction of anaesthesia and at half-hourly intervals during the operation. A further sample was obtained at the termination of the operation before the administration of the radioactive fibrinogen.

The investigations were continued daily after the operation for a period of 1 week. Five patients had to be excluded from the investigation because it proved impossible to obtain repeated blood-samples without the use of a tourniquet.

Eighty-nine patients have been investigated in the manner described.

Investigation of Venous Thrombosis.—Fifty-five patients undergoing major surgery were investigated using radioactive fibrinogen. All the patients were undergoing operations of a similar or greater magnitude to cholecystectomy, and all were over 40 years of age. A consecutive series of patients who fulfilled these two criteria was investigated.

Investigation of the Diurnal Variation.—There is known to be a normal diurnal variation in fibrinolysis (Buckell and Elliott, 1959). During the morning hours there is an increase in fibrinolytic activity. Ten normal volunteers and 12 preoperative patients were confined to bed and kept in the fasting state. The normal diurnal variation was suppressed in all those who were investigated, i.e., the normal shortening of blood-clot lysis time between 8.00 a.m. and 12.00 midday did not occur.

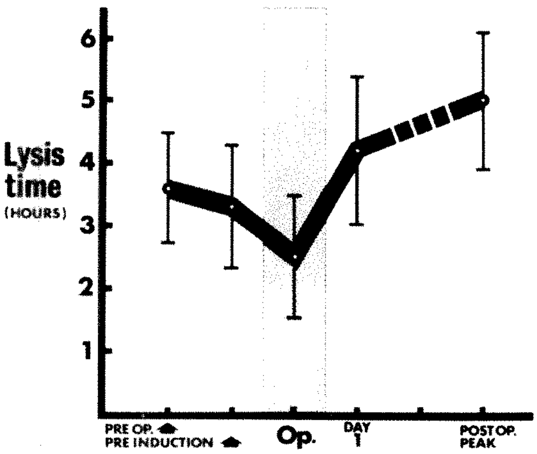

FIG. 2.—Changes in the euglobulin lysis time during and following operation.

RESULTS

Fig. 2 shows the mean values of the euglobulin lysis time in the 89 patients who were investigated during the operation period. Similar results were obtained for the dilute blood-clot lysis time. In the majority of patients there was a small increase in fibrinolysis before the induction of anaesthesia. There was a significant difference ($P < 0{\cdot}001$) between the preoperative values and the lowest value obtained during operation. It was concluded therefore that fibrinolytic activity is increased during surgery. On the first postoperative day this increase in activity was reversed and the patients either returned to their normal preoperative level of activity or had a lower level of activity on the first postoperative day. Although the graph of the results demonstrates an increase in fibrinolysis during operation, 20 per cent of the patients investigated failed to show this increase in activity. With 1 exception, however, the patients who remained normal during the operation were undergoing only minor surgery.

The pre-induction value appears to be affected by premedication. Thus, 13 out of 14 patients who received diazepam (Valium) as the premedication did not show any increase in fibrinolytic activity. The significance of suppressing fibrinolysis at this time is not known.

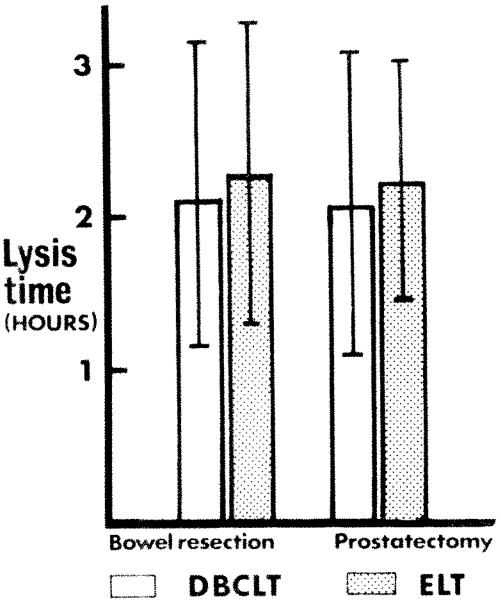

FIG. 3.—Lysis times during prostatectomy and bowel resection. DBCLT, Dilute blood-clot lysis time. ELT, Euglobulin lysis time.

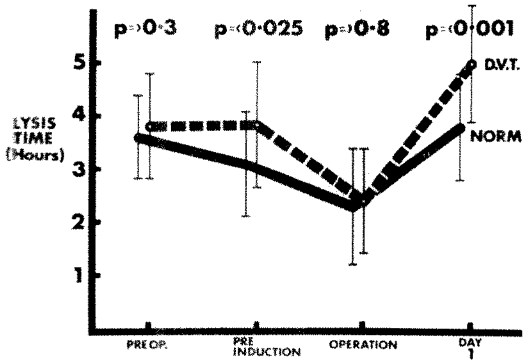

FIG. 5.—Euglobulin lysis time in normal patients and in patients who developed deep-vein thrombosis.

Two groups of patients were compared to see if there was any increase in fibrinolysis resulting from prostatectomy, which has often been stated to be associated with a high level of fibrinolysis. Nine patients undergoing prostatectomy were compared with 10 patients undergoing large-bowel resection. Both the dilute blood-clot lysis time and the euglobulin lysis time were shortened by these operations, but there was no significant difference between the operations (*Fig.* 3). These techniques simply measure fibrinolysis in the peripheral blood and local fibrinolytic activity is not taken into account by these methods.

Postoperative Lysis Time.—Prolongation of lysis time occurred in the postoperative period. All the patients showed a reduction in fibrinolysis time at some stage during the postoperative period as compared with their preoperative fibrinolytic activity. In the majority of patients the decrease occurred on the fifth or sixth postoperative day, but it was observed that in some patients it occurred on the first postoperative day.

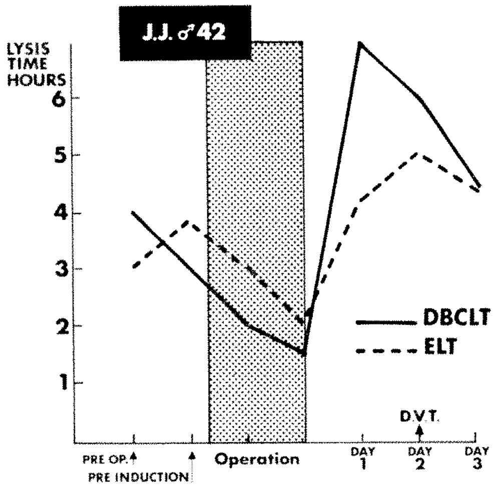

FIG. 4.—Lysis times in a patient who developed a deep-vein thrombosis. DBCLT, Dilute blood-clot lysis time. ELT, Euglobulin lysis time.

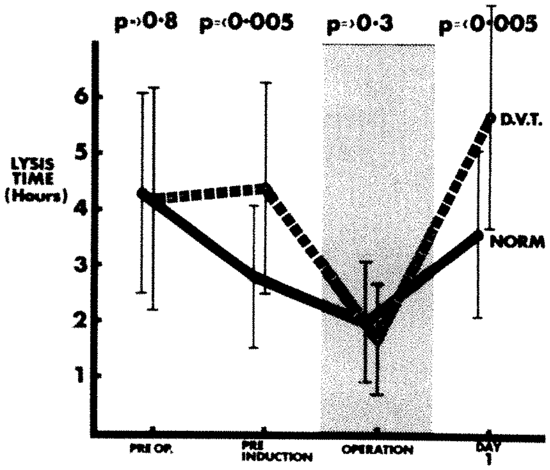

FIG. 6.—Dilute blood-clot lysis time in normal patients and in patients who developed deep-vein thrombosis.

Results of Investigations with ^{125}I-fibrinogen.—The alterations in fibrinolytic activity occurring in a patient who developed deep-vein thrombosis (as shown by radioactive fibrinogen studies) are shown in *Fig.* 4. It can be seen that there is an increase in fibrinolysis during the operation which is similar to that obtained in the larger group of patients. On the first postoperative day, however, there is a marked diminution in fibrinolytic activity which in this patient was particularly noticeable in the dilute blood-clot lysis time.

Two groups of patients have therefore been compared: those who developed signs of deep-vein thrombosis, as shown by the ^{125}I-fibrinogen test, and those who remained normal in this respect throughout their postoperative recovery. The investigations were exactly the same as for the 89 patients undergoing routine surgery. *Fig.* 5 shows the changes in euglobulin lysis time, and *Fig.* 6 demonstrates the alteration in the dilute blood-clot lysis time for the same group of patients. In both of these investigations it can be seen that there is an increase in fibrinolysis during the operation. These results are the same as those found in the overall group of patients. There was no significant difference in the lysis time of the two groups during the operation nor was there any significant difference between the two groups on their preoperative investigation.

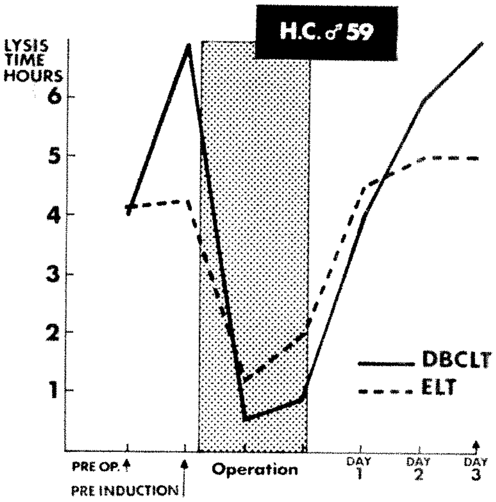

FIG. 7.—A further example of the changes in lysis time occurring in a patient who developed a venous thrombosis. DBCLT, Dilute blood-clot lysis time. ELT, Euglobulin lysis time.

Differences, however, emerge between the two groups in the pre-induction investigation, when those patients who later developed venous thrombosis failed to show the normal increased fibrinolytic activity prior to the induction of anaesthesia. The significance of this is not certain as there are so many factors which influence fibrinolytic activity at this time. Both groups of patients, however, were treated identically.

In the postoperative period the normal patients returned to a level of fibrinolytic activity which was similar to their preoperative level, but the patients developing a deep-vein thrombosis showed a marked and early prolongation of their lysis time, that is, diminished fibrinolytic activity on the first postoperative day. When the results on the first postoperative day were compared for the two groups employing Student's t-test, they gave $P < 0{\cdot}005$ for the dilute blood-clot lysis time and $P < 0{\cdot}001$ for the euglobulin lysis time. There is, therefore, a significant difference between the two groups at this time.

A further example of the alterations occurring in an individual patient is shown in *Fig.* 7. This patient went on to develop a venous thrombosis on the third postoperative day. There was a marked prolongation in the clot lysis time in the early postoperative period.

DISCUSSION

Previous investigations have shown that the majority of patients who develop venous thrombosis do so either during or shortly after their operation. It is known that there is an increased coagulability of the blood at that time and it is not unexpected to find that there is an increase in fibrinolysis during the period of the operation.

Chakrabarti and others (1969) were the first to point out that a reduction in fibrinolysis occurs in the postoperative period. Morrell and Dunnill (1968), in post-mortem studies, showed that in recurrent pulmonary embolism the thrombus in the pulmonary vessels failed to lyse in the normal manner. They postulated that the emboli may have occurred in a period of reduced fibrinolytic activity in the blood.

The present investigation has confirmed that there is a period of reduced fibrinolytic activity in the postoperative period. In patients who develop venous thrombosis there is a significant reduction in fibrinolysis on the first postoperative day at a time when the risk of thrombus formation is high.

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EXPERIMENTAL ORGAN PRESERVATION

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SUMMARY

An experimental model for the study of organ preservation based on the isolated, biologically perfused rat heart is described. Using this model a standard storage solution has been evolved for use with initial perfusion and hypothermic storage. This solution contains Dextran 40 and insulin. Various perfusion characteristics including *p*H and infusion volume have also been studied. This solution has been modified and compared with two currently available storage solutions—Collins's C4 solution and the Gelin technique—and found to be superior to both. The technique consists of two parts; first, the organ is flushed with 0·5 per cent lignocaine in a buffered solution and is then perfused with the Dextran-40-based solution containing insulin and lignocaine. Further modification of the solution to contain a high magnesium concentration has resulted in a further improvement in survival after storage. These results are now being confirmed in the dog kidney.

The gradual acceptance of prospective tissue typing in organ transplantation has meant that more organs are now being transported to centres where recipients with the best tissue match are available (Batchelor and Joysey, 1969; Van Rood, 1969). With this development the need for simple and efficient methods of preservation during transportation has become more necessary. Many perfusates in conjunction with hypothermia have been recommended for short-term organ preservation, but the important constituents of each and their optimal concentrations have not been clearly defined. Two solutions in particular have been widely used for organ preservation. Collins, Bravo-Shugarman, and Terasaki (1969a, b) recommended a solution with an intracellular electrolyte composition which also contained phenoxybenzamine. This solution allowed efficient storage for periods of up to 36 hours. Although this perfusate may be very useful clinically, the importance of each individual constituent is still not definitely known. Similarly organ preservation using the Gelin technique (Brunius, Bergentz, Ekman, Gelin, and Westberg, 1968; Sells and Pena, 1970) involves a three-stage perfusion before storage: first, the organ is flushed with lignocaine (0·5 per cent w./v.) and heparin; secondly, the organ is perfused with a Dextran-40-based solution; and, finally, a fructose-bicarbonate solution is infused into the organ. It is not clear yet whether each step is of importance, or whether one particular aspect is the crucial one in preservation of the organ. For these reasons we have developed the technipue reported here based on a small animal model, which has allowed us to investigate single factors and analyse the results statistically. In this way it is hoped that the important constituents can eventually be aggregated into an ideal method for short-term clinical organ preservation, the small animal model being used as a screening technique prior to assessment with the dog kidney.

Our aim has been to investigate initial perfusion with hypothermic storage as technically the simplest method available. This paper reports on several aspects of organ preservation. First, the development of a simple, reliable, and reproducible method for assessing organ storage, a preliminary report of which has already been published (Calman, Macpherson, Wood, and Bell, 1970; Calman and Bell, 1971). Secondly, basic perfusion characteristics such as *p*H of the infusion, organ weight, infusion volume, and colloid content of the infusion medium have been studied. Thirdly, substances thought to enhance organ preservation, such as insulin, chlorpromazine, phenoxybenzamine, and lignocaine, have been assessed both individually and in combination in an attempt to analyse in detail the perfusion solutions widely used at present. Finally, the solution so evolved has been compared with the Collins solution and the Gelin technique.

MATERIALS AND METHODS

Experimental Model.—The isolated, biologically perfused rat heart was chosen as the experimental model for a variety of reasons. First, the method is cheap and allows large numbers of animals to be used for subsequent statistical analysis; secondly, viability of the organ is easy to assess within a short period of time; and, thirdly, the donor heart can be rapidly removed, cannulated, and stored in a variety of ways.

After precise time intervals the heart can be revascularized by attaching it in the manner to be described to a second rat referred to as the recipient (*Fig.* 1). Outbred Wistar rats weighing 200–400 g. were used throughout the experiments and anaesthetized with intraperitoneal pentobarbitone (6 mg. per 100 g.). Storage was timed from the start of the thoracotomy, prior to the removal of the heart, until revascularization was achieved.

Preparation of the Donor Heart.—The donor heart is exposed and the superior and inferior vena cava ligated. Forceps are then passed into the transverse sinus and the aorta and pulmonary artery are separated and cannulated using 18-gauge polythene cannulae. Finally, the pulmonary veins are ligated *en masse*. The heart is then removed by dividing the superior and inferior vena cava and pumonary veins (*Fig.* 2). This procedure takes, on average, 5 minutes to complete but there are several important points to note. First, during the mass ligature of the pulmonary veins care should be taken not to ligate the atria inadvertently. Secondly, the coronary artery must not be occluded by the cannula and, in practice, this means tying the cannulae in place as far from the heart as possible. Thirdly, the heart must not be unduly manipulated.

Preparation of the Recipient.—The abdomen of the anaesthetized recipient rat is opened and the aorta and inferior vena cava cannulated with 18-gauge polythene cannulae (*Fig.* 1). In order to maintain the recipient in the best possible condition several factors require attention:—

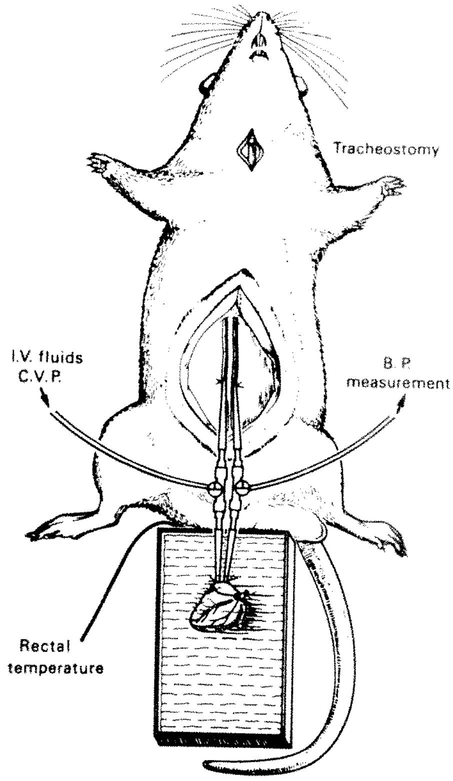

FIG. 1.—The preserved heart is revascularized by attaching it to cannulae previously inserted into the donor aorta and vena cava. The blood-pressure of the recipient is maintained by intravenous infusion of blood or saline.

a. Heparinization (500 U. per 100 g.) of the recipient is essential in order to prevent clotting in the cannulae.

b. Central venous pressure: The inferior vena caval catheter is connected to a T-piece, the long end of which is kept upright and open to the air. This serves as a central venous pressure monitor and allows transfusion of the recipient if this becomes necessary (*Fig.* 1).

c. Blood-pressure: Experience has shown that a systolic blood-pressure of at least 70 mm. Hg must be maintained in order to allow adequate perfusion of the donor heart. The blood-pressure is intermittently monitored via the aortic cannula using a three-way tap connected to a mercury manometer and is maintained as necessary by infusions of saline, dextran, or autologous rat blood.

d. Temperature: The recipient rat, lying exposed, very rapidly loses heat. Accordingly its temparature is maintained using a 100-W. light bulb. Rectal temperature is recorded during the procedure and kept at a constant level.

e. Respiratory function: The recipient, lying supine for periods of up to 4 hours, may retain secretions in the trachea. Tracheostomy is therefore performed so that secretions can be readily removed.

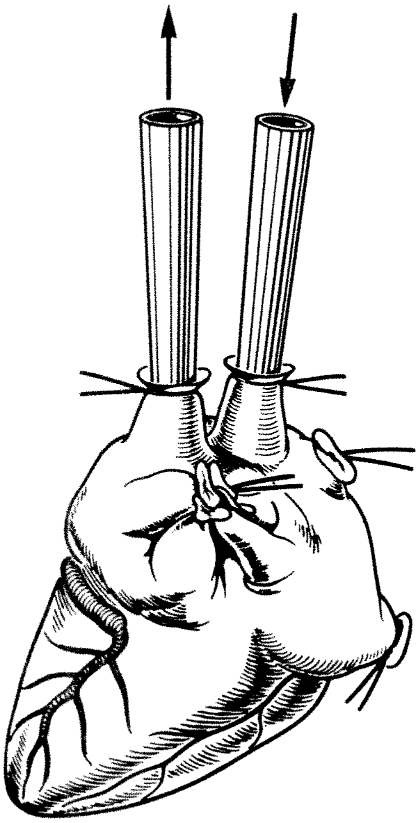

FIG. 2.—Cannulae are inserted into the aorta and pulmonary artery. When the heart is revascularized blood flows through the coronary system.

All of these factors are aimed at maintaining the circulation of the recipient rat so that error due to poor perfusion of the preserved heart can be eliminated.

Experimental Procedure.—Following removal, the donor heart is perfused and stored in the medium under investigation. It is then connected to the recipient in the manner shown in *Fig.* 1. Circulation of the donor heart is established for a period of 10 minutes, during which time the viability of the organ is assessed. It has been found over a series of 2000 rats that if the heart does not beat within 10 minutes it will not do so at all. On the other hand, if the heart beats within a few minutes of establishing the circulation and continues to do so for at least 10 minutes it will continue to beat for some hours afterwards. Using this technique, up to 20 donor hearts can be assessed using a single recipient, each heart being removed after a 10-minute observation period.

Criteria of Viability.—For a heart to be scored as viable all of the following criteria must be satisfied:—

1. There must be adequate perfusion of the donor heart. In practice this means that the blood-pressure of the recipient must be at least 70 mm. Hg.

2. The heart must beat and continue to beat for at least 10 minutes.
3. Venous return from the heart must be adequate.
4. Electrocardiographic evidence of electrical activity must be obtained.

RESULTS AND DISCUSSION

Establishment of the Experimental Model.—A previous report (Calman and Bell, 1971) has described the initial experimental work with this model and only the important features will be outlined here. The model was found to be reproducible and easy to use; large numbers of animals could be used in each experiment, making it possible for statistical analysis to be performed; the model was cheap to use and results could be rapidly obtained. One particularly useful feature was the sharp cut-off in viability (*Fig.* 3), making it possible to distinguish relatively small changes in the survival of groups of rat hearts treated in different ways. The model has, however, two main disadvantages. For clinical application of the results of this study in human kidney transplantation account has to be taken of the fact that the model utilizes the heart (a different organ) and the rat (a different species). It will be clear from the results presented, however, that though these differences must be recognized much useful information can still be obtained.

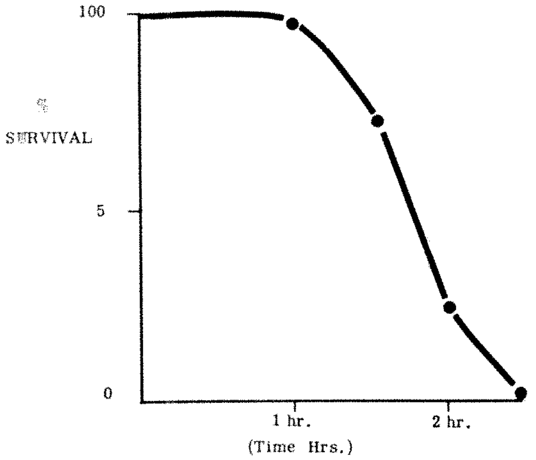

FIG. 3.—Illustrating the sharp cut-off in survival which occurs using the rat heart. The experiment shown was performed at 25° C. but similar results are obtained even if the storage time is prolonged by preservation at low temperatures.

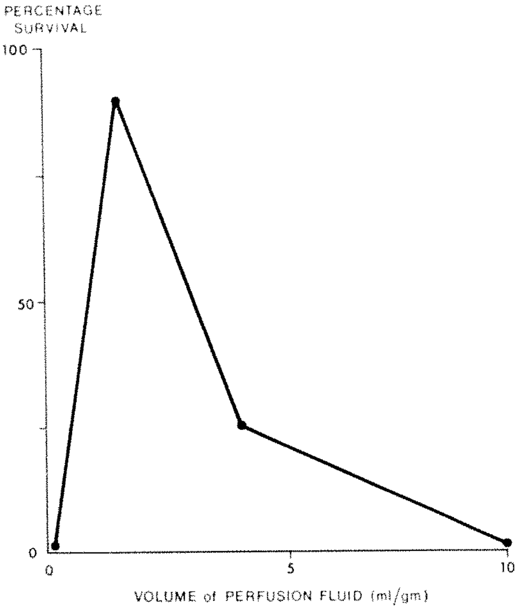

FIG. 4.—The viability of preserved hearts decreased with an increase in perfusion volume. Storage for 14 hours at 5° C.

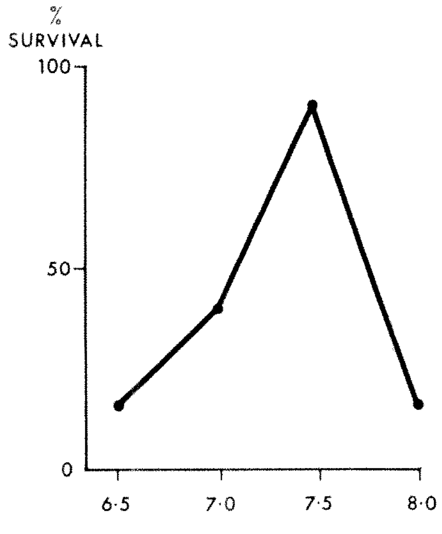

FIG. 5.—A *p*H of 7·5 at 5° C. was found to be optimal for organ storage, using a balanced salt solution with Rheomacrodex and a Tris buffer. Storage for 14 hours.

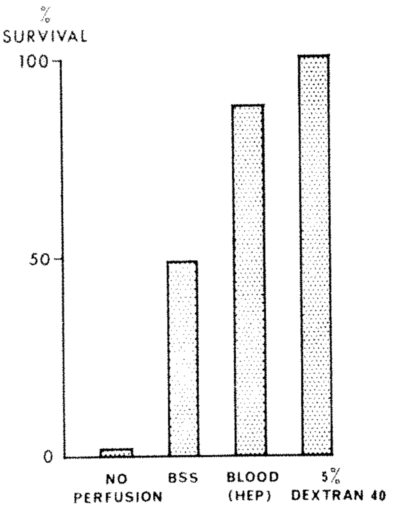

FIG. 6.—Dextran 40, 5 per cent, was found to be the best colloid for preservation of the rat heart. Storage for 10 hours at 5° C.

Throughout this paper results are expressed as the percentage survival of groups of rat hearts. In all cases these groups contained not less than 10 animals and usually 20. Thus each point or column in the results represents at least 10 animals.

Basic Perfusion Characteristics.—

1. *Rat Heart Weight.*—As an initial experiment the effect of rat heart weight was investigated. Two groups of animals, weighing 200 and 400 g. respectively, were studied using the same perfusate and perfusion was of the same volume per unit weight of the heart. The results showed that larger hearts of the heavier rats were easier to preserve ($P < 0{\cdot}02$). It may be that this is a phenomenon related only to the heart, since the myocardial cells enlarge with increase in organ size rather than increase in number. The experiment, however, is of importance in the design of experiments using the rat heart. In each series of experiments the rat weight was kept constant. This explains the differences recorded for the same solution between different experiments.

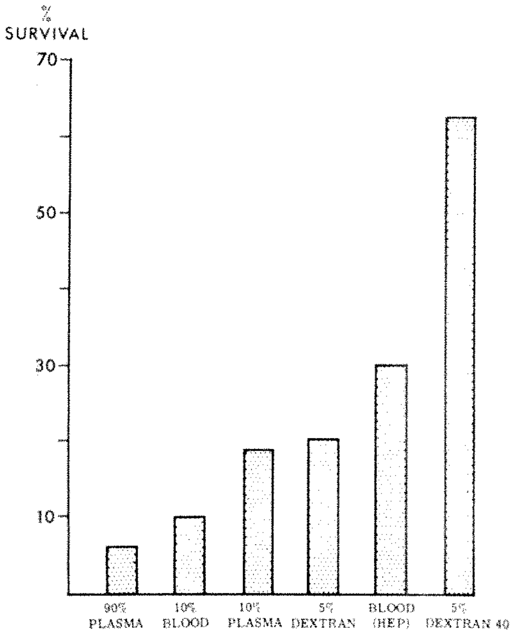

FIG. 7.—Extension of the storage time to 14 hours confirmed the superiority of 5 per cent Dextran 40 to preserve the rat heart.

2. *Effect of Infusion Volume.*—A series of rat hearts was perfused with different amounts of a standard solution. The results are shown in *Fig.* 4. Storage was at 5° C. for 14 hours. These results show that as the volume was increased over 2 ml. per g. the survival of the hearts decreased. These results have been confirmed using different storage times and solutions. It is likely that the damage is related to the washing out of essential substrates or ions (Keeler, Swinney, Taylor, and Uldall, 1966).

3. *The Effect of* pH.—Using a standard solution in which pH could be readily varied, the effect of pH on organ preservation was studied. The results are shown in *Fig.* 5. The optimum pH at 5° C. would appear to be 7·5. During this study the importance of temperature on the pH of the buffer was studied. It was found, for example, that if a Tris buffer (THAM) was used the pH varied by 0·5 unit over the temperature range 5–20° C. Thus the results could be significantly affected by the temperature at which the pH was standardized. A brief report on these results has been published (Calman, Quin, Macpherson, and Bell, 1971).

4. *The Effect of Colloid on Organ Preservation.*—The importance of different colloids on preservation of the rat heart was studied next. Groups of rat hearts were perfused with a variety of solutions each based on a balanced salt solution buffered with Tris-HCl (BSS). The results are shown in *Figs.* 6 and 7. These results show that the most suitable colloid is Dextran 40 and this is significantly better than other colloids ($P < 0{\cdot}05$). Dextran 40 has therefore been used as the colloid in all subsequent experiments.

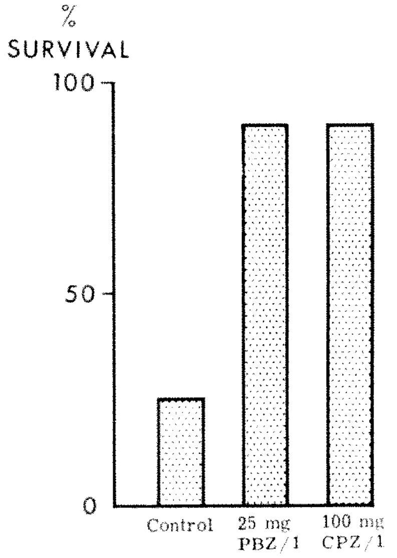

FIG. 8.—Phenoxybenzamine (PBZ) and chlorpromazine (CPZ) both improved organ survival significantly ($P < 0{\cdot}001$) when each was added to the preservation solution. Storage for 14 hours at 5° C.

At this stage in the study, therefore, a solution had been devised which would successfully preserve the rat heart for up to 14 hours. This solution contained a balanced salt content, buffered with Tris-HCl at pH 7·5 at 5° C., 1 g. glucose per litre, and 5 per cent Dextran 40.

Effect of Various Additives on Organ Preservation.—

1. *Phenoxybenzamine and Chlorpromazine.*—These compounds have been used in various preservation solutions because of their effect on the stabilization of lysosomes; they also may improve flow through the organ (Belzer, Reed, Pryor, Kountz, and Dunphy, 1970; Collins and others, 1969a, b; Fonkalsrud, Rangel, Byfield, Bruckner, Stevens, and Dinbar, 1969; Rangel, Bruckner, Byfield, Adomian, Dinbar, and Fonkalsrud, 1970). In the present experiments phenoxybenzamine was used at a concentration of

25 mg. per litre and chlorpromazine at 100 mg. per litre. The results are shown in *Fig.* 8. Both compounds significantly increase survival over that of the controls ($P < 0{\cdot}001$). There is thus good evidence that these compounds should be used in organ-storage solutions. One disquieting feature, however, is the recent report that phenoxybenzamine in dilute physiological solution may decompose rapidly (Bird, 1970).

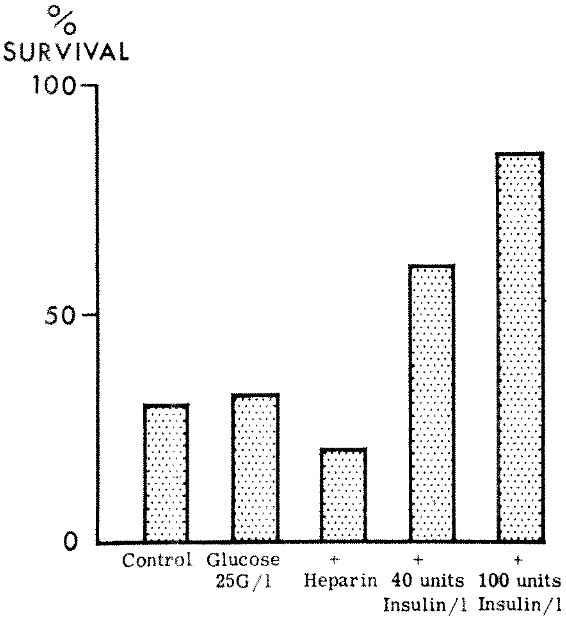

FIG. 9.—The addition of insulin (40 U. per litre) to the solution significantly increased organ survival ($P < 0{\cdot}01$). Preservation was further improved when the concentration of insulin was increased to 100 U. per litre ($P < 0{\cdot}001$). The addition of heparin or increasing the glucose concentration did not significantly increase survival. Storage for 14 hours at 5° C.

Table I.—COMPOSITION OF STANDARD SOLUTION

Sodium	140 mEq./l.
Potassium	13·0 mEq./l.
Calcium	1·6 mEq./l.
Magnesium	2·1 mEq./l.
Chloride	145 mEq./l.
Phosphate	10·0 mEq./l.
Glucose	1 g./l.
Insulin	100 U./l.

5 per cent Dextran 40
0·01 M Tris buffer, *p*H 7·5, at 5° C.
2 ml./g. of tissue infused
Storage temperature: 5° C.

2. *Effect of Heparin, Glucose, and Insulin.*—The addition of heparin (10,000 U. per litre), glucose (25 g. per litre instead of the 1 g. per litre used in the control solution), and insulin (40 and 100 U. per litre) was assessed in the rat heart model. Whereas the use of the increased glucose concentration or of heparin did not increase organ survival, the addition of either 40 or 100 U. of insulin per litre did significantly increase the survival ($P < 0{\cdot}01$ and $P < 0{\cdot}001$). The results are shown in *Fig.* 9.

3. *Combinations of Additives.*—The three compounds, phenoxybenzamine, chlorpromazine, and insulin, have been used in combination. There was no significant increase in survival over the results with each compound used alone. The only significant feature was that when phenoxybenzamine and chlorpromazine are used together there is a definite decrease in survival ($P < 0{\cdot}02$). On this evidence, therefore, there is no justification for using more than one of these compounds in a preservation solution.

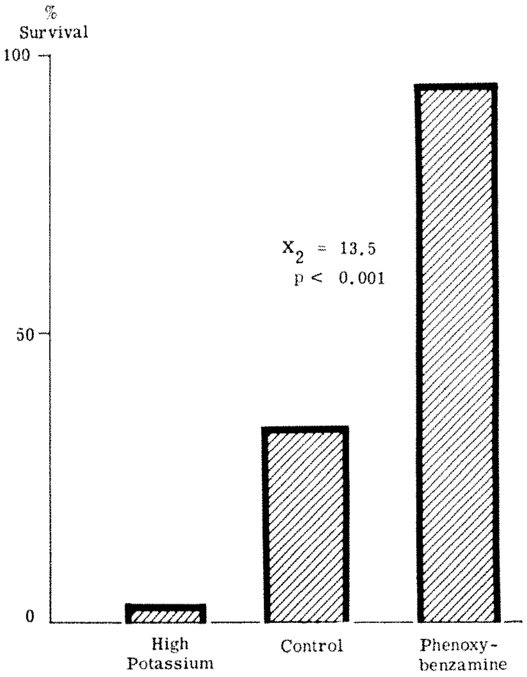

FIG. 10.—A potassium concentration of 115 mEq./l. significantly decreased organ survival ($P < 0{\cdot}01$), whereas phenoxybenzamine added to the control solution improved survival ($P < 0{\cdot}001$). Storage for 14 hours at 5° C.

At this point a standard solution was devised, the composition of which is shown in *Table I*. Insulin, at 100 U. per litre, was chosen rather than phenoxybenzamine or chlorpromazine because of its greater stability in solution. This solution will be referred to as the standard solution in subsequent experiments.

Comparison with Collins's and Gelin Techniques.—

1. *Comparison with Collins's C4 Solution.*—The standard solution was significantly better than the Collins's solution ($P < 0{\cdot}01$) for 16 hours' storage at 5° C. To find out why this was so the standard solution was modified to contain either a high potassium concentration (115 mEq./l.) or phenoxybenzamine. The results with phenoxybenzamine have already been described. When a high potassium concentration was used the results were significantly worse ($P < 0{\cdot}01$) (*Fig.* 10). Thus, the poor results with the Collins's solution may be related to the high potassium value. It is of interest that in a recent publication Collins, Hartley, and Clunie (1972) suggest that this concentration of potassium may in fact be too high. This has also been pointed out by other workers (Abouna, 1968; Calman and Bell, 1971).

2. *Comparison with the Gelin Technique.*—When the standard solution was compared with the Gelin

echnique (*Fig.* 11) it was found to be an inferior organ-preservation solution ($P < 0{\cdot}01$). This was at first surprising since the *p*H values of the three basic solutions of the Gelin technique are outside the physiological range, being *p*H 6, 6, and 8 respectively. An analysis was then made of the component parts of the Gelin technique by assessing each part separately in ombination with the standard solution. The results are shown in *Fig.* 12. When the lignocaine flush (0·5 per cent w./v.) was used before the standard solution or when lignocaine (2 per cent w./v.) was added to the standard solution there was a significant increase in survival ($P < 0{\cdot}05$). On the other hand, if fructose/bicarbonate (10 per cent fructose/1·4 per cent bicarbonate in equal volumes) was used there was a significant decrease in survival ($P < 0{\cdot}01$).

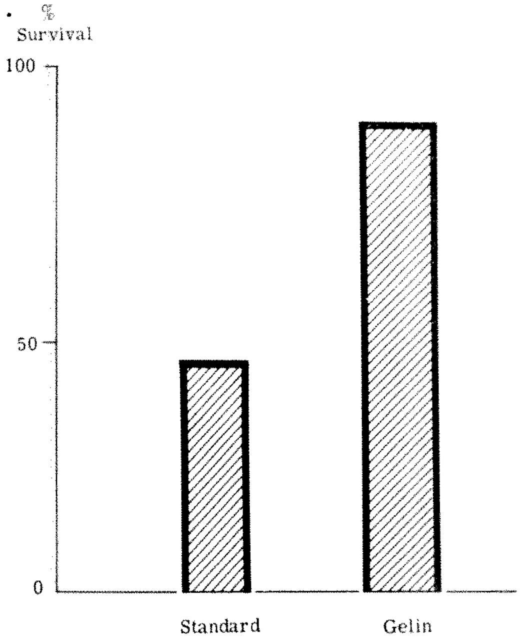

Fig. 11.—The Gelin technique was found to be significantly better ($P < 0{\cdot}01$) than the standard solution. Storage for 16 hours at 5° C.

Table II.—Composition of Modified Standard Solution

Solution 1

Sodium	140 mEq./l.
Potassium	13·0 mEq./l.
Calcium	1·6 mEq./l.
Magnesium	1·6 mEq./l.
Chloride	145 mEq./l.
Phosphate	10 mEq./l.
Glucose	1 g.

0·01 M Tris buffer, *p*H 7·5, at 5° C.
0·5 ml./g. of tissue infused

This is made up to 750 ml. and 60-ml. aliquots are taken. To these aliquots 20 ml. of 2 per cent lignocaine are added, giving a final concentration of 0·5 per cent lignocaine; 5000 U. of heparin are then added

Solution 2

As in standard solution (*Table I*).
25 ml. of 2 per cent lignocaine are added per litre.
1·5 ml./g. of tissue infused

With this information a modified standard solution was then devised (*Table II*) based on the standard solution, incorporating the 0·5 per cent lignocaine flush in a buffered solution and 2 per cent lignocaine, but without the fructose/bicarbonate. The results show that this solution (*Fig.* 13) is significantly better ($P < 0{\cdot}05$) than the Gelin technique. It is important to note that the storage time has been prolonged over the previous experiment and this accounts for the

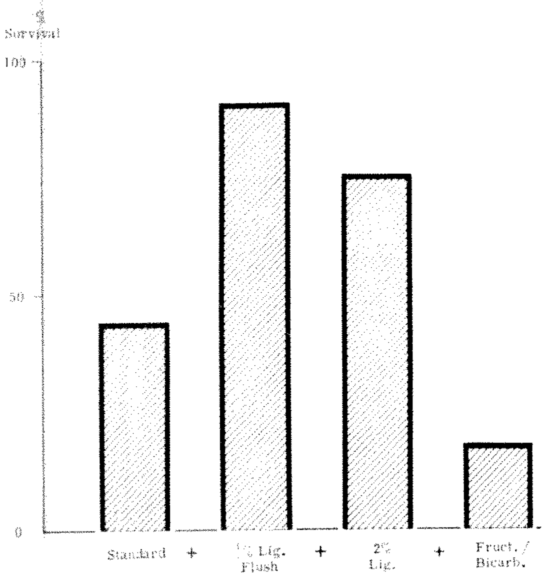

Fig. 12.—Fructose/bicarbonate added to the standard solution decreased organ survival. In contrast, a 0·5 per cent lignocaine flush prior to infusion or the incorporation of lignocaine (2 per cent) in the solution significantly enhanced survival ($P < 0{\cdot}05$). Storage for 16 hours at 5° C.

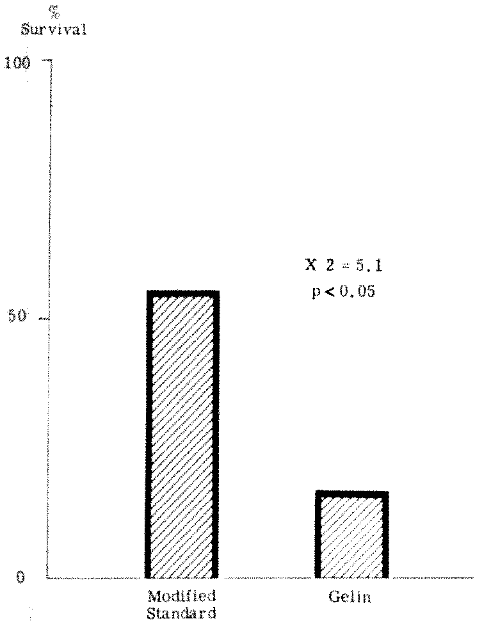

Fig. 13.—The modified standard solution (infusion preceded by 0·5 per cent lignocaine flush with 2 per cent lignocaine in the preservation solution) was superior to the Gelin technique ($P < 0{\cdot}05$) with 17 hours' storage at 5° C.

difference in survival rate from the previous results (*Fig.* 11).

3. *Effect of High Concentrations of Magnesium.*—Several workers have suggested that a high magnesium concentration is important, both in the dog kidney (Collins and others, 1972) and the rat heart (Kamiyama, Webb, and Ecker, 1970). To assess this the second part of the modified standard solution was altered to contain 60 mEq. magnesium sulphate per litre with a corresponding reduction in the sodium concentration (*Table III*). When this solution was compared with the modified standard solution it was found to be significantly better ($P < 0{\cdot}05$).

Table III.—COMPOSITION OF HIGH-MAGNESIUM SOLUTION

Solution 1

As in *Table II.*
0·5 ml. per g. of tissue infused

Solution 2

Sodium	70 mEq./l.
Potassium	13·0 mEq./l.
Calcium	1·6 mEq./l.
Magnesium*	60 mEq./l.
Chloride	70 mEq./l.
Phosphate	10 mEq./l.
Glucose	1 g./l.
Insulin	100 U./l.

5 per cent Dextran 40
0·01 M Tris buffer, *p*H 7·5, at 5° C.
2 per cent lignocaine: 25 ml./l.

* As magnesium sulphate.
1·5 ml./g. infused.

CONCLUSIONS

The rat heart is a convenient model for the study of organ preservation. The physiology and biochemistry of this organ have been extensively investigated and the electrocardiographic patterns in various disease states elucidated (Schever and Stezoski, 1968; Cooper, 1969). The rat heart has also previously been used in organ-preservation investigations and the effects of both freezing and various perfusates studied (Karow, Webb, and Stapp, 1965; Webb, Dodds, Unal, Karow, Cook, and Daniel, 1966; Ancona, Frasson, Perracchia, Tonini, and Tremolada, 1970). The method used here is unique in that the viability is assessed after biological perfusion. This has theoretical advantages in that the donor heart is perfused with blood at the correct temperature and oxygen content and with pulsatile flow. In addition, the technique is simple, rapid, and allows statistical evaluation of the results. Viability after storage has been confirmed in this investigation by heterotopic transplantation of the rat heart using the method of Ono and Lindsay (1969). Prolonged survival of these preserved transplants in inbred strains of Wistar rats confirms that our criteria for viability are acceptable.

In this paper the isolated, biologically perfused ra heart has been used to assess a number of aspects o organ preservation. The aim of the present study wa to analyse the constituents of various preservatio media and to develop the most suitable preservatio solution for organ storage. Such a technique has bee developed using a 0·5 per cent lignocaine flus followed by a Dextran-40-based, high-magnesiu solution containing lignocaine and insulin. Sub sequently this solution will be tested with the do kidney, an essential step for validation of the mode prior to its use in humans.

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THE EFFECT OF ISCHAEMIC INJURY ON KIDNEYS PRESERVED FOR 24 HOURS BEFORE TRANSPLANTATION

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SUMMARY

Kidneys have been preserved for 24 hours by three methods—continuous hypothermic perfusion with plasma protein fraction (P.P.F.), simple ice storage using the method of Collins, Bravo-Shugarman, and Terasaki (1969), and a combination of simple ice storage followed by continuous perfusion. Prior to preservation the kidneys were subjected to warm ischaemic intervals varying from 0 to 180 minutes.

Kidneys preserved without warm ischaemia functioned immediately whichever method was used. Kidneys preserved by perfusion after up to 60 minutes of warm ischaemia returned to normal function; kidneys preserved by Collins's method did not function after ischaemic injury.

The period of storage of ischaemically injured kidneys initially preserved by Collins's method can be extended to 24 hours by subsequent continuous perfusion, but the results are not as good as with perfusion alone. A fall in perfusate pH was a reliable indication that kidneys would not function after 24 hours' storage.

SUCCESS in transplanting human cadaver kidneys depends on good tissue typing and on the ability to distribute the kidneys to the best-matched recipients. These two factors lose their value if the kidney cannot be sufficiently well preserved to ensure immediate function, since even short periods of impaired renal function may mask early rejection which may then progress unrecognized to beyond control.

Twenty-four-hour renal preservation with immediate return of function has often been achieved in the laboratory (Belzer, Ashby, and Dunphy, 1967; Collins, Bravo-Shugarman, and Terasaki, 1969; Scott, Morley, and Swinney, 1969). These laboratory results are not easily applied to the clinical situation because human cadaver kidneys have been exposed to injury whereas the kidneys of laboratory animals are fresh.

Warm ischaemia is an important cause of injury, the severity of which increases with the duration of ischaemia. The warm ischaemic interval is defined as that period between circulatory arrest and effective cooling of the donor organ. In human cadaveric renal transplantation such an interval is unavoidable.

The duration of warm ischaemia compatible with 24-hour preservation is not known; neither is it known which of the methods available best preserves ischaemically injured kidneys.

The aim of the present work was to investigate the effect of warm ischaemic injury on kidneys preserved for 24 hours either by simple ice storage (Collins and others, 1969) or by continuous perfusion with oxygenated plasma-protein fraction (Johnson, Anderson, Flear, Murray, Swinney, and Taylor, 1971).

Since facilities for continuous perfusion are not generally available in this country the practicability of combining short periods of ice storage followed by 24-hour perfusion has also been studied.

During perfusion the physical and biochemical characteristics of the kidney were recorded in an attempt to predict subsequent function after reimplantation.

MATERIALS AND METHODS

Adult trail hounds, weighing between 15 and 30 kg., were used. Each dog was anaesthetized with Nembutal, the trachea was intubated, and anaesthesia maintained with nitrous oxide and oxygen.

Table I.—C4 SOLUTION (COLLINS AND OTHERS, 1969)

KH_2PO_4	2·05 g./l.
$K_2HPO_4.3H_2O$	9·70 g./l.
KCl	1·20 g./l.
$NaHCO_3$	0·84 g./l.
$MgSO_4.7H_2O$	7·38 g./l.
Procaine HCl	0·10 g./l.
Heparin	5000 I.U./l.
Phenoxybenzamine	0·025 g./l.
Glucose	25 g./l.
pH	7·0 at 25° C.

Phenoxybenzamine was added immediately before use; when the cloudiness disappeared glucose and magnesium sulphate were added as 50 per cent solutions. C4 was used only if the solution was clear and free from crystals.

Nephrectomy.—The right kidney was exposed through a loin incision. The kidney was handled as little as possible; the renal artery and vein were clamped close to their origins and divided. Kidneys being exposed to a warm ischaemic interval were then allowed to remain undisturbed in the peritoneum for periods up to 180 minutes.

Initial Cooling.—After removal, the kidneys were immersed in iced saline slush, the artery and vein were cannulated, and the kidneys were washed through with cold solution by gravity infusion from 150 cm. During this initial wash-out rate of flow was measured by collecting consecutive minute samples of the venous effluent in separate pots.

Wash-out Solutions.—

1. C4 *Solution.*—This solution was made up as described by Collins and others (1969); its final composition is shown in *Table I.* The Collins's method of ice storage simply comprised washing the kidneys out with cold C4 solution which approximates in composition to intracellular fluid and then placing them in a bag containing C4 solution in a refrigerator at 4° C.

2. *Saline Wash-out.*—Kidneys being prepared for continuous perfusion were washed out with sodium chloride (0·94 per cent w./v.) containing phenoxybenzamine (2·5 mg. per cent w./v.) and procaine hydrochloride (2·5 mg. per cent w./v.).

After wash-out the venous cannula was removed.

Perfusion Apparatus.—(This apparatus was designed and built in the Department of Surgery, University of Newcastle upon Tyne, by Mr. D. F. Scott and Mr. W. G. Leslie.) The apparatus comprises a Perspex kidney box, a disk oxygenator, a Watson-Marlow roller pump, and a Churchill heat-exchange unit (*Fig.* 1). The perfusion fluid recirculates through polyvinylchloride tubing. A manometer, a bubble trap, and a filter are included in the circuit.

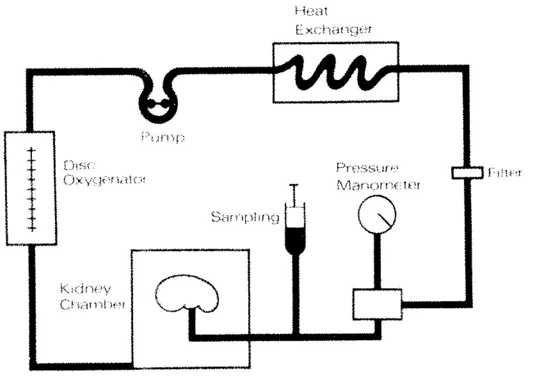

FIG. 1.—The perfusion circuit designed and built by Mr. W. G. Leslie and Mr. D. F. Scott in the Department of Surgery, University of Newcastle upon Tyne.

Table II.—ADJUSTMENTS TO PLASMA-PROTEIN FRACTION

P.P.F.$_{(1)}$ (Normal $[K]^+$)		P.P.F.$_{(2)}$ (High $[K]^+$)	
$NaHCO_3$	4 mEq./l.	H_2O	1 : 4
KCl	2 mEq./l.	$KHCO_3$	15 mEq./l.
*p*H 7·05–7·15		*p*H 7·55–7·65	

MgCl	2 mEq./l.
Insulin	40 I.U.
Glucose	150 mg. per cent
Hydrocortisone	100 mg.
Ampicillin	500 mg.

Table III.—FINAL COMPOSITION OF P.P.F.$_{(1)}$ AND P.P.F.$_{(2)}$

	P.P.F.$_{(1)}$	P.P.F.$_{(2)}$
Na^+	140–160 mEq./l.	125–135 mEq./l.
K^+	4·5 mEq./l.	15–20 mEq./l.
Mg^{++}	5–7 mg. per cent	5–7 mg. per cent
Ca^{++}	4·4 mg. per cent	4·4 mg. per cent
Cl^-	100–110 mEq./l.	100–110 mEq./l.
HCO_3^-	20–25 mEq./l.	25–30 mEq./l.
Total protein	4·3–4·5 g. per cent	3·4–4·0 g. per cent
Albumin	4·3–4·5 g. per cent	3·4–4·0 g. per cent
Glucose	130 mg. per cent	150 mg. per cent
Fat	15–20 mg. per cent	10–15 mg. per cent
Osmolality	300 m.osmol./l.	275 m.osmol./l.

Perfusion Solution.—Plasma-protein fraction (P.P.F.) was used. Its composition was modified in two ways to make two solutions: P.P.F.$_{(1)}$ which resembles serum, and P.P.F.$_{(2)}$ which has an increased potassium concentration in an attempt to minimize the cellular leakage of this electrolyte which has been shown to occur at low temperatures (Keeler, Swinney, Taylor, and Uldall, 1966). An evaluation of P.P.F. as a perfusion solution has previously been published (Johnson, Anderson, Flear, Murray, Swinney, and Taylor, 1972). The preparation and final compositions of P.P.F.$_{(1)}$ and P.P.F.$_{(2)}$ are shown in *Tables II* and *III*.

During perfusion the oxygen tension was maintained between 200 and 400 mm. Hg by using 95 per cent oxygen and 5 per cent carbon dioxide. The flow rate was maintained at 1 ml. per g. of kidney per minute. Flow was only adjusted if a systolic pressure of 40 mm. Hg could not be sustained.

The temperature of the perfusion fluid was adjuste to give a renal core temperature of 6° C.

Measurements.—

Perfusion pressure was continuously recorded on Recklar D.B.G.M. air displacement manometer.

*Oxygen tension and p*H were measured on fres samples using an Astrup Blood Micro System B.M.S. (Radiometer, Copenhagen); *p*H values were correcte to 37° C. Lactic dehydrogenase (L.D.H.) wa measured by using a Boehringer T.LAC Biochemic test kit combination.

Renal core temperature was measured with a needl probe, Nihon Kohden MGA III 219.

Reimplantation.—After 24-hour storage th kidney was reimplanted in the dog's pelvis as an auto graft. The renal vein was anastomosed end to side t the common iliac vein and the renal artery wa anastomosed end to end to the external iliac artery The ureter was reimplanted into the base of th bladder through a short submucous tunnel.

Contralateral nephrectomy was performed eithe immediately or on the nineteenth day.

Following contralateral nephrectomy, daily measurements of plasma creatinine and plasma urea were mad until they returned to normal or until the dog die All surviving dogs were killed at 3 months.

RESULTS

Group 1: Kidneys preserved for 24 Hour *without* Warm Ischaemia.—

a. Simple Ice Storage (Collins's Method), wit Immediate Contralateral Nephrectomy.—Five kidney were preserved in this manner; warm ischaemic inter vals were very short, not exceeding 3 minutes. Eac kidney became pink on reimplantation and all 5 mad urine immediately. Following immediate contralater nephrectomy, all 5 kidneys rapidly assumed norm function (*Fig.* 2 A). The highest plasma creatinine wa 3 mg. per cent, and in each instance the plasma creatinine level was less than 2 mg. per cent by th third postoperative day.

Table IV.—RESULTS OF 24-HOUR PRESERVATION B COLLINS'S TECHNIQUE FROM THE DAY AFTER CONTRA LATERAL NEPHRECTOMY

WARM ISCHAEMIA TIME	NO. OF DOGS	NO. OF SURVIVORS	PERCENTAGE SURVIVING	MEAN NO. OF DAYS TO REACH BIO-CHEMICAL NORMALIT	
				Creatinine	Urea
Zero	5	5	100	5	8
30 minutes	8	2	25	28	—
40 minutes	2	0	0	—	—

b. Continuous Perfusion with P.P.F. at 6° C., wit Immediate Contralateral Nephrectomy.—Five kidney were preserved by this method; again contralater nephrectomy was immediate. All 5 kidneys becam pink and made urine at reimplantation. Four kidney rapidly assumed normal function (*Fig.* 2 B). Th highest post-reimplantation plasma-creatinine lev was 2·8 mg. per cent. The remaining dog was foun to have a completely obstructed ureter; this wa treated by reimplantation on the third postoperativ day; subsequent return to normal function wa rapid.

Group II: Kidneys preserved for 24 Hours after 30 to 40 Minutes of Warm Ischaemia.—

a. Simple Ice Storage (Collins's Method), with Delayed Contralateral Nephrectomy (Table IV).—Ten kidneys had 30–40 minutes of warm ischaemia; only 2 functioned sufficiently to sustain life even after contralateral nephrectomy had been delayed until the nineteenth postoperative day. The kidneys generally had a bluish hue when the circulation was opened and though they all eventually became pink only 1 made urine during reimplantation.

Neither of the 2 kidneys which functioned after warm ischaemia returned completely to normal function although 1 of the dogs had a plasma creatinine of less than 2 mg. per cent after 30 days (*Fig.* 3).

In each of the 8 failures the dog was moribund within 5 days of delayed contralateral nephrectomy. Histology of the 2 survivors showed numerous areas of cortical fibrosis with hypertrophy of the residual tubules. The 8 failures all had cortical necrosis.

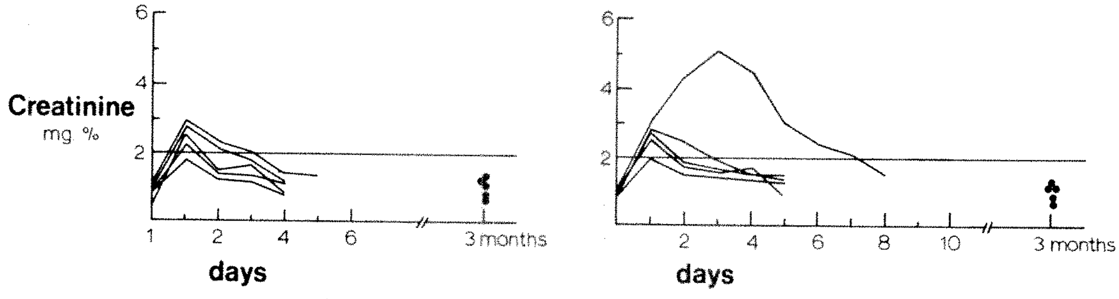

FIG. 2.—Kidneys preserved for 24 hours without warm ischaemia. A, By Collins's method. B, By continuous hypothermic perfusion.

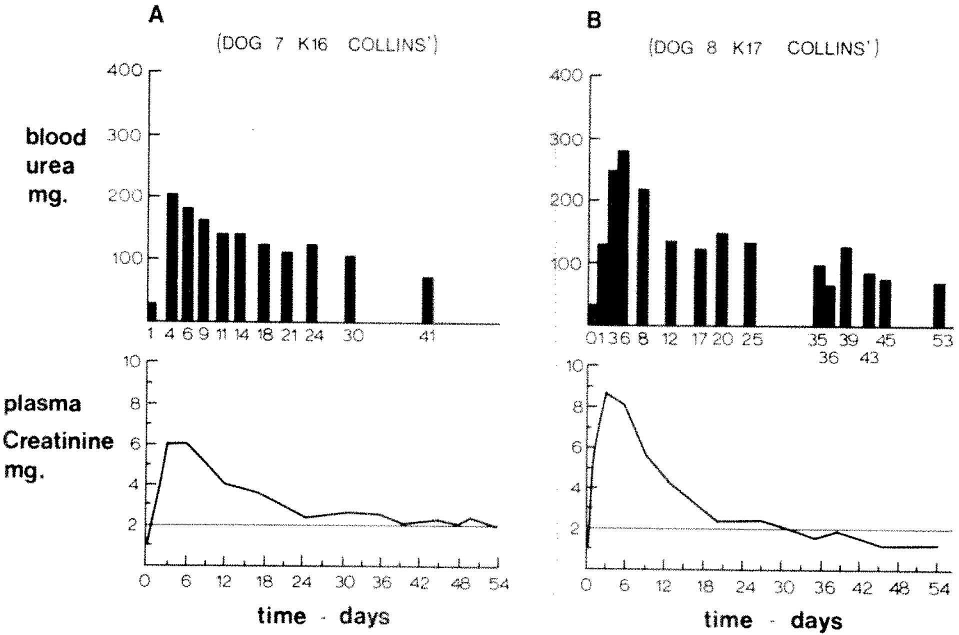

FIG. 3.—Kidneys preserved by Collins's method after 30 minutes of warm ischaemia, with delayed contralateral nephrectomy.

b. Continuous Perfusion with P.P.F.$_{(1)}$ *at 6° C., with Delayed Contralateral Nephrectomy (Table V).*—Seven kidneys had up to 40 minutes of warm ischaemia; all returned rapidly to normal function after delayed contralateral nephrectomy. The plasma-creatinine levels commonly rose during the first 3 days; the highest value was 4·6 mg. per cent, but in every instance the plasma-creatinine level was normal by the seventh day.

Table V.—RESULTS OF 24-HOUR PRESERVATION USING P.P.F.$_{(1)}$, WITH DELAYED CONTRALATERAL NEPHRECTOMY

WARM ISCHAEMIA TIME	NO. OF DOGS	NO. OF SURVIVORS	PERCENTAGE SURVIVING	MEAN NO. OF DAYS TO REACH BIO-CHEMICAL NORMALITY	
				Creatinine	Urea
15	2	2	100	< 5	< 12
30	5	5	100	10	25
40	2	2	100	10	25
60	3	2	66·6	8	25
100	1	—	—	—	—
180	3	—	—	—	—

c. Continuous Perfusion with P.P.F.$_{(2)}$ at 6° C., with Immediate Contralateral Nephrectomy.—Six kidneys were preserved by continuous hypothermic perfusion with P.P.F.$_{(2)}$ at 6° C. The kidneys all became pink on reimplantation. Five made urine immediately. Though all 6 dogs survived immediate contralateral nephrectomy postoperatively plasma-creatinine levels rose to high peaks (maximum, 12 mg. per cent; *Fig.* 4) and there was a delay of up to 14 days before all had returned to normal function.

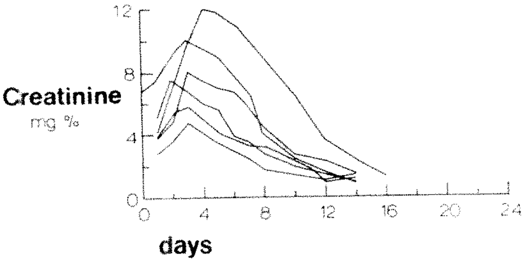

FIG. 4.—Kidneys preserved by continuous perfusion for 24 hours after 30–40 minutes of warm ischaemia, with immediate contralateral nephrectomy.

Recovery of function was heralded by a marked increase in urinary output between the second and fourth postoperative days. Two dogs became quite dehydrated as a result of this diuresis and required support with subcutaneous Ringer's lactate.

Group III: Kidneys preserved for 24 Hours after 60–180 Minutes of Warm Ischaemia (*Table V*).—All the kidneys in this group were preserved by continuous perfusion with P.P.F.$_{(1)}$ at 6° C. Three kidneys received 60 minutes of warm ischaemia; all 3 became pink on revascularization but none made urine. Two dogs survived delayed contralateral nephrectomy and their transplanted kidneys resumed completely normal function. The third dog was killed on the fifth postoperative day. Histology of the kidney showed cortical necrosis.

Four kidneys had warm ischaemic intervals of 100–180 minutes. None of these functioned and all 4 had cortical necrosis.

Group IV: Kidneys preserved for a Short Preliminary Period in Ice followed by Continuous Hypothermic Perfusion with P.P.F.$_{(2)}$ to 24 Hours.—

a. No Warm Ischaemia.—Three kidneys were stored in ice for 6 hours and then removed from ice and placed on the perfusion circuit and perfused for a further 18 hours (*Fig.* 5). All 3 kidneys supported life following immediate contralateral nephrectomy, but the postoperative plasma-creatinine levels were much higher than in those kidneys preserved without warm ischaemia by perfusion alone or by ice storage alone. The highest recorded creatinine was 6 mg. per cent.

b. Thirty Minutes' Warm Ischaemia (*Table VI*).—

i. Four kidneys were stored for 3 hours in ice prior to perfusion. Three were immediately able to sustain life; the fourth dog died of renal failure.

ii. Eight kidneys were stored in ice for 6 hours prior to perfusion; 5 were immediately able to support life. Three dogs died of renal failure. The renal function in 1 of the survivors had not returned to normal even at 3 months (plasma creatinine, 2·8 mg. per cent; plasma urea, 110 mg. per cent).

The remaining 4 dogs all returned to biochemical normality. The highest plasma creatinine was 14 mg. per cent and the longest duration of abnormal function was 17 days.

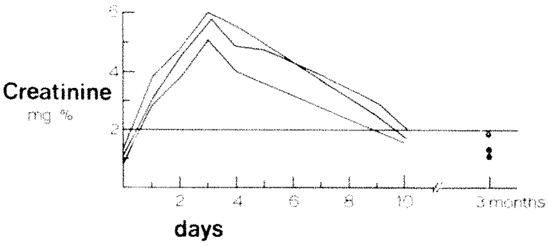

FIG. 5.—Kidneys preserved for 24 hours by the combined method of 6 hours of ice storage followed by 18 hours of perfusion without warm ischaemia, with immediate contralateral nephrectomy.

Table VI.—RESULTS OF 24-HOUR PRESERVATION AFTER 30 MINUTES' WARM ISCHAEMIA, WITH IMMEDIATE CONTRALATERAL NEPHRECTOMY

GROUP	NO. OF DOGS	NO. OF SURVIVORS	MEAN NO. OF DAYS TO REACH BIOCHEMICAL NORMALITY	
			Creatinine	Urea
Perfusion alone	6	6	7	23
3 hours in ice	4	3	9·6	25
6 hours in ice	8	5	9·9	25

Flow Characteristics.—

1. *Rate of Initial Wash-out.*—The time required to flush 200 ml. of fluid through the kidney by gravity infusion from 150 cm. increased progressively with the warm ischaemic interval, indicating an increase in renal vascular resistance (*Fig.* 6). Blood-staining of the venous effluent continued throughout the entire wash-out period in kidneys subjected to prolonged periods of warm ischaemia, whereas the venous effluent cleared rapidly when the warm ischaemic interval was short.

2. *Perfusion Pressure* (*Figs.* 7, 8).—The perfusion pressure of kidneys injured by 30–40 minutes of warm ischaemia was raised during the first hour when compared with uninjured kidneys (*Fig.* 7). This difference, however, failed to reach statistical significance. All the kidneys in these two groups functioned normally on reimplantation. When the perfusion pressures of those kidneys which failed to function on reimplantation were compared with the normal range (*Fig.* 8), it was found that only the initial reading was significantly different from normal ($0{\cdot}1 < P > 0{\cdot}05$); thereafter the pressure fell rapidly into the normal range.

Change in Weight.—All the kidneys gained weight during perfusion. The range of weight-gain for those kidneys which functioned immediately was 4–22 per cent. The range of weight-gain for those kidneys which failed to function was 5–24 per cent.

Change in Perfusate *p*H.—Kidneys which nctioned immediately after reimplantation were mpared with those which failed to function even en contralateral nephrectomy was delayed (*Fig.* 9). here was a highly significant difference between the o groups especially during the first hour of perfuon. Those kidneys which had been subjected to olonged warm ischaemia (1 hour or more) exhibited profound drop in *p*H during the first hour from 24 to 6·97 ± 0·04, whereas those kidneys which nctioned immediately exhibited only a very small ll in *p*H during the first hour from 7·25 to 7·15 ± 0·04. his difference was statistically significant (*t* = 4·3, '> 0·001).

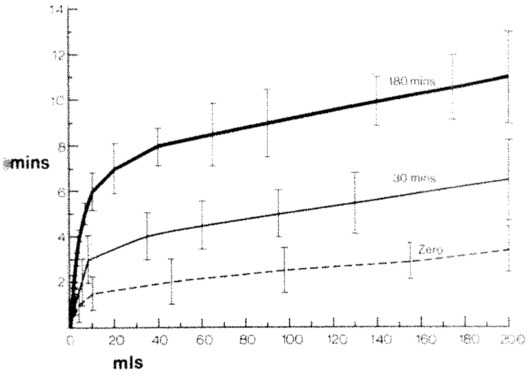

FIG. 6.—Rate of venous outflow during initial wash-out. ▬▬, 180 minutes of warm ischaemia (mean of 3). ——, 30 minutes of warm ischaemia (mean of 10). - - -, No warm ischaemia (mean of 10). All the results are ± 2 S.E.

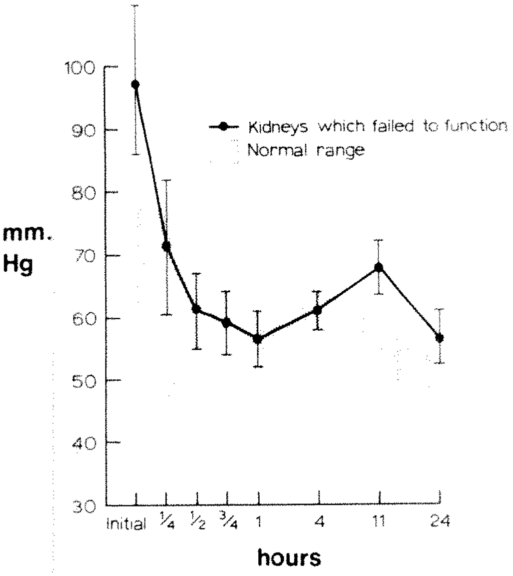

FIG. 8.—Change in perfusion pressure over 24 hours.

After the first hour the *p*H rose in both groups: in e survivor group the *p*H returned to normal at 24 ours; in the failure group the *p*H plateaued at 6·99 ± ·05 and then fell again to 6·9 ± 0·1 at 24 hours.

Perfusate L.D.H.—L.D.H. accumulation in the erfusion fluid was compared for those kidneys which functioned immediately and those which failed to function at all. The range of L.D.H. among the survivors was 190–512 I.U. compared with 376–419 I.U. for the failures. Although the failures were always in the 300–400 range there was no significant difference between the two groups.

DISCUSSION

When a warm ischaemic interval was excluded canine kidneys were preserved equally well by either simple ice storage using Collins's method or continuous perfusion with plasma-protein fraction. Postoperative plasma-creatinine levels followed very similar patterns and in neither group did they rise above 3 mg. per cent. These results confirm the findings of other worker in the field (Belzer and others, 1967; Collins and others, 1969; Collste, Bjorken, Collste, and Groth, 1970; Liu, Humphries, Russell, Stoddard, and Moretz, 1971).

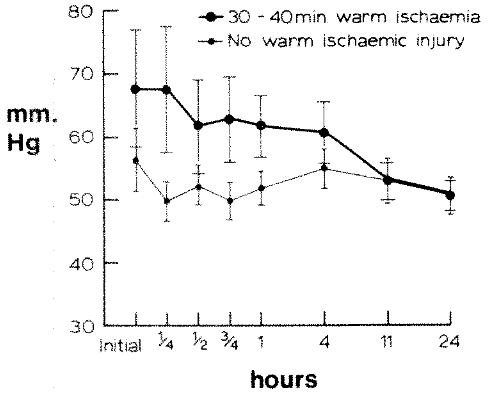

FIG. 7.—Change in perfusion pressure over 24 hours.

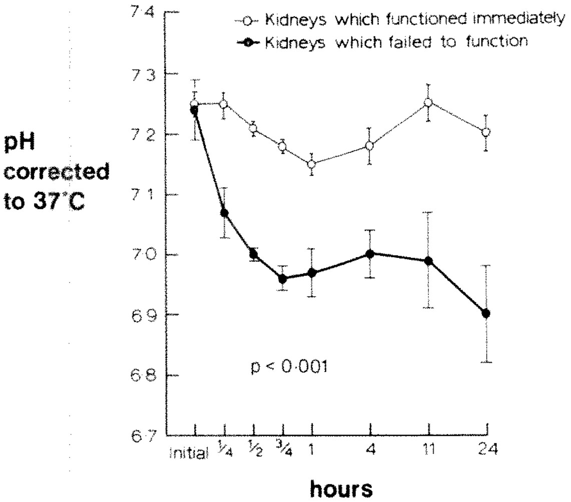

FIG. 9.—Changes in perfusate *p*H over 24 hours.

The introduction of a warm ischaemic interval of 30 minutes produced a very significant difference in the results obtained from these two preservation methods. Kidneys preserved by Collins's method either failed to function completely or were just able to sustain life even when protected by delayed contralateral nephrectomy, whereas using continuous perfusion kidneys returned to normal function after up to 60 minutes of warm ischaemia when protected by delayed contralateral nephrectomy. A warm ischaemic interval of 40 minutes was compatible with immediate life-sustaining function after 24-hour perfusion.

Simple ice storage by Collins's method followed by continuous perfusion can be used to give 24-hour preservation with immediate return of function in kidneys injured by 30 minutes of warm ischaemia. However, the quality of immediate postoperative renal function is not as good as when kidneys are preserved by perfusion alone, neither are the results so reliable. After 6 hours' ice storage only 5 out of 8 kidneys could sustain life and only 4 of the 5 returned completely to normal function. The duration of ice storage would appear to be critical; when it exceeds 6 hours, delayed return of function is the best result that can be expected.

What then is the effect of a warm ischaemic interval and how can it produce such a radical difference between two preservation methods which are well established for storing healthy kidneys?

We have observed that as the warm ischaemic interval increased there was a proportional increase in renal vascular resistance as evidenced by a diminished rate of flow of the initial wash-out solution, higher initial perfusion pressures, and increased blood-staining of the perfusate. There was also a fall in *p*H during the first hour of perfusion; this was most profound in those kidneys subjected to prolonged warm ischaemic injury. None of these kidneys functioned subsequently and the changes in perfusate *p*H that they exhibited differed very significantly from the *p*H changes of both fresh and ischaemically injured kidney that did function immediately ($t = 4 \cdot 3$, $P < 0 \cdot 001$). A fall in the surface *p*H of rabbit kidneys exposed to warm ischaemic injury has previously been reported (Dmochowski, Couch, Kempf, and Appleton, 1966; Couch, Maginn, Middleton, Appleton, and Dmochowski, 1967; Couch and Middleton, 1968), but because in most perfusion systems it is necessary to adjust the *p*H continuously in order to maintain stability of the perfusion solution a fall in the perfusate *p*H has not previously been correlated with function after transplantation.

The absence of oxygen precludes the utilization of the citric acid cycle and forces the renal cells to metabolize glucose in such a manner that only 8 per cent of the total potential energy available through the oxidation of glucose is released (White, Handler, and Smith, 1964). Without continuous perfusion marked suppression of aerobic metabolism occurs within minutes (Wilhelmi, Russel, Engle, and Long, 1945). The maintenance of cellular volume is an active energy-consuming process which is dependent on the active extrusion of sodium at the cell membrane (Leaf, 1959). Lack of energy causes pump failure which leads to accumulation of sodium and water in the cells and cellular swelling. The accumulation of lactic acid and the other by-products of anaerobic metabolism leads to a fall in *p*H which causes further cellular swelling. Cellular swelling and metabolic acidosis account for the increased vascular resistanc and for the profound fall in perfusate *p*H.

Simple hypothermia by suppressing metabolis also causes some cellular swelling; provided that th kidney is cooled rapidly this swelling is usuall minimal, but in the presence of established ischaem injury further periods of cold anoxia may have cumulative effect, whereas continuous hypotherm perfusion with an oxygenated energy-rich solutic should arrest and reverse anoxic injury by allowir aerobic metabolism to recommence even at a ver reduced rate and by washing out, diluting, an buffering the by-products of anaerobic metabolism.

In conclusion, continuous hypothermic perfusic with oxygenated plasma-protein fraction is the be way to preserve ischaemically injured kidneys. Up 60 minutes of warm ischaemia is compatible wit normal function after 24 hours' perfusion. Combin tions of up to 6 hours' ice storage and 18 hour perfusion are practicable but perfusion alone preferable.

A profound fall in *p*H during the first hour perfusion is a clear indication that the kidney irreversibly injured. This indication is reinforced the fall in *p*H is sustained or continues througho the 24-hour period.

Changes in perfusion pressure, kidney weight, an perfusate L.D.H. gave no indication of subsequer failure to function.

Acknowledgements.—I should like to than Professor John Swinney for his support and guidanc with this work; in addition I have received invaluab help from Professor Ivan D.A. Johnston, Mr. R. M. F Taylor, Dr. C. T. G. Flear, and Mrs. Marilyn Andersor I am indebted to Mrs. Dorothy Adams for typing th manuscript.

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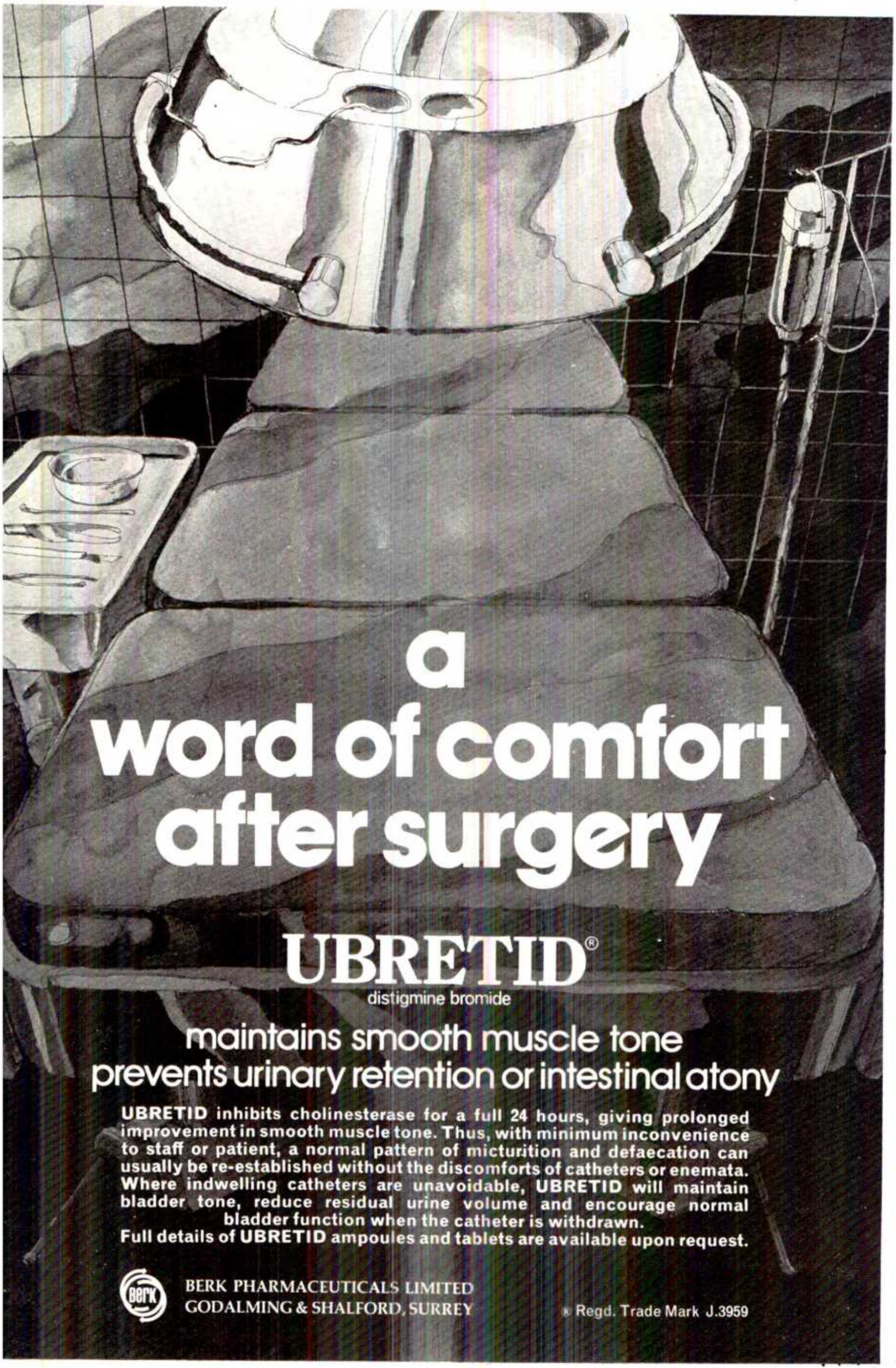

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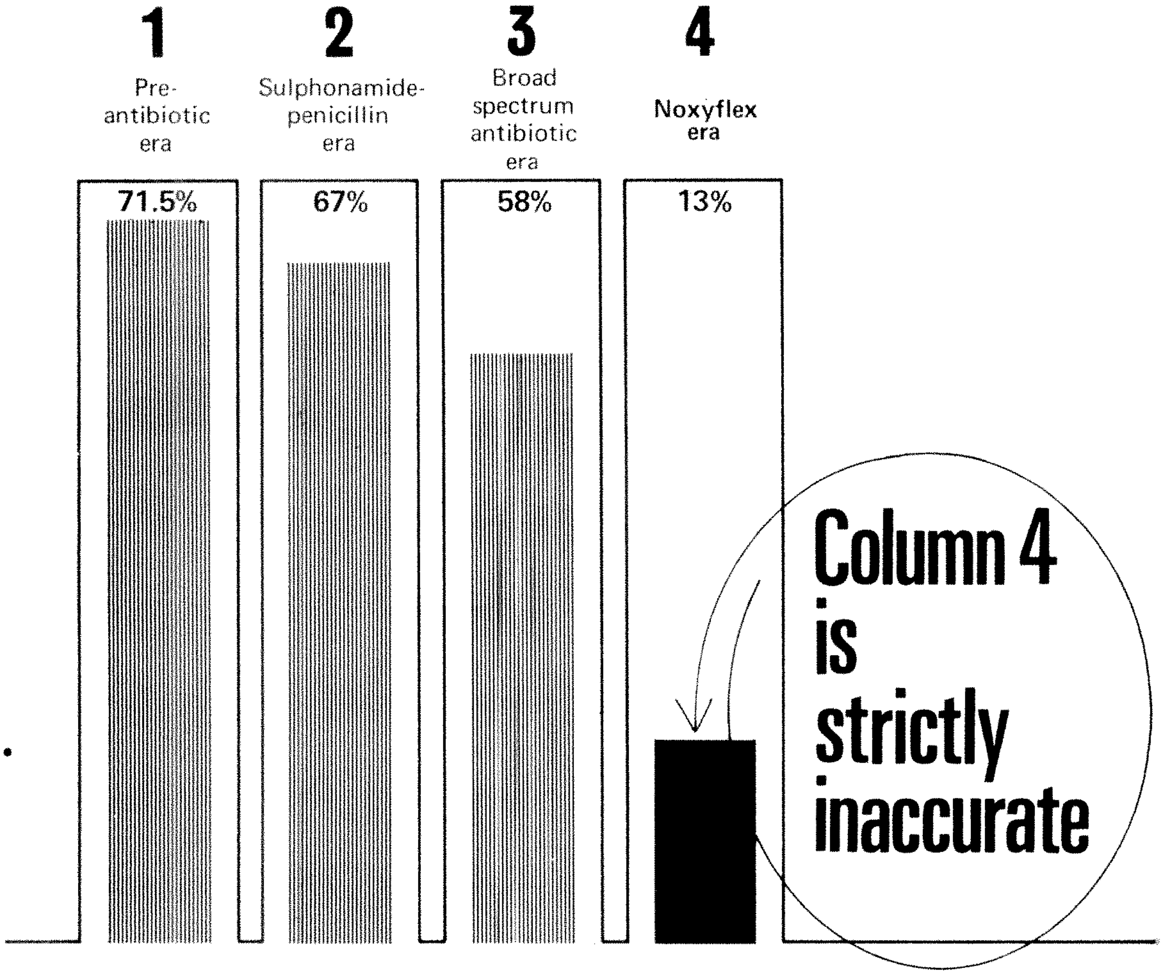
It is not pedantically accurate because its sources differ. But the point is fairly made.



Why inaccurate? Because column 4 refers to 23 cases of faecal peritonitis which were treated successfully with Noxyflex. But the *3 deaths which occurred were due to causes other than peritonitis - as post-mortem revealed. **The mortality rate due to peritonitis can therefore be regarded as zero.**

* The whole graph, and the causes of the deaths referred to are the subject of the new Noxyflex folder "Why three deaths?" You will receive at least one copy!

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A MODEL WHICH CAN BE USED TO IMPROVE THE TREATMENT OF ACUTE HEPATIC FAILURE

By JOHN WINCH

DEPARTMENT OF SURGERY AND LIVER UNIT, KING'S COLLEGE HOSPITAL MEDICAL SCHOOL, LONDON

SUMMARY

A model using the pig from which the liver has been removed for isolated perfusion, as a subject showing some of the features of acute hepatic failure for later treatment by cross-circulation with its own perfused liver, is described. Effects of such a procedure on the glucose and halothane metabolism and intravascular coagulation and bleeding are detailed.

THE main clinical problem with which the present paper is concerned is the treatment of a patient in fulminant hepatic failure. Such a patient, whether the necrotizing agent affecting the liver is the hepatitis virus or a chemical compound such as paracetamol, presents a challenging clinical syndrome (Trey and Davidson, 1970). The acute failure of the *excretory* function of the liver allows accumulation in the blood of bilirubin, ammonia and amino-compounds, and any natural or administered toxic substance whose route of excretion should involve the hepatic metabolism. The inexorable accumulation of such products leads to neurological disturbances, probably occurring first in the brain-stem reticular formation, producing coma (*Fig.* 1), progressing to depression of the respiratory and vasomotor centres, and finally leading to respiratory and cardiac arrest. The biochemical changes are as complex as the neurological abnormalities, with respiratory alkalosis, metabolic alkalosis (James, Nashat, Sampson, Williams, and Garassini, 1969) associated with loss of potassium, probable renal failure, and impairment of carbohydrate metabolism with hypoglycaemia (Leading article, 1971) associated with high levels of circulating insulin (Knell, Pratt, Curzon, and Williams, 1972). The failure of the synthetic function of the liver is reflected by a low serum albumin and a lowering of the circulating fibrinogen and all except Factor VIII of the coagulation factors. The bleeding tendency is worsened by the necrotic tissue in the liver acting as a focus for intravascular coagulation (Rake, Flute, Shilkin, Lewis, Winch, and Williams, 1971), thus adding a consumptive element to the bleeding tendency.

Much can be done to support the patient but there comes a stage when the patient is unconscious, on a ventilator, and tending to bleed from the slightest stimulus when the surgeon is called, for then the patient needs the benefit that can only come from a functioning extra liver. The rationale of such treatment lies in the remarkable powers of regeneration of the liver (Blumgart, Leach, and Karren, 1971), for if temporary liver function is provided for the patient (Winch, 1971) eventual regeneration of the patient's own liver may result in recovery. In this country the most easily available extra liver is that of the pig, although primate or cadaver human livers may prove to be better (Abouna, Serrou, Boehmig, Amemiya, and Martineau, 1970). In an earlier communication a circuit suitable for perfusing the pig liver with human blood was described and the biochemical evidence of adequate function of the liver was presented (Winch, Fleisher, Hague, Kolthammer, Bentley, Shilkin, and Williams, 1971). The next step was to develop a technique of cross-circulating an isolated perfused liver with a suitable subject.

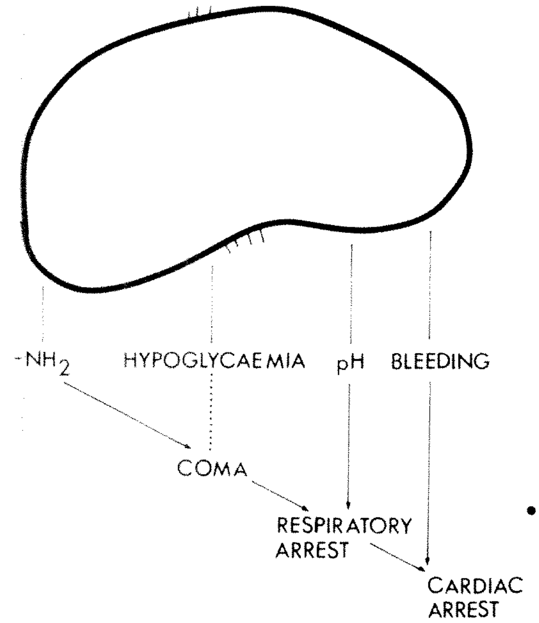

FIG. 1.—Clinical and metabolic consequences of fulminant hepatic failure.

The aims of the present study were therefore:—

1. To study the metabolic consequences of cross-circulation of a perfused pig liver with an animal which was preferably in hepatic failure.
2. To gain technical experience of such a cross-circulation.

CHOICE OF ANIMAL

It is difficult to produce the picture of human hepatic failure in an animal since the hepatitis virus does not affect animals and preparing a succession of animals with hepatic necrosis induced by chemical insult would be a major undertaking in itself. However, each time a pig liver was perfused in an isolated circuit directly after hepatectomy an animal was being discarded which because it had no liver should show a pure picture of hepatic failure, uncomplicated by the toxic overlay of the presence of a large mass of necrotic tissue.

It was therefore decided to retain the pig from which a liver was obtained for perfusion, to maintain it in an anhepatic state while the liver was being studied in an isolated circuit, and later to cross-circulate the pig with its own liver.

This paper reports three experimental periods (*Fig.* 2): first, the anhepatic pig and, secondly, the isolated perfused liver, both studied concurrently during 3 hours, and, thirdly, a period immediately following this when the liver was cross-circulated with the anhepatic pig for 1½ hours.

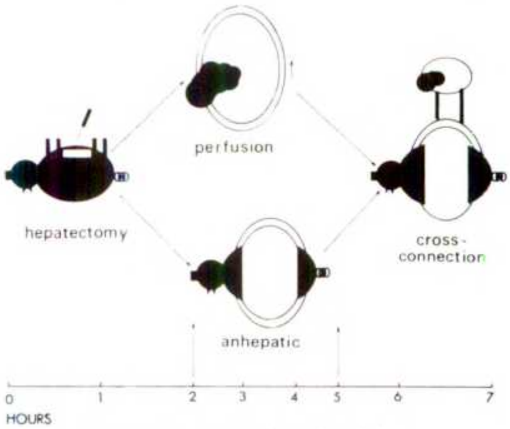

FIG. 2.—Plan of experimental periods.

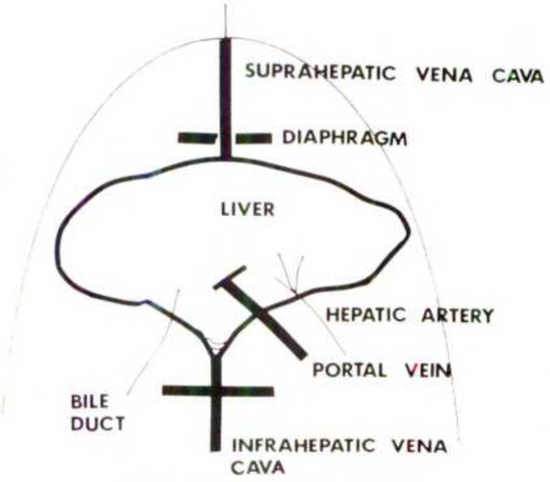

FIG. 4.—Liver prepared for removal.

THE NEEDS FOR A BY-PASS SHUNT

The first problem in developing this use of the anhepatic pig was that the pig (Terblanche, Peacock, Bowes, and Hobbs, 1968), like the calf (Battersby, Balderson, Winch, and Burnett, 1971), but unlike the monkey (Milnes and Child, 1949) or man (Starzl, Groth, Brettschneider, Penn, Fulginiti, Moon, Blandshard, Martin, and Porter, 1968), will not survive acute ligation of the portal vein. Pre-hepatectomy portacaval shunt would not provide a drainage for the portal system, for in the pig the inferior vena cava passes through the liver, thus necessitating removal of a long section of the vena cava during hepatectomy. An external shunt was therefore indicated which for ease of maintenance of circulation should be made to decompress the abdominal inferior vena cava as well as the portal vein.

The shunt that was designed (*Fig.* 3) consists of a short length of polyvinylchloride tubing (Portex, 9·5 mm. diameter) with two cannulae (Bardic venou cannula 1061/20) at one end, for the portal vein and ven cava respectively, and a cannula (Bardic 1060/18) at th other end for insertion into the right external jugula vein. This external shunt functioned well without an pump being necessary, giving a flow in excess o 250 ml. per minute into the external jugular vein Since two connecting points would later be needed i the pig for cross-circulation, two side-arms whic could be opened when cross-circulation was starte were added to the shunt.

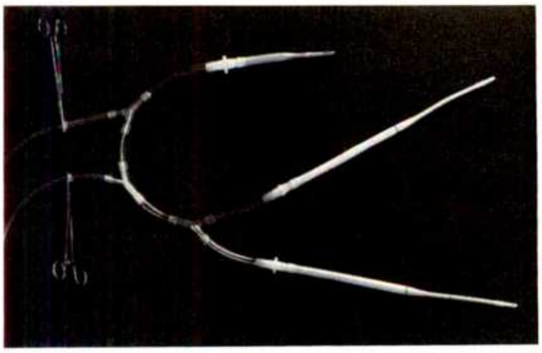

FIG. 3.—By-pass shunt for the portal vein and the intrahepatic vena cava. No external pump was necessary. Note the connexions for later cross-circulation.

ANAESTHESIA AND MONITORING CANNULAE

Each experiment began with induction of anaesthesia in a 20-kg. pig by means of halothane and snout mask. This was followed by endotrache intubation and maintenance of anaesthesia with halothane administered by intermittent positive-pressur respiration. A short vertical incision was then mad in the neck to cannulate the right internal jugular vei for a slow dextrose infusion and a central venou pressure manometer. The right common caroti artery was cannulated to provide continuous blood pressure monitoring. The right external jugular vei was exposed for later cannulation with the upper en of the by-pass shunt. Heparin, 5000 U., was give intravenously to prevent coagulation in the cannula or shunt.

PREPARATION FOR HEPATECTOMY

Through a midline abdominal incision the fir structure to be identified and cannulated was th common bile-duct, which was allowed free drainag during the subsequent operative procedures. Th gall-bladder was isolated by ligation in continuity the cystic duct. The liver was then dissected free of a except its main vascular connexions (*Fig.* 4): the ver cava was defined just above the right adrenal vein, th liver was dissected free of the diaphragmatic crura posteriorly, and the diaphragm was opened to expose the vena cava above the liver, taking care to ligate the large phrenic veins. The portal vein was exposed and the large pancreatic and splenic tributaries were tied, with particular dissection well into the pancreatic tissue to provide placement for the decompressing portal vein shunt. The common hepatic artery was similarly exposed and all the branches to the pancreas, duodenum, and stomach were ligated. During the whole of this procedure the circulation of the liver was not obstructed.

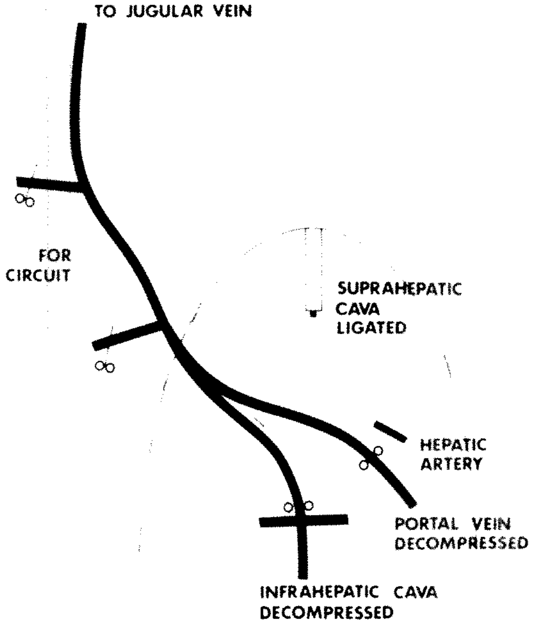

FIG. 5.—By-pass shunt in place after hepatectomy.

COMPLETION OF HEPATECTOMY AND INSERTION OF A BY-PASS SHUNT

When the preliminary work was completed the by-pass shunt was primed with saline and the upper end was inserted into the external jugular vein. The vena cava below the liver was cannulated in the direction of the hind-legs by one half of the lower end of the shunt (*Fig.* 5). The caval by-pass was then opened and the vena cava below the liver was clamped and divided. The portal vein was cannulated in the direction of the liver to enable cooling of the liver to begin with an infusion of a balanced solution of electrolytes (approaching intracellular concentration), heparin, and Rheomacrodex at 7° C. The pancreatic side of the portal vein was cannulated with the other half of the by-pass shunt, the shunt was opened, and the portal vein was divided. The common hepatic artery was then clamped and divided and the only remaining vascular connexion, the suprahepatic vena cava, was dealt with similarly.

TECHNIQUE OF ISOLATED PERFUSION

Flushing of the liver was continued outside the abdomen while the hepatic artery and the vena cava below the liver were cannulated. The vena cava above the liver was ligated, taking care not to obstruct the hepatic veins. The fully prepared liver could now be transferred to float in the saline which forms the physical support for the liver in this circuit (*Fig.* 6). The perfusate was fresh, heparinized pig blood buffered with bicarbonate and allowed to flow into the liver as an oxygenated supply through the portal vein under gravity and through the hepatic artery in a pulsatile manner, with a total flow through the liver of 1 ml. per g. of liver per minute. A solution of mixed bile-salts was infused into the circuit at a constant rate to compensate for the interrupted enterohepatic circulation of bile-salts. The first 30 minutes of isolated perfusion were spent in slowly rewarming the liver to 38° C. Warm perfusion was then continued for 3 hours.

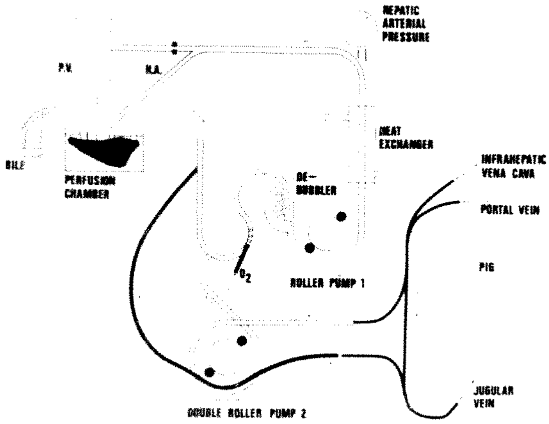

FIG. 6.—Circuit diagram for isolated perfusion and cross-circulation. Liver circulation is provided by pump 1, while cross-circulation is effected independently by pump 2.

MAINTENANCE OF THE ANHEPATIC PIG

The first three attempts to maintain the pig alive after hepatectomy failed largely because of technical difficulties in swiftly cannulating the portal vein in opposite directions. However, once the technique was mastered, maintenance was possible with constant monitoring of the arterial and central venous pressure.

TECHNIQUE OF CROSS-CIRCULATION

Cross-circulation was prepared simply by unclamping the cross-connecting lines and starting the second (double-headed) pump (*Fig.* 6). The speed of the second pump was increased to the maximum flow in both directions that was possible without the flow in the midpart of the by-pass shunt reversing (i.e., up to the maximum flow that was emerging from the combined portal vein and inferior vena cava); this was usually 250 ml. per minute. The main pump in the circuit remained at a constant speed throughout the cross-circulation (usually 900 ml. per minute), for the circuit design allows the flow into the liver to be independent of the flows to and from the anhepatic pig.

The first attempt at cross-circulation was followed within a few minutes of the start by a dramatic fall in the blood-pressure of the anhepatic pig. Cardiac arrest occurred shortly after. Resuscitation with internal cardiac massage and intravenous calcium was possible, and it was observed that the pig's blood-pressure could be titrated against the rate of calcium infusion. This provided a clue to the cause of cardiac arrest and subsequent analysis revealed that the pig's serum potassium at the time was well over 8 mEq./l. This high level derived from the high level in the liver circuit, which in turn derived from loss from the liver substance during the ischaemic period of preparation (Abouna, 1968) and in part from the flushing solution still remaining in the liver at the time of connexion to the circuit. After this experiment the first 350 ml. of blood which had passed through the liver were discarded when isolated circulation was begun. From then on no further technical problems were encountered and 11 successful studies were performed with this model.

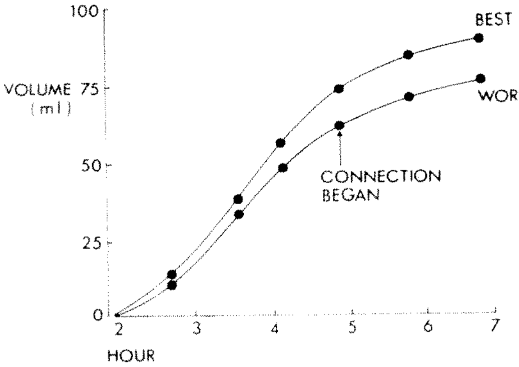

FIG. 7.—Cumulative bile volumes produced by the perfused liver. Bile continued to flow during cross-circulation.

Table I.—BIOCHEMICAL ASSESSMENT OF THE PERFUSED LIVER

GROUP	BILE VOLUME (ml. per 3 hr.)	$T_{\frac{1}{2}}$ BSP IN PERFUSATE (min.)	BSP IN BILE (percentage of loading dose)	$T_{\frac{1}{2}}$ GALACTOSE IN PERFUSATE (min.)
Isolated perfused liver: (n = 11)	45 ± 11·9	67 ± 21	62 ± 12·3	18 ± 10·8
Intact pig (n = 6)	75 ± 17·3	10 ± 2·8	70 ± 13·8	11 ± 5·9

All the results are given as the mean ± S.D.

ASSESSMENT OF LIVER FUNCTION

Excretion in the Perfused Liver.—The biochemical function of the isolated liver was assessed by its ability to deal with administered doses of 100 mg. bromsulphthalein (BSP) and 5 g. of galactose as well as by the rate of bile production. The rates of disappearance of both BSP and galactose from the perfusate were calculated by estimation of serial samples taken from the circuit, to give an indication of the ability of the liver to take up these substances from the blood circulating through it. After uptake BSP is stored, some is conjugated, and both conjugated and free forms are excreted into bile (Whelan, Hoch, and Combes, 1970). The amount of BSP that was excreted into the bile produced during the 3-hour perfusion was also measured to give perhaps a more valid estimate of liver function than does uptake alone (Ham, Pirola, and Elmslie, 1969). Figures for these biochemical assessments are shown in *Table I* together with comparative figures obtained in other studies with intact anaesthetized pigs. The function of the isolated liver is adequate but is less than that in the intact pig where there has been no hepatectomy and cannulation to produce ischaemia. These figures compare well with reduction to two-thirds of the intact liver values that have been reported by other workers (Tygstrup, Funding, Juul-Nielsen, Keiding, Kondahl, Ramsöe, and Winkler, 1971). The only indication of continuing biochemical activity of the perfused liver during cross-circulation was the rate of bile-flow which continued in all the experiments (*Fig.* 7) at an acceptable rate.

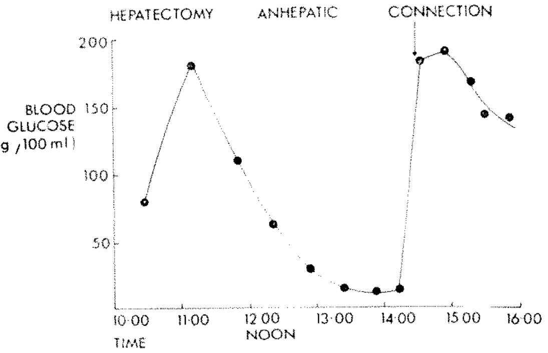

FIG. 8.—Blood-glucose in the pig during one typical experiment. Glucose is infused during hepatectomy but not thereafter.

Excretion in the Anhepatic Pig.—The period (3 hours) of the anhepatic phase was too short to allow accumulation of any detectable amounts of bilirubin or amino-compounds in this series.

Glucose.—The amount of glucose in the perfusate of the isolated liver was maintained at a high level throughout the perfusion without the addition of exogenous glucose. In the anhepatic pig there was a rapid and profound fall in blood-glucose (*Fig.* 8) which remained at extremely low levels until corrected by cross-circulation. There are at least two major factors contributing to this hypoglycaemia of the anhepatic pig: absence of production of glucose by the liver and lack of uptake by the liver of insulin, allowing excessive insulin action peripherally. Correction of the hypoglycaemia by cross-circulation could be due to restoration of either or both of these deficiencies. At least part of the rise was due to the high level of glucose existing in the circuit, but continued normal levels during the 1½-hour period of cross-circulation suggested active liver function.

Synthetic Function of the Liver.—Evidence of synthesis of albumin and fibrinogen by the liver in both the circuit and the pig was sought during the study but no significant changes were found. This reflects either the slower metabolic turnover of protein compared with that of glucose or that protein synthesis was more affected by the less efficient function of the isolated lever compared with that of a normal liver.

EFFECT OF HALOTHANE ON THE ANHEPATIC PIG

One other indication of liver function was obtained virtually as a by-product of the experimental method. Anaesthesia was maintained in the pig by the administration of halothane carried in oxygen and nitrous oxide through a ventilator. The depth of anaesthesia was monitored indirectly by observing the effect of halothane on the pig's blood-pressure—a very sensitive indicator. Excess halothane causes a rapid fall in pressure, while too little allows the blood-pressure to rise and the pig begins to awake from anaesthesia. During hepatectomy continuous administration of halothane was necessary (*Fig.* 9) but within minutes of hepatectomy being complete evidence of halothane excess was seen by a falling blood-pressure. This could only be prevented by stopping the administration of halothane completely during the anhepatic phase. A few minutes after cross-circulation was started the animal began to awake unless halothane administration was recommenced.

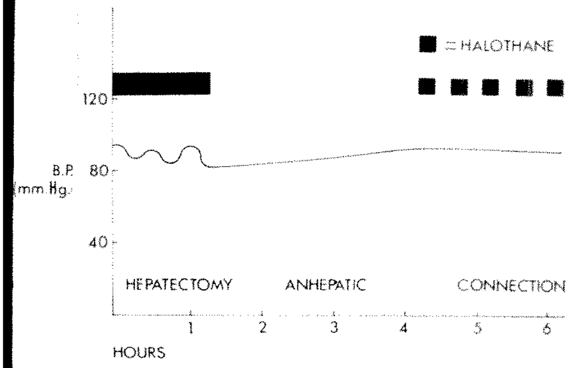

FIG. 9.—Halothane requirements for adequate anaesthesia during the experiments. The blood-pressure is satisfactory throughout. No additional halothane is required after the completion of hepatectomy until the liver is reconnected to the pig.

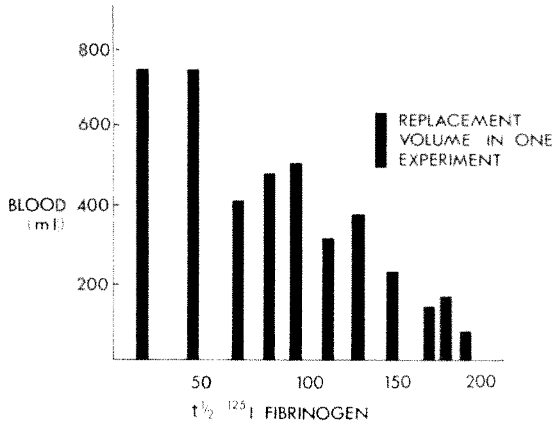

FIG. 11.—Volume of blood required to replace loss from the pig during cross-circulation compared with estimations of intravascular coagulation in the perfused liver using ^{125}I-fibrinogen.

Previously halothane was regarded as a metabolically inert anaesthetic but some 20 per cent of the administered dose has been shown to be metabolized (Rehder, Forbes, Alter, Hessler, and Stier, 1967), as indicated by the urinary appearance of metabolites. The present observations suggest that the site of this metabolism is the liver and the need for less halothane in the cross-circulation period than for the intact pig again reflects the reduction in efficiency of the isolated liver.

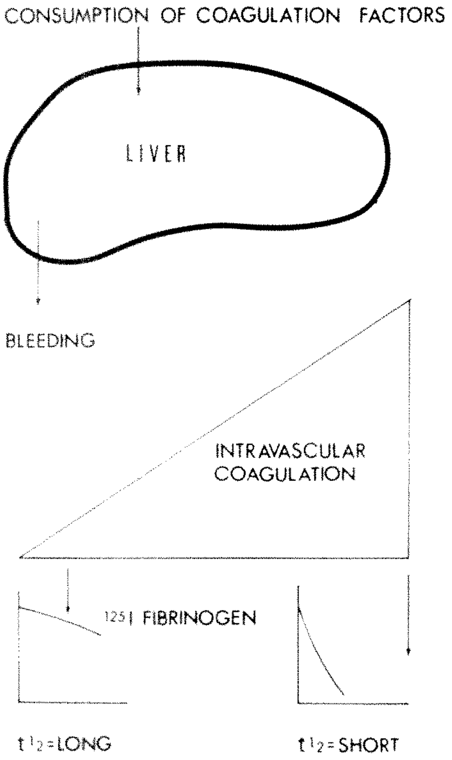

FIG. 10.—Intravascular coagulation in the perfused liver indicated by the disappearance of ^{125}I-fibrinogen from the perfusate.

INTRAVASCULAR COAGULATION IN THE PERFUSED LIVER AND ITS EFFECT ON THE ANHEPATIC PIG

Each isolated liver was assessed during perfusion for the occurrence of intravascular coagulation by the administration of ^{125}I-fibrinogen (10 μc.) to the perfusate and by serial sampling to estimate its rate of disappearance. This has previously been demonstrated to be a useful method of assessment of the likely effects on the recipient's coagulation state if the perfused liver were to be used for cross-circulation (Winch and others, 1971). A rapid fall in the labelled fibrinogen indicates excessive intravascular coagulation, which in turn would lead to bleeding when the recipient's coagulation factors were consumed once cross-circulation was begun (*Fig.* 10).

In the series of cross-circulations presented here there was often considerable bleeding from the cut surfaces in the anhepatic pig, beginning shortly after cross-circulation commenced. To maintain circulation additional blood was required. The amount of blood needed was more when there was a short $T_{\frac{1}{2}}$ of ^{125}I-fibrinogen (*Fig.* 11), indicating significant intravascular coagulation, than when a longer $T_{\frac{1}{2}}$ was found.

This relationship of bleeding to intravascular coagulation as indicated by ^{125}I-fibrinogen agrees with previous theoretical predictions.

CONCLUSION

The use of the model described has fulfilled the two aims of the present work, in that efficient cross-circulation of a functioning isolated liver with an animal having absent hepatic function and a study of the metabolic effects of such a procedure have been carried out. The perfused liver restores glucose metabolism to the anhepatic pig when cross-circulation is performed. The use of this model also suggests hepatic metabolism of halothane, which earlier was regarded as being metabolically inert. Theoretical ideas concerning intravascular coagulation and bleeding were supported, and a need to reduce the circulating potassium in the perfusion circuit before using the method on a patient was discovered. Further work is required to study the method of preparation of the perfused liver, such that its function more nearly reaches that existing before hepatectomy and cannulation cause deterioration. This is necessary in order that the full possible benefit of temporary hepatic function may be offered to a patient in fulminant hepatic failure.

Acknowledgements.—I wish to thank Dr. Roger Williams, Professor J. G. Murray, and Mr. C. T. Howe for their help and encouragement. This work was supported by a generous grant from the Wates Foundation.

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REGRESSION OF AXILLARY LYMPH-NODES IN CANCER OF THE BREAST

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SUMMARY

A multicentre, prospective trial on the treatment of Stage-I and Stage-II breast cancer by simple mastectomy plus radiotherapy versus simple mastectomy alone is described. So far 1050 patients have been collected within 2 years. Data on the first 161 patients treated by simple mastectomy alone are analysed. Axillary lymph-nodes have regressed within 3 months of mastectomy in 75 per cent of patients in clinical Stage II. Regression may be due to resolution of reactive changes in lymph-nodes following removal of the primary tumour.

Cancer of the breast is the commonest malignant disease in women in the United Kingdom, but we still do not know with certainty which form of treatment at present confers benefit on the patient, which has little effect, or which may be harmful (Editorial, 1969). Experience indicates that only prospective, randomized clinical trials are likely to provide firm facts upon which rational decisions can be based. Few such clinical trials have been carried out (Brinkley and Haybittle, 1966; Easson, 1968; Kaae and Johansen, 1968; Fisher, Slack, Cavanaugh, Gardner, and Ravdin, 1970). In all these trials it was assumed that treatment to the regional lymph-nodes was necessary, reflecting a radical approach based on a traditional view of the spread of cancer of the breast. It is believed that malignant disease is autonomous and spreads centrifugally through the surrounding tissues, along lymphatic pathways to the local lymph-nodes, and at a later stage by the blood-stream to form distant metastases. Therefore, if the breast and regional lymph-nodes are treated effectively patients in whom the tumour has not spread further should be cured, but treatments of a lesser degree should fail in a greater proportion of patients. All radical types of treatment are justified by this concept of cancer spread. No significant differences so far have been detected in th overall survival rates when any two radical treatments have been compared (Brinkley and Haybittle, 1966; Easson, 1968; Kaae and Johansen, 1968; Fisher and others, 1970).

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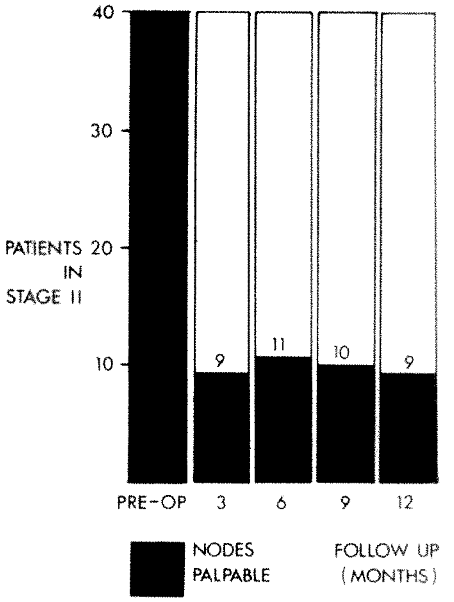

FIG. 1.—Progress of axillary lymph-nodes in 40 patients in Stage II.

In recent years evidence has been accumulating in support of a more conservative approach to treatment. In the Manchester trial (Easson, 1968) radical mastectomy with postoperative radiotherapy was compared with radical mastectomy alone. In the latter régime no treatment was given to the internal mammary nodes and yet the survival rate in this group of patients was similar to that in the group which did receive treatment to the nodes. Again, Crile (1968) reported a series in which patients fared as well without axillary clearance as those treated with axillary clearance. There is some evidence that routine treatment of regional lymph-nodes by radiotherapy may even reduce the survival rate (Bond, 1967). The assumption that there is a moment in time when metastases from a breast tumour have not spread beyond the local tissues has been strongly challenged by the findings of Galasko (1971). At least 20 per cent of patients with apparently early breast cancer have significant bony metastases demonstrable by scintiscanning. It is not unlikely that tiny foci of tumour cells are already present throughout the whole body at the time of detection of the primary tumour. Abundant evidence, mainly from animal sources, suggests that the body plays an active part in the control of tumour growth and that the reticulo-endothelial system may be largely responsible (Fisher, 1971). Indeed, Gewant, Chasin, Tilson, Rutledge, and Goldenberg (1972) have shown that in breast-cancer patients the axillary lymph-nodes show a definite activity *in vitro* against the presence of the primary tumour. It may well be important to preserve lymphatic tissue even in the presence of microscopic deposits of tumour.

As a result of widespread doubts about the value of radical treatment and the lack of precise information about the results of conservative measures, a large prospective clinical trial supported by the Cancer Research Campaign was launched in 1970 to compare a radical with a conservative régime in a methodical and scientific manner (Edwards, Baum, Magarey, and Myson, 1971).

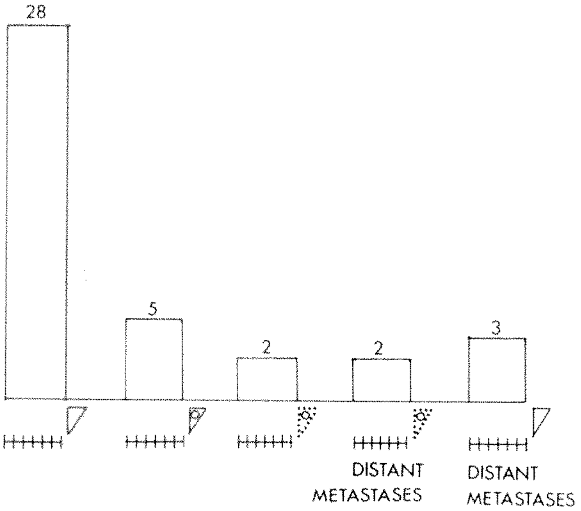

FIG. 2.—Progress of 40 patients in Stage II.

Simple mastectomy followed by routine irradiation to the regional lymphatic field was chosen as the best example of an established and widely used form of radical treatment (Editorial, 1969). It was to be compared with the conservative treatment of simple mastectomy alone with preservation of the regional lymph-nodes. The lymph-nodes would not be treated in the latter régime unless there was evidence of local progression of the disease. This conservative régime represents a fresh approach to the management of early breast cancer, and participants and critics alike are awaiting the first comparative results which will be available in 2–3 years. However, there is particular interest in the fate of the lymph-nodes which have not been treated. It is the purpose of this paper to describe the early progress of patients in the conservative treatment group.

PATIENTS

Women under the age of 70 years with Stage-I and Stage-II (T_1+T_2, N_0+N_1, M_0) breast cancer are eligible for the trial. A standardized simple mastectomy is performed on all patients. The procedure consists of removing the whole breast including the axillary tail while avoiding deliberate excision of the axillary lymph-nodes. After operation the patients are divided randomly into two groups. In one, the *irradiated group*, a standardized course of radiotherapy is given to the skin-flaps and the axillary, supraclavicular, and internal mammary lymph-node areas. In the second, the *'watch policy' group*, no treatment is given to the regional lymph-nodes after simple mastectomy unless there is evidence of progression of the disease. In this group there is no intention of allowing lymph-nodes to progress to the extent that symptoms may arise. The criteria which are regarded as evidence of active growth of tumour in nodes include progressive enlargement and the development of fixation.

All the patients are examined at 3-monthly intervals and clinical information including the presence or absence of local lymph-nodes and recurrences is recorded. Any other initial treatment, such as oophorectomy or the administration of hormones or cytotoxic drugs, is not permitted.

In the first 22 months of the study 1050 patients have been accepted from 85 centres in the United Kingdom, Eire, Scandinavia, Switzerland, and New Zealand. Over 2000 patients are expected to have been included by 1973. It has now been agreed that comparisons will be made with patients in the National Surgical Adjuvant Breast Project in the United States of America.

RESULTS

So far, 161 patients in the 'watch-policy' group have have been followed up for a period of 12 months and the results are available for study.

Of 40 patients judged to be in Stage II, in no less than 75 per cent the axillary lymph-nodes have regressed (*Fig.* 1). The regression was apparent at the first follow-up examination 3 months after mastectomy and has persisted. In 5 patients (*Fig.* 2) the nodes remained palpable but unchanged, and in 2 patients treatment has been given for progressive enlargement of lymph-nodes in the absence of distant metastases. In 5 other patients distant metastases have developed but only in 2 of them was treatment required for axillary node progression.

Of 121 patients in Stage I, 11 patients had palpable axillary nodes which have not progressed during the first year of follow-up (*Fig.* 3). In addition, 4 patients have received treatment for progression of axillary lymph-nodes in the absence of distant metastases. Seven patients have developed distant metastases with or without lymph-node progression, and of these 7, 3 patients have died.

DISCUSSION

There has always been doubt about the prognostic significance of palpable axillary nodes in patients with carcinoma of the breast and uncertainty about how to treat them. The fact that in the present trial the great majority of palpable nodes have regressed following simple mastectomy (Stage II reverting to Stage I) highlights this dilemma.

There is evidence that the enlargement is due to sinus histiocytosis in about one-third of lymph-nodes (Black and Speer, 1958). It may be that a proportion of the nodes which undergo spontaneous regression do so because of the removal of the tumour and consequently the stimulus to the sinus histiocytosis. There is increasing evidence that such changes in th regional lymph-nodes may be part of a defenc mechanism, helping to contain the malignant growth to some extent (Editorial, 1969). Again, it may be that the defence mechanism involved the reticulo-endothelial system as a whole and that the regional lymph-nodes are only part of this mechanism. Radiotherapy, as it is traditionally employed following simple mastectomy, interferes not only with the function of the regional lymph-nodes but also with other aspects of the reticulo-enthothelial system (Magarey and Baum, 1970) and if this is so then routine postoperative radiotherapy to the regional lymph-nodes may be harmful in a proportion of patients (Editorial, 1969).

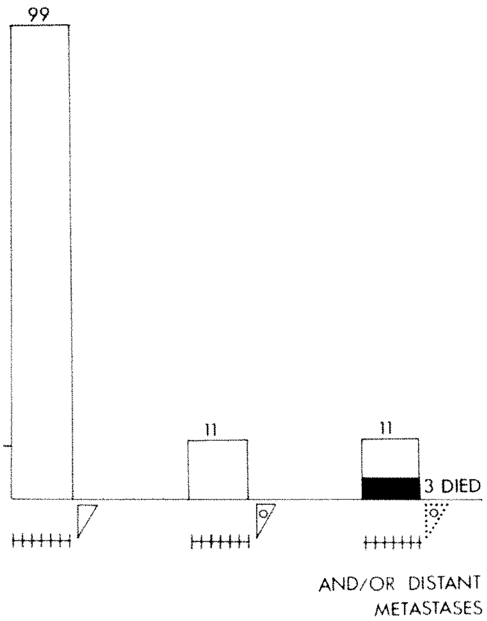

FIG. 3.—Progress of 121 patients in Stage I.

On the other hand, histological studies of radical mastectomy specimens show that in 50 per cent of patients with palpable lymph-nodes there is metastatic disease in the axillary nodes (Wallace and Champion, 1972). Thus a proportion of the nodes in the present study which have regressed are likely to contain malignant cells. Is it possible that under certain circumstances some of these lymph-nodes containing malignant cells are still capable of exerting some protective process against further growth of these cells? The present trial, for the first time, compares a radical form of treatment involving radiotherapy with a conservative approach without radiotherapy. Only with a longer follow-up and larger numbers of patients within this trial will the dilemma be resolved.

Acknowledgements.—We are very grateful to Professor J. S. Mitchell, Professor J. G. Murray, and over 300 clinicians for their support and encouragement.

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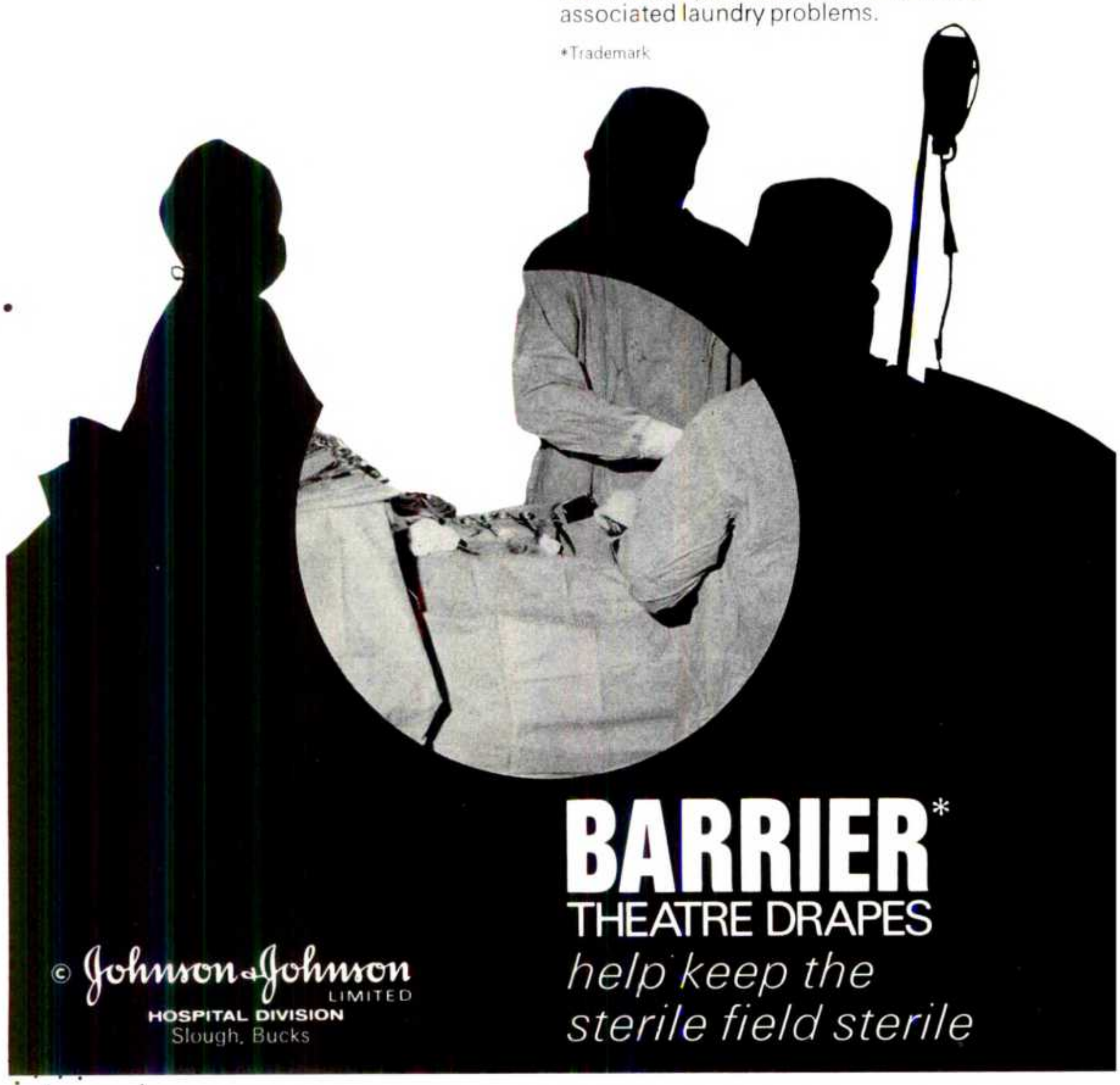

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THE VALUE OF PRESERVING THE PYLORUS IN THE SURGERY OF DUODENAL ULCER

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SUMMARY

Highly selective vagotomy without a drainage procedure (H.S.V.) has been used in the surgical treatment of 120 cases of duodenal ulcer in Leeds over the past 3 years. In this operation preservation of the vagal nerve-supply to the antral region of the stomach permits preservation of an intact pylorus. In the present paper the results which have been achieved are assessed, both clinically and experimentally, by comparison with the results in patients after truncal or selective vagotomy and pyloroplasty at a comparable stage after operation.

Studies of gastric emptying provide no evidence of gastric stasis after H.S.V., and symptoms of flatulence and food vomiting are found no more frequently than after vagotomy and pyloroplasty. After both truncal and selective vagotomy and pyloroplasty gastric emptying and small-bowel transit were abnormally fast, whereas after H.S.V. there was much less departure from the values found in preoperative ulcer patients. At the clinical and experimental level dumping and diarrhoea were significantly less frequent after H.S.V. than after vagotomy and pyloroplasty.

To date there has been no operative mortality, no case of recurrent ulcer, and no reoperation for gastric stasis after H.S.V. Preservation of a more normal pattern of gastric emptying, by reducing the incidence of dumping, diarrhoea, and bile vomiting, has led to better overall (Visick) results after H.S.V. than after truncal or selective vagotomy and pyloroplasty.

THERE is now considerable evidence that many of the sequelae of gastric surgery which may mar otherwise good results arise from abnormalities of gastric emptying (Colmer, Davies, Owen, and Shields, 1969; McKelvey, 1970; Cobb, Bank, Marks, and Louw, 1971). The operation of highly selective vagotomy without a drainage procedure (H.S.V.) (Johnston and Wilkinson, 1970) combines an effective attack on the acid- and pepsin-secreting proximal part of the stomach with an attempt to preserve the mechanisms which normally control gastric emptying. This is achieved by denervating the parietal cell mass of the stomach and preserving, in addition to the hepatic and coeliac branches of the vagus, the parasympathetic nerve-supply to the antrum of the stomach—the nerves of Latarjet. No drainage procedure is added to this vagotomy so that an intact and innervated antrum, pylorus, and duodenum are left to regulate gastric emptying.

H.S.V. has been performed in 120 patients with chronic duodenal ulcer in Leeds over the past 3 years. This paper attempts an assessment of this operation by comparing and contrasting the results obtained with those found after the conventional operations of truncal and selective vagotomy with pyloroplasty performed in the same surgical unit.

MATERIALS AND METHODS

Clinical Study.—The clinical results are derived from the assessment made at the Gastric Follow-up Clinic at Leeds. The patients were interviewed by a panel of surgeons and physicians who were unaware of the nature of the operations the patients had undergone until after they had reached an agreement. In this way an unbiased assessment was possible. Follow-up data 1–2 years after operation were available for 62 patients who had undergone H.S.V. for duodenal ulcer. These results were compared with the results 1–2 years after bilateral selective vagotomy and pyloroplasty in 67 patients, and the results 2 years after truncal vagotomy and pyloroplasty in 158 patients; the latter results have already been published from this unit (Goligher, Pulvertaft, de Dombal, Clark, Conyers, Duthie, Feather, Latchmore, Matheson, Harrop-Shoesmith, Smiddy, and Willson-Pepper, 1968). In order to achieve a greater degree of objectivity in the assessment of symptoms of alimentary dysfunction 50 patients who had undergone appendicectomy, herniorrhaphy, or varicose-vein operations 1 year previously were included in the Gastric Follow-up Clinic without the prior knowledge of the interviewing panel. These patients constitute the control series.

Experimental Studies.—A number of experimental studies have been performed to obtain more precise information about gastric emptying and small-bowel transit time and to highlight any differences which might exist in the liability to such symptoms as dumping and diarrhoea. The patients chosen for these studies were representative of the larger groups with respect to individual symptoms and overall Visick grading. Patients with duodenal ulcer before operation were also investigated as a control group. The numbers of patients in each study are indicated in the results.

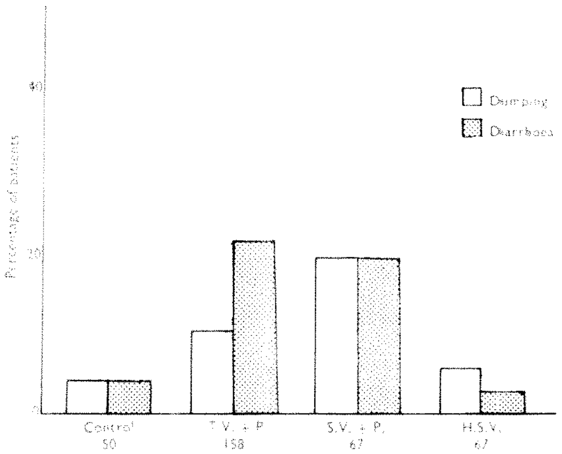

FIG. 1.—Incidence of dumping and diarrhoea 1–2 years after operation.

Table I.—SYMPTOMS OF ALIMENTARY DYSFUNCTION 1–2 YEARS AFTER OPERATION

SYMPTOM	T.V. + P. (Percentage of 158 Cases)	S.V. + P. (Percentage of 67 Cases)	H.S.V. (Percentage of 62 Cases)
Nausea	26	21	13
Bile vomiting	11	9	0
Food vomiting	8	13	8
Epigastric fullness	47	52	30
Early dumping	10	19	6
Late dumping	3	6	2
Flatulence	31	27	16
Heartburn	18	18	13
Dysphagia	1	0	1
Diarrhoea	22	19	3

T.V. + P., Truncal vagotomy with pyloroplasty. S.V. + P., Selective vagotomy with pyloroplasty. H.S.V., Highly selective vagotomy without a drainage procedure.

Hypertonic Glucose Meal.—This consisted of 350 ml. of a 25 per cent solution of glucose to which phenol red had been added to a concentration of 250 parts per million. Gastric emptying was measured by the percentage of the test meal leaving the stomach in 20 minutes, the method and calculations being based on the test described by George (1968). Similar tests were performed with the patients standing upright and without aspiration of the stomach in an attempt to provoke the onset of dumping and diarrhoea.

Food and Barium Meal.—A standard meal of toast and butter, scrambled eggs, and a cup of tea was homogenized with 30 ml. of barium suspension to a semi-fluid consistency. The serial radiographs taken after eating this were reviewed by an experienced radiologist who was not aware which operation had been performed. Gastric emptying has been expressed in terms of whether the stomach was completely empty by 90 minutes after the start of the meal, and small-bowel transit time by whether the head of the meal had reached the caecum in this time interval.

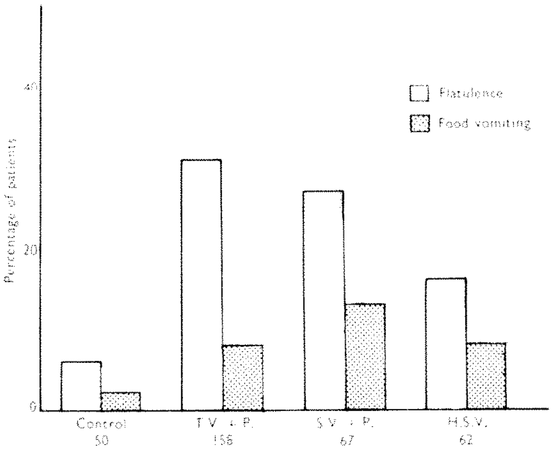

FIG. 2.—Incidence of flatulence and food vomiting 1–2 years after operation.

Table II.—OVERALL (VISICK) GRADING 1–2 YEARS AFTER OPERATION

VISICK GRADING	T.V. + P. (Percentage of 158 Cases)	S.V. + P. (Percentage of 67 Cases)	H.S.V. (Percentage of 62 Cases)
1	37 } 64	39 } 64	59 } 86
2	27	25	27
3	24	25	6
4	12	11	8

For abbreviations *see Table I.*

RESULTS

Clinical Study.—The individual symptoms recorded at the Gastric Follow-up Clinic 1–2 years after operation are shown in *Table I.* The incidence of dumping and diarrhoea—symptoms which are related to abnormally rapid gastric emptying—is shown in *Fig.* 1, whilst *Fig.* 2 shows the incidence of flatulence and food vomiting. There is no evidence that H.S.V. is followed by more flatulence or food vomiting than is vagotomy and pyloroplasty. Both dumping and diarrhoea, particularly the latter, have been reduced in incidence by H.S.V. It is noteworthy that bile vomiting has not been recorded after this operation, whilst the incidence is about 10 per cent after both truncal and selective vagotomy and pyloroplasty.

The overall clinical grading is shown in *Table II* and *Fig.* 3. The incidence of outright failures (Visick grade 4) is similar after each of the operations at 8–12 per cent. However, the incidence of Visick grade 3 results (unsatisfactory clinical results because of severe symptoms of alimentary dysfunction which cannot be controlled by modifications of diet) is much less after H.S.V., only 6 per cent of the patients falling into this category compared with 25 per cent after vagotomy and pyloroplasty. By reducing the incidence of symptoms such as dumping, diarrhoea, and bile vomiting H.S.V. has led to a considerable increase in the number of good and excellent results (*Fig.* 3).

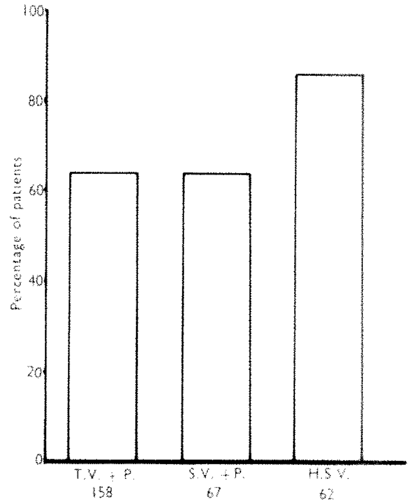

FIG. 3.—Proportion of good to excellent clinical results (Visick I and II) 1–2 years after operation.

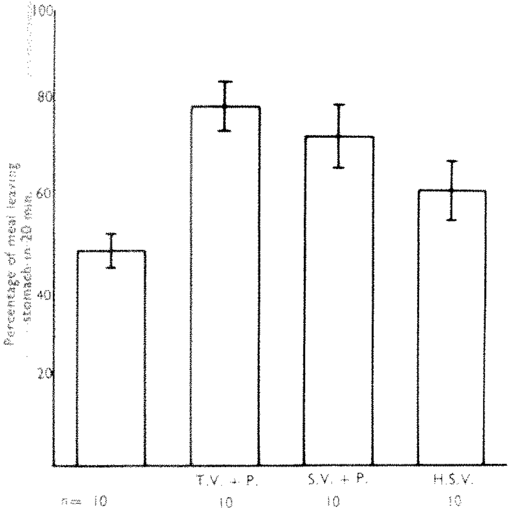

FIG. 4.—Gastric emptying of hypertonic glucose: percentage of meal leaving the stomach in 20 minutes. Mean ± 1 S.E.M.

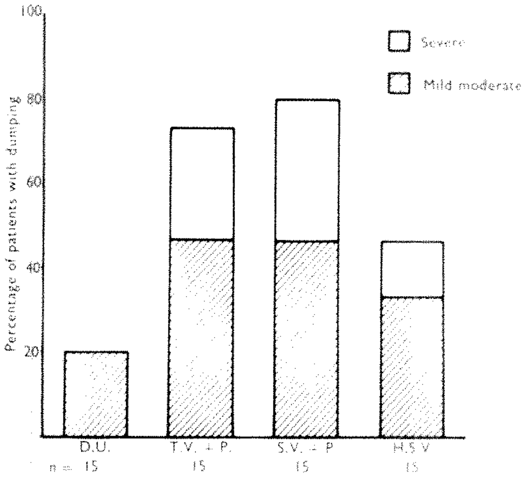

FIG. 5.—Incidence of dumping after the ingestion of hypertonic glucose.

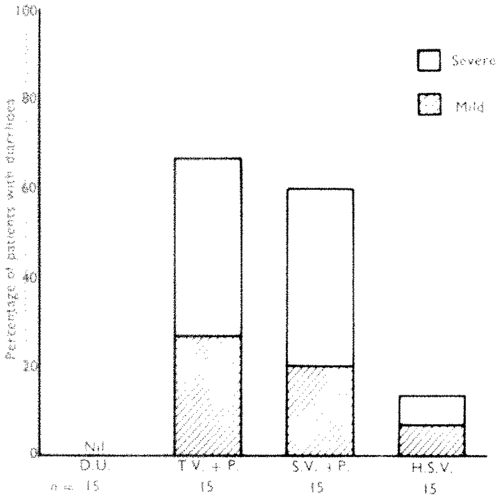

FIG. 6.—Incidence of diarrhoea after the ingestion of hypertonic glucose.

Experimental Studies.—

Gastric Emptying of a Fluid Meal.—The mean percentage of the test meal leaving the stomach in 20 minutes is shown in *Fig.* 4. After both truncal and selective vagotomy and pyloroplasty significantly greater amounts of the meal left the stomach than in the preoperative ulcer patients ($P < 0{\cdot}05$). Although the rate of emptying was faster in the H.S.V. patients than in the preoperative patients, it was not significantly so.

When the same meal was drunk without aspiration of the stomach, the onset of dumping and/or diarrhoea was provoked in a proportion of patients. The incidence of dumping and diarrhoea after oral glucose is shown in *Figs.* 5 and 6. Both dumping and diarrhoea occurred significantly more frequently after vagotomy and pyloroplasty than after H.S.V. ($P < 0{\cdot}02$).

Food and Barium Meal.—The percentage of patients whose stomachs had emptied within 90 minutes of eating the meal is shown in *Fig.* 7. Gastric emptying of this semi-fluid meal was significantly faster than in the preoperative patients after both truncal ($P < 0.002$) and selective ($P < 0.01$) vagotomy and pyloroplasty but not after H.S.V. Small-bowel transit time was significantly reduced after all three operations when compared with the preoperative patients. The head of the meal had reached the caecum in 36 per cent of the patients after H.S.V. ($P < 0.03$) compared with 60 per cent after selective vagotomy ($P < 0.01$) and 83 per cent after truncal vagotomy ($P < 0.001$).

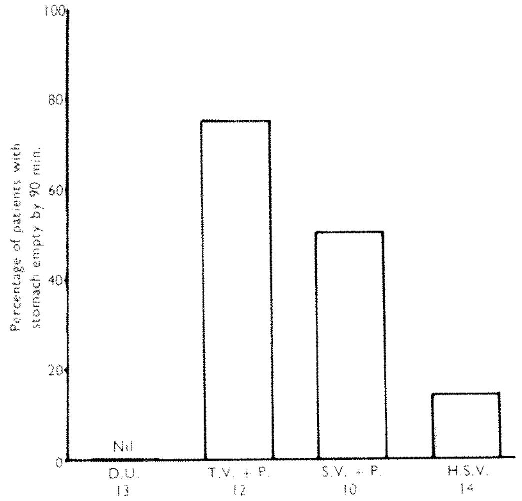

FIG. 7.—Gastric emptying of food and barium meal: percentage of patients with complete emptying of the stomach by 90 minutes.

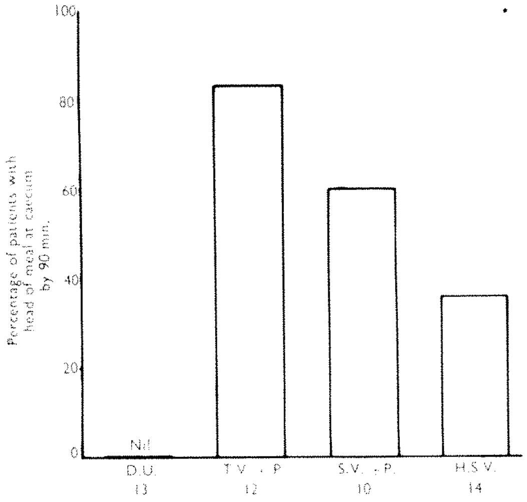

FIG. 8.—Small-bowel transit of food and barium meal: percentage of patients in whom the head of the meal had reached the caecum by 90 minutes.

DISCUSSION

One defect of the present study must be admitted at the outset, namely that the results obtained are not derived from a prospective randomly controlled clinical trial. However, the operations were all performed in the same surgical unit where the indications for operation have not changed. Moreover, the results have been assessed in a 'blind' manner by a panel, so that we feel that any advantages we have shown for one operation are more likely to be due to differences between the operations themselves rather than to dissimilarities in the patients coming to operation.

An operation for chronic duodenal ulcer which preserves the pylorus and deliberately retains an innervated antrum must be examined critically on two counts: recurrent ulceration and gastric stasis. H.S.V. has been performed on more than 250 patients in Leeds and Copenhagen (Amdrup, 1972) over the past 3 years without a single recurrent duodenal ulcer to date. Holle (1969) has performed more than 300 proximal selective vagotomies with either pyloroplasty or antrectomy and reports a recurrent ulcer rate of only 7 per cent. There is no reason to expect that H.S.V. will be followed by a higher incidence of recurrent ulceration than vagotomy and pyloroplasty since basal acid output, maximal acid output to pentagastrin, and peak acid output to insulin are all reduced as effectively by H.S.V. as by truncal or selective vagotomy (Johnson and Wikinson, 1970; Wilkinson, Humphrey, Mason, Smith, and Johnston, 1971). The innervated antrum does not lead to an excessive release of gastrin in response to meat extract (Johnston, Humphrey, Smith, and Wilkinson, 1971).

Even though H.S.V. has been performed on some patients with considerable scarring of the duodenum we have not had to reoperate on any patient for gastric retention. Symptoms of gastric stasis, flatulence, and food vomiting do not occur more frequently after H.S.V. than after vagotomy and pyloroplasty. The studies of gastric emptying are particularly reassuring as they show that gastric emptying of both fluid and semi-fluid meals is slightly more rapid than in the preoperative patient. Omission of a drainage procedure does not lead to gastric stasis, provided that the propulsive power of the gastric antrum is retained.

The studies of gastric emptying of hypertonic glucose confirm previous reports (George, Connell, and Kennedy, 1968; Hall and Read, 1970; McKelvey, 1970) that a fluid meal leaves the stomach more rapidly after vagotomy and drainage than in the preoperative subject. Indeed, as McKelvey (1970) has so aptly put it, after vagotomy and pyloroplasty the stomach is incontinent of a fluid meal. This picture of uncontrolled gastric emptying is not seen after H.S.V. Moreover small-bowel transit time is nearer to normal after H.S.V. than after vagotomy and pyloroplasty. Preservation of the pylorus—more properly the antropyloroduodenal segment—enables controlled emptying to occur from the stomach. The corollary of this is that the incidence of unpleasant alimentary side-effects is reduced by H.S.V., leading to an increase in the proportion of good to excellent clinical results. These findings are in agreement with the observations of others that preservation of the pylorus after partial gastrectomy is accompanied by a better pattern of gastric emptying and fewer side-effects (Friesen and Rieger, 1960; Killen and Symbas, 1962; Amdrup, Nielsen, and Jensen, 1970; Hennessy, Weir, and D'Auria, 1972).

A gradation may be observed in both the physiological changes in gastric emptying and the incidence of the side-effects of operation, from the 'normal' preoperative stomach, through highly selective and selective vagotomy, to truncal vagotomy. It seems, not unreasonably, that the more that gastro-intestinal anatomy and physiology are unnecessarily interfered with, the worse may be the side-effects of surgery. H.S.V. does not give perfect results. For instance, one-third of the patients experience epigastric fullness which in some necessitates a reduction in the size of meals. However, by restricting the surgical attack to the acid- and pepsin-secreting part of the stomach only and by preserving all other parts H.S.V. seems to achieve a cure for ulcer dyspepsia without imposing too high a price in terms of 'post-vagotomy' symptoms.

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SHORT PAPERS

PYLOROPLASTY ALONE IN THE MANAGEMENT OF PATIENTS WITH A NEGATIVE EXPLORATION FOR DUODENAL ULCER

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SUMMARY

If a preoperative diagnosis of duodenal ulcer is not confirmed at laparotomy an exploratory pyloroduodenotomy may be closed as a pyloroplasty without adding a vagal section. This study concerns 32 patients in whom this was done. As a group these patients tended to have somewhat atypical ulcer symptoms and indefinite radiological signs. Within a mean follow-up period of 3½ years more than one-third of these patients developed recurrent ulcer symptoms, which in 4 patients to date have been successfully treated by vagotomy. The functional result could not be predicted by the preoperative symptoms or radiological changes. The incidence of diarrhoea and post-cibal fullness, vomiting, dumping, colic, and hypoglycaemia was almost identical with that seen after vagotomy and pyloroplasty. The wisdom of using pyloroplasty without vagotomy in patients with ulcer symptoms is therefore questioned.

THE inability to confirm at laparotomy a previously diagnosed duodenal ulcer is an uncommon but recurring problem. Because of the well-established risk of unpleasant sequelae there is a reluctance to submit these patients to what may be unnecessary ulcer surgery. Weinberg, Sempien, Movius, and Dnagadi (1956) advocated inspection of the mucosa of the duodenal cap and pyloric canal via a longitudinal incision, and if no sign of ulcer disease was found closing this as a pyloroplasty without proceeding to vagal section. However, little attention has been given to the long-term results of this policy or to the incidence of side-effects, although pyloroplasty alone has been used in the past for the treatment of duodenal ulcers (Horsley, 1926; Judd and Nagel, 1927) and more recently for gastric ulcers (Gilchrist, 1956; Farris and Smith, 1961).

In the present report the functional result in patients who underwent pyloroplasty without vagotomy after negative exploration for duodenal ulcer is assessed. These patients are compared with a matched group of patients who had a complete truncal vagotomy and pyloroplasty to establish the relative incidence of post-cibal symptoms.

MATERIALS AND METHODS

During the 6½ years from October 1964 to March 1971, 595 patients have undergone surgical treatment for duodenal ulcer in the Department of Surgery, Sheffield. Thirty-two of these patients had a Heineke-Mikulicz pyloroplasty performed without vagal section after exploration failed to confirm the presence of a duodenal ulcer or scar. These patients formed the study group. They were matched for sex, age, and length of time from operation with patients who had a Heineke-Mikulicz pyloroplasty and complete truncal vagotomy. The vagotomy was deemed complete if two insulin tests were negative by Hollander's criteria 2 weeks and 6 months respectively after surgery.

The patients were randomized and interviewed by a person who was unaware of the nature of the patients' operations. An assessment was made of the functional state according to a modification of the Visick classification (Visick, 1948). Careful inquiry was made as to the presence, frequency, and severity of side-effects attributable to the surgery. Symptoms were recorded only if they occurred at least three times a year. The following definitions were used:—

Dumping: Weakness, faintness, trembling, and sweating within 30 minutes of a meal. Severity was judged by whether patients had to sit or lie down and the time taken for recovery.

Diarrhoea: Three or more loose bowel actions in 1 day.

Hypoglycaemia: Weakness, faintness, trembling, sweating, and hunger occurring 2–4 hours after a meal.

Ulcer Symptoms: The presence of post-prandial epigastric pain, other than central abdominal colic, was taken as evidence of failed treatment. In view of the difficulty in making an absolute radiological or fibre-optic diagnosis of recurrent ulcer after pyloroplasty, clinical assessment only was used in this follow-up.

The case notes of all the patients were scrutinized in the same random order without knowledge of the type of operation, and an assessment was made of the preoperative clinical and radiological evidence for duodenal ulcer disease. Note was only taken of symptoms specifically recorded as being present or absent. Radiological features were taken from the original barium-meal reports.

RESULTS

All the patients were interviewed except 1 who had moved from the area and who was assessed by correspondence with the surgeon attending him.

The composition of the study group was similar to that of the matched vagotomized patients (*Table I*).

Preoperative Clinical State.—There were several differences between the two groups regarding the nature of the pain. By every criterion the patients in whom no ulcer was found tended to have less typical symptoms. This difference was statistically significant with regard to past or present relief of pain with food or alkali and to radiation of pain through to the back (*Table II*). In each group 4 patients with a history of haematemesis or melaena had required blood transfusion. The incidence of vomiting was not significantly different for the two groups. Preoperative acid studies revealed a lower mean output in the study group (34·0 mEq. per hour) than in the vagotomized group (43·5 mEq. per hour) although this difference was not significant.

Table I.—COMPOSITION OF THE GROUPS STUDIED

	Pyloroplasty	*Vagotomy and Pyloroplasty*
No. of patients	32	32
Male : female ratio	25 : 7	25 : 7
Age at operation (yr.)	42·6	45·0
Duration of symptoms (mth.)	118	130
Length of follow-up (mth.)	46·5	39·3

Table II.—PREOPERATIVE SYMPTOMS

SYMPTOM	PYLOROPLASTY		VAGOTOMY AND PYLOROPLASTY	
	No. of Patients	Per cent	No. of Patients	Per cent
Episodes of remission				
Absent	9	33·3	3	10·0
Present	18	66·7	27	90·0
Pain related to meals				
Absent	9	31·0	3	16·7
Present	20	69·0	25	83·3
Relief with alkali*				
Absent	8	27·6	1	3·1
Present	21	72·4	31	96·9
Pain at night				
Absent	11	37·9	5	15·6
Present	18	62·1	27	84·4
Back pain**				
Absent	20	74·1	11	36·7
Present	7	25·9	19	63·3
Haematemesis and melaena				
Absent	18	60·0	21	65·6
Present	12	40·0	11	34·4

Patients are only included where a symptom was specifically recorded as being absent or present.

* $\chi^2 = 5·42$, degrees of freedom = 1, $P < 0·025$.

** $\chi^2 = 6·58$, degrees of freedom = 1, $P < 0·01$.

Table III.—PREOPERATIVE RADIOLOGICAL CHANGES

RADIOLOGICAL CHANGES	PYLOROPLASTY		VAGOTOMY AND PYLOROPLASTY	
	No. of Patients	Per cent	No. of Patients	Per cent
No changes or irritable duodenal cap	8	25	0	
Mild deformity	8	25	3	9·4
Moderate deformity or probable ulcer crater	8	25	15	46·9
Gross deformity or definite ulcer crater	8	25	14	43·7
Total	32		32	

Radiological Evidence.—The reports of the examining radiologists were classified according to the degree of changes noted. Normal findings or 'irritable' duodenal cap were classed as no change and gross deformity or a definite ulcer crater as marked hange. Varying degrees of deformity or suggestion of an ulcer crater were classed as mild or moderate hanges. Those patients with a negative exploration had significantly less severe changes (*Table III*). The mean length of time from barium meal to operation was virtually identical in the two groups, being 6·7 and 6·3 months for pyloroplasty alone and for vagotomy and pyloroplasty respectively. However, in those 8 patients with marked changes but a negative exploration this delay was somewhat longer at 8·7 months (2 weeks to 2 years).

Table IV.—FUNCTIONAL RESULTS ACCORDING TO THE VISICK CLASSIFICATION

GRADE	PYLOROPLASTY		VAGOTOMY AND PYLOROPLASTY	
	No. of Patients	Per cent	No. of Patients	Per cent
	10	31·3	14	43·8
	6	18·8	9	28·1
a	4	12·5	8	25·0
b	0		0	
	12	37·5	1	3·1
Total	32		32	
Good (grades 1 and 2)	16	50	23	71·9
Satisfactory (grade 3a)	4	12·5	8	25·0
Poor (grades 3b and 4)	12	37·5	1	3·1
Total	32		32	

Comparison between the individual grades showed a significant difference. $\chi^2 = 11{\cdot}90$, degrees of freedom $= 3$, $P < 0{\cdot}01$.

Table V.—ANALYSIS OF POOR RESULTS

Symptoms	*No. of Patients*
Pyloroplasty	
Ulcer symptoms leading to vagotomy	4
Recurrent or persistent ulcer symptoms	5
Melaena (also a major preoperative symptom)	1
Daily vomiting (also a major preoperative symptom)	2
Total	12
Vagotomy and pyloroplasty	
Recurrent ulcer symptoms	1

Table VI.—DETAILS OF PATIENTS HAVING A SECONDARY VAGOTOMY

No. of patients	4
Symptom-free period after pyloroplasty (mth.)	4 (range, 2–6)
Period between pyloroplasty and vagotomy (mth.)	24 (range, 13–32)
Length of follow-up since vagotomy (mth.)	27 (range, 10–37)
Functional result (No. of patients)	
Good	3
Satisfactory	1

Postoperative Assessment.—The patients having pyloroplasty alone after a negative exploration fared badly according to the Visick classification (*Table IV*). The difference between the two groups was significant and a similar result was noted when grades 1 and 2 were grouped together. No patient in either group fell into grade 3b, which is also regarded as a poor result. Clinical evidence only was used to classify patients with poor results as even at reoperation it is often impossible to distinguish between scarring due to pyloroplasty and that due to recurrent ulceration (*Table V*).

Further details and the subsequent functional result of the 4 patients who underwent secondary vagotomy are shown in *Table VI*.

Postoperative Non-dyspeptic Symptoms.—The overall incidence of symptoms usually associated with vagotomy and drainage was virtually the same after pyloroplasty alone and after pyloroplasty and complete truncal vagotomy (*Table VII*). Apart from 2 patients who had persistent daily vomiting, in no case were the symptoms disabling. Where there was a clear difference in the severity of symptoms the more severe ones, e.g., episodic diarrhoea, tended to occur in the vagotomized group.

Table VII.—POSTOPERATIVE SYMPTOMS

SYMPTOM	PYLOROPLASTY (28 patients)		VAGOTOMY AND PYLOROPLASTY (32 patients)	
	No. of Patients	Per cent	No. of Patients	Per cent
Fullness	13	46·4	11	34·4
Vomiting	4	14·5	2	6·3
Colic	4	14·5	4	12·5
Diarrhoea	5	17·9	7	21·9
Dumping	4	14·5	8	25·0
Hypoglycaemia	4	14·5	6	15·6

Comparison between the two groups revealed no significant difference for any symptom.

Table VIII.—CORRELATION OF THE FUNCTIONAL RESULT WITH THE PREOPERATIVE EVIDENCE FOR DUODENAL ULCER

FUNCTIONAL RESULT	CLINICAL EVIDENCE		RADIOLOGICAL EVIDENCE	
	Weak	Strong	Weak	Strong
Good and satisfactory (Visick grades 1, 2, and 3a)	8	12	8	12
Poor (Visick grade 4)	5	7	8	4
	13	19	16	16

Comparison between those with weak evidence and those with strong evidence for duodenal ulcer showed no significant difference in the incidence of poor results.

Correlation of Postoperative Results with Preoperative State.—The 32 patients who had pyloroplasty alone were classified according to the features of their pain as listed in *Table II*. They were then grouped according to whether the clinical evidence for duodenal ulcer was weak or strong. The poor results were equally divided between these two groups (*Table VIII*).

A similar comparison was made using the radiological features. Although more of those with weak evidence for ulcer did poorly than those with strong evidence, this difference was far from significant (*Table VIII*).

Preoperative acid studies were available for 20 of the 32 patients and the proportion of poor functional results was similar whether the output was greater or less than 25 mEq. per hour (40 per cent and 30 per cent respectively).

DISCUSSION

The problem of the disappearing ulcer is far from negligible, arising in 5·3 per cent of all clinically diagnosed duodenal ulcers requiring surgical treatment in our department. This incidence is somewhat unreal because of the retrospective nature of the study. It was not possible to determine whether all the patients who received definitive ulcer surgery had signs of ulcer disease demonstrable at operation. Similarly the patients were not classified preoperatively although obviously the diagnosis of duodenal ulcer was made with varying degrees of conviction.

The matched group of vagotomized patients was included to avoid bias in the postoperative assessment and to afford a comparison of postoperative side-effects. The incidence of preoperative symptoms and radiological signs is in accord with common experience. In comparison, the study group tended to have atypical symptoms and less definite radiological changes, which possibly reflects a heterogeneous composition.

The patients who had pyloroplasty alone did very badly, with 37·5 per cent poor functional results. The matched group of vagotomized patients did rather better than an unselected series. This was due to the low risk of recurrent ulcers by virtue of the completeness of their vagotomy. They were probably further selected in that submitting successfully to two intubations (insulin tests) would tend to eliminate some 'unsatisfied' patients.

Could the poor results achieved by pyloroplasty alone be anticipated? It seems reasonable to speculate that those patients in whom no ulcer was found at operation may have consisted of several subgroups. First, there are those who had true ulcer disease which was missed at surgery because of healing without noticeable scarring or because of a post-bulbar position. Up to one-half of such patients could be expected to develop recurrent ulcer if their course was to parallel that after gastro-enterostomy alone (Lewisohn, 1954; Tanner, 1959) despite the early encouraging reports of the use of pyloroplasty alone (Horsley, 1926; Judd and Nagel, 1927). Secondly, there are those patients with the pseudo-ulcer syndrome. Barfred (1959) described a significant percentage of patients with duodenal ulcer symptoms, some with an irritable cap on barium studies, whom he considered not to have duodenal ulcer but rather functional pyloroduodenal irritability which could be likened to spastic colon. Many of his patients, in fact, had a high acid output and nearly one-third developed duodenal ulcers at a later date, so that a high proportion of patients in this subgroup could be expected to develop recurrent ulcer symptoms. One can only surmise that if any patients had an entirely functional disorder some might be improved and the remainder would continue to have symptoms of epigastric distress indistinguishable from a peptic ulcer syndrome. The subsequent satisfactory results from secondary vagotomy lends strength to the suggestion that at least some of these patients actually had a duodenal ulcer or preduodenal ulcer state. Thirdly, the possibility of undiagnosed, unrelated disease does exist despite a diligent search at operation, and symptoms due to this would persist after pyloroplasty.

Unfortunately it does not seem possible to preselect these patients on clinical grounds. Despite the obvious tendency of these patients as a group to have a less than typical pattern of pain, it is well established that all genuine duodenal ulcers do not provoke classic symptoms. Radiological signs will frequently confirm the diagnosis but up to 10 per cent of later proved duodenal ulcers will not be diagnosed b routine investigation. Thus, the few patients wit normal barium-meal examinations should not necessarily have been denied surgery. Minor changes suc as an irritable cap are just as likely as not to b associated with a duodenal ulcer (Templeton, 1965) whereas persistent deformities of the duodenal ca are found not to be due to duodenal ulcer disease i less than 5 per cent of cases (Bockus, 1963). Th patients with moderate or marked changes o barium-meal examination and no ulcer at operatio may have included these few exceptions. Alternatively the months between radiographic examination an operation may have allowed healing without noticeabl scarring.

Finally, a true peptic ulcer syndrome may develo after pyloroplasty owing to gastric ulceration. It ha recently been suggested that pyloroplasty may b ulcerogenic on the grounds of prolonged antral gastri release due to delayed gastric emptying of solid foo and antral neutralization with alkaline reflux (Lulu Lawson, and Dragstedt, 1971). Indeed, Woodward Eisenberg, and Dragstedt (1967) warn agains pyloroplasty alone for the treatment of gastric ulce and report 3 recurrences after such a procedure.

Although there is a temptation to regard pyloroplasty as a non-destructive operation there is accumulating evidence to the contrary. Animal experiment have shown that pyloroplasty results in altere contraction patterns of the antrum and the first par of the duodenum so that the two contract simultaneously, preventing a pressure gradient betwee them (Ludwick, Whiley, and Bass, 1969). There i also evidence of delayed emptying for semi-solid food after pyloroplasty alone in dogs but more rapi emptying with liquids (Lulu and others, 1971) Buckler (1967) found a tendency for a small group o patients to have delayed emptying of semi-solid foo after pyloroplasty. Aylett, Wastell, and Wise (1969 found rapid emptying of a liquid meal after vagotom and pyloroplasty which they believed to be due largel to the pyloroplasty. This has been shown to be du to an 'incontinent stomach' and to be dependent o posture (McKelvey, 1970). Thus the effects o pyloroplasty on gastric emptying are similar to thos of vagotomy and pyloroplasty. As the genera consensus holds that many of the post-cibal symptom are due to the rapid emptying of hyper-osmola liquid into the small intestine, it is not surprising t find these symptoms to be present to virtually th same extent after both pyloroplasty alone an complete vagotomy and pyloroplasty. The incidenc found in the present study closely resembles that fo combined large series of patients after vagotomy an pyloroplasty (Cox, Spencer, and Tinker, 1969). similar experience of dumping symptoms afte pyloroplasty alone has been recently reporte (Amdrup, Nielson, and Jensen, 1970).

It is not to be supposed that the vagotomy i without effect. Rapid emptying of hyperosmola glucose solution was found after vagotomy alone when compared with normal controls (Hall and Read 1970). Diarrhoea, which is undoubtedly a majo complication after vagotomy, appeared to be les severe when drainage was added (Pollock, 1952). I the same study there was a notable incidence o hypoglycaemia after vagotomy alone. There is als evidence that selective (gastric) vagotomy reduces the incidence of diarrhoea to a certain extent (Kennedy and Connell, 1970; Kronberg, Malmstrom, and Christiansen, 1970).

Withholding vagal section does not protect the patient from at least moderate post-cibal symptoms, as found in the group of patients presented here. More than one-third of patients can be expected to have recurrent ulcer symptoms. It is not possible to predict on clinical or radiological grounds which patients will do badly. We therefore recommend that all patients requiring surgery in whom a reasonable diagnosis of duodenal ulcer is made should have a definitive ulcer operation even if no ulcer is obvious at exploration, provided that careful laparotomy excludes other pathology. The wisdom of this advice can only be confirmed by a prospective clinical trial.

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TREATMENT OF GASTRIC ULCER BY HIGHLY SELECTIVE VAGOTOMY WITHOUT A DRAINAGE PROCEDURE: AN INTERIM REPORT

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SUMMARY

Fourteen patients with gastric ulcer alone and 5 patients with combined gastric and duodenal ulceration have been treated by highly selective (parietal-cell) vagotomy without a drainage procedure (H.S.V.) in the past 3 years. Before operation no evidence of gastric stasis was found, clinically, radiologically, or during tests of gastric secretion. Spontaneous acid output was low. Acid output in response to a test meal of meat extract was also found to be low. There was no evidence that in the patients with gastric ulcer alone the ulcer was due to pyloric channel disease with excessive release of gastrin by the antrum.

Each gastric ulcer was proved by frozen-section examination to be benign at the time of operation. No problems with gastric stasis were encountered in the early postoperative period. The vagotomy was shown to be complete on insulin testing in each of the 17 patients tested.

Follow-up ranges from 1 month to 3 years. The clinical progress of the patients has been good, and none has symptoms suggestive of recurrent ulceration or of gastric retention. Barium-meal examination in 11 patients who were followed up for more than 9 months showed satisfactory gastric emptying, without recurrent ulceration. While the need for much longer follow-up is obvious, these preliminary results are encouraging. Further trial of H.S.V. for gastric ulcer, preferably in the form of a prospective, randomized comparison with Billroth-I gastrectomy, now seems desirable.

PROVIDED that his ulcer could be induced to heal and his stomach to empty satisfactorily, the patient with a gastric ulcer would probably be better off with his pylorus than without it; better with his whole stomach than bereft of half of it. Encouraged by our results with highly selective vagotomy for duodenal ulcer (Johnston and Wilkinson, 1970) we have treated 19 patients who had benign gastric ulcer without evidence of gastric stasis by highly selective vagotomy without a drainage procedure (H.S.V.). In this operation only the acid- and pepsin-secreting parts of the stomach are vagally denervated, the vagal nerve-supply to the antral 'pump' being carefully preserved (Amdrup and Jensen, 1970; Johnston and Wilkinson, 1970). The antrum, pylorus, and duodenum are left completely intact. Compared with Billroth-I gastrectomy, this operation should have a lower operative mortality, produce fewer side-effects such as dumping, and be followed by less weight-loss and anaemia in the long term.

PATIENTS AND METHODS

Patients.—Full details are given in *Table I.* Of the 19 patients, 16 were male and 3 were female. Many of the patients were underweight. Fourteen had gastric ulcer alone, and 5 had gastric ulceration with scarring of the duodenum. The duodenal ulcer appeared to be active in only 2 patients. Most of the patients with gastric ulcer alone had received full medical treatment, including carbenoxolone sodium, and were referred for surgery either because the ulcer had failed to heal or because it had recurred. One patient was operated on as an emergency for haematemesis. Thirteen of the ulcers were situated near the incisura angularis or more distally, 2 were in the middle of the lesser curvature, and 4 were in the upper third of the stomach. At the time of operation 15 of the 19 ulcers were found to be active and 4 had healed. Initially, for technical reasons, only a few selected patients with gastric ulcer were treated by H.S.V., but with increasing experience it was found possible to treat all patients in this way, and the last 14 patients form a consecutive series.

The possibility of ulcer cancer was excluded in each patient by the use of a combination of tests: barium-meal examination, fibrescopy, studies of acid output, and finally by excision of the ulcer with frozen-section examination by an experienced pathologist at the time of operation. Cancer was not found unexpectedly at frozen-section examination in any patient with gastric ulcer.

The possibility that the gastric ulcer had arisen as a result of gastric stasis was excluded by clinical methods, supplemented by the information obtained from barium-meal examination and by measurement of the volume of resting juice in the stomach at the start of preoperative tests of gastric secretion. At operation the absence of pyloroduodenal narrowing was confirmed in each patient by the passage of a finger or Hegar's dilators through the pylorus and proximal duodenum.

Tests of Gastric Secretion.—

1. *Spontaneous Acid Output (B.A.O.) and Maximal Acid Output (P.A.O.(PG)).*—Before operation spontaneous acid output (in 1 hour) and the response to intramuscular pentagastrin (Johnston and Jepson, 1967), in a dose of 6 μg. per kg. body-weight, were measured in 17 patients. The pentagastrin response was expressed as P.A.O.(PG) (output in the peak 20-minute period × 3, in mEq. per hour). Measurement of B.A.O. and P.A.O.(PG) was repeated 4–8 days after operation in each patient. The dose of pentagastrin used then was 10 μg. per kg. body-weight (Jepson, Lari, and Johnston, 1968).

2. *Response to Meat Extract (Oxo)* (Welbourn and Burns, 1964; Giles and Clark, 1966; Johnston, Humphrey, Smith, and Wilkinson, 1971).—This test was used as a measure of the activity of the gastric antrum. Gastrin release was stimulated by placing 100 ml. of Oxo solution at pH 7 and room temperature into the stomach via a nasogastric tube. Nine patients, all of whom had gastric ulcer alone, underwent this test before operation. Acid outpu expressed as P.A.O.(Oxo) (peak 20-minute output × 3, in mEq. per hour).

3. *Hollander Insulin Test* (Hollander, 1948).— test was performed 4–8 days after operation i patients and omitted in 2 on account of age and ca vascular disease. The dose of insulin used was o per kg. Venous blood-samples withdrawn 30 an minutes after the insulin injection established tha blood-glucose concentration had decreased to less 35 mg. per 100 ml. in each test. Acid output expressed as P.A.O.(I) (peak 30-minute output in mEq. per hour).

The methods used in these tests have been descr previously (Johnston and Jepson, 1967; Johnston Wilkinson, 1970; Johnston and others, 1 Titration was to the pH 7 end-point, but B.A.O. also expressed as 'free' acid, with titration to 3·5.

Clinical Result.—This was judged at the Ga Follow-up Clinic by a panel of observers who kept in ignorance of the preoperative diagnosis the type of operation which had been performed they had written down their collective assessme accordance with a modified Visick classifica (Visick, 1948). Visick grade 1 signifies a pe result; 2, near perfection with only trivial side-ef easily controlled by care; 4 means failure du recurrent ulceration or severe side-effects, whi signifies a satisfactory result with freedom from pain but somewhat marred by side-effects which not be entirely avoided. No formal assessment attempted in 8 patients who were followed up less than 9 months. Their clinical progress has satisfactory to date.

Barium-meal Examination.—This was ca out in 11 patients who had been followed up f least 9 months after operation.

Operative Technique.—The technique of H. for duodenal ulcer has been described previousl detail (Amdrup and Jensen, 1970; Johnston Wilkinson, 1970) (*Fig.* 1). The presence of a ga ulcer poses special problems: first, because the is usually close to the antral nerves (nerve Latarjet) which must be preserved, and, secon because the ulcer must be excised and submitte frozen-section examination to exclude the possib of malignancy. At first these factors deterred us f using H.S.V. in any except the occasional cas gastric ulcer, but with increasing experience we found it possible to treat all cases of gastric ulce this way. A transgastric approach to the ulcer vi appropriately sited gastrotomy incision is prefe (*Fig.* 2) because it is difficult to excise the ulcer f outside the stomach without damaging the nerve Latarjet. The entire ulcer, together with a dis surrounding mucosa, is excised with the diathe blade or scalpel. The fibrous base of the ulcer usually so thick that the stomach wall was perfor during this manœuvre in only 6 of the 19 ca Bleeding was controlled by deeply placed interru catgut sutures. The gastrotomy incision is m longitudinally and is placed, whenever possible the proximal three-quarters of the stomach whic to be vagally denervated. The incision is cl longitudinally. In the case of an ulcer that is dist the incisura the gastrotomy has to be made in

Table I.—CLINICAL DETAILS OF THE PATIENTS IN THE PRESENT SERIES

CASE NO.	AGE AND SEX	WEIGHT (kg.)	LENGTH OF ULCER HISTORY (yr.)	GASTRIC SECRETION									CLINICAL RESULT	
				B.A.O. (titre to *p*H 7)		P.A.O. (PG)			P.A.O. (Oxo)		P.A.O. (I)			
				B (mEq./hr.)	*A* (mEq./hr.)	*B* (mEq./hr.)	*A* (mEq./hr.)	*Reduction* (per cent)	*B* (mEq./hr.)	*Percentage of P.A.O. (PG)*	*A* (+ve/−ve)	*A* (mEq./hr.)	*Length of Follow-up* (mth.)	*Visick Grade*
1	39 M.	70	20	4·06	0·79	18·75	9·75	48·00	—	—	−ve	0·38	36	2
2	37 M.	59	15	2·08	0·30	25·53	8·43	66·99	15·12	59·23	−ve	0·62	30	1
3	47 M.	70	3	1·26	0·00	27·90	5·13	81·61	—	—	−ve	0·00	17	2
4	33 M.	61	2	2·88	0·00	28·38	2·16	92·39	6·00	21·14	−ve	0·00	14	3
5	26 M.	43	3	0·24	0·15	18·06	7·86	56·48	0·57	3·16	−ve	0·00	13	2
6	41 M.	65	5	2·87	0·61	28·71	11·34	60·50	8·32	28·98	−ve	0·00	12	2
7	60 M.	58	3	0·03	0·32	18·60	10·80	41·94	—	—	−ve	0·00	9	2
8	54 F.	76	2	6·58	0·00	44·61	14·91	66·58	12·48	27·98	−ve	0·00	12	3
9	48 M.	65	4	3·21	0·12	13·83	3·81	72·45	—	—	−ve	0·00	9	1
10	55 M.	57	2	4·50	0·34	33·84	9·09	73·14	0·30	0·89	−ve	1·24	6	—
11	71 M.	63	0	—	1·05	—	17·85	—	—	—	Not performed		5	—
12	50 M.	64	10	0·00	0·00	26·19	8·46	67·70	0·00	0·00	−ve	0·00	1	—
13	60 F.	54	12	2·10	1·55	15·75	9·42	40·19	3·27	20·76	−ve	0·00	1	—
14	48 M.	54	5	0·46	0·00	19·83	5·04	74·58	4·41	22·24	−ve	0·00	1	—
Mean of 13 cases ± 1 S.E. (Nos. 2–14)	48·46 ± 3·38	60·69 ± 2·27	5·08 ± 1·24	2·19 ± 0·58 (12) Mean reduction 76·4 ± 10 per cent	0·29 ± 0·13 (12)	25·10 ± 2·50 (12)	8·04 ± 1·03 (12)	66·21 ± 4·33 (12)	5·61 ± 1·81 (9)	20·49 ± 6·16 (9)	All −ve		7·69 ± 2·22	— — —
15	45 M.	61	18	4·57	0·80	50·31	17·01	66·19	—	—	−ve	0·30	22	1
16	48 M.	76	29	7·32	0·00	59·67	25·44	57·37	—	—	−ve	0·00	26	2
17	71 M.	57	10	3·43	0·35	48·00	26·25	45·31	—	—	−ve	0·38	7	Short follow-up
18	54 F.	58	25	0·82	0·62	23·64	9·24	60·91	—	—	−ve	0·56	3	—
19	63 M.	58	30	—	0·00	—	17·40	—	—	—	Not performed		2	—
Mean	50·00 ± 2·75 (19)	61·53 ± 1·82 (19)	22·40 ± 3·75 (5)	4·04 ± 1·35 (4) 74·2 ± 17 per cent reduction	0·45 ± 0·17	45·41 ± 7·68 (4)	19·49 ± 4·00 (4)	57·45 ± 4·43 (4)	—	—	All −ve		11·89 ± 2·35 (19)	3 with grade 1 6 with grade 2 2 with grade 3 (11 patients at 9 months or more after operation)

Cases 1–14 had gastric ulcer alone; *Cases* 15–19 had both gastric and duodenal ulcers. *Cases* 2–19 were treated by H.S.V. alone; *Case* 1 had a 70-g. segmental gastric resection in addition to H.S.V. *B*, Before operation. *A*, 5–9 days after operation.

antral region, on whose motility gastric emptying will depend. The incision should then be placed not in the middle of the anterior gastric wall but along the greater curvature, so that denervation of the inferior half of the anterior wall of the antrum may be avoided. Again the incision is closed longitudinally. Edge-to-edge apposition without inversion is the aim. Oedema and fibrosis around the ulcer often obliterate the normal plane of dissection between the lesser curvature of the stomach and the lesser omentum which contains the nerves to the antrum. This problem can be overcome by the use of a combined approach from the front and from the lesser sac after mobilization of the greater curvature, and by the ligation of tissues in continuity with transfixion sutures placed close to the wall of the stomach. A finger, or a Hegar's dilator, is passed through the pylorus into the second part of the duodenum and if the 'pyloric channel' does not admit the distal finger-joint or a 14-mm. dilator (Kirk, 1970) some degree of obstruction to the gastric outlet must be suspected. In these circumstances it might be advisable to resort to gastric resection or to a vagotomy with drainage procedure instead of H.S.V. Stenosis was found in only 1 of our patients and was treated by simple digital dilatation.

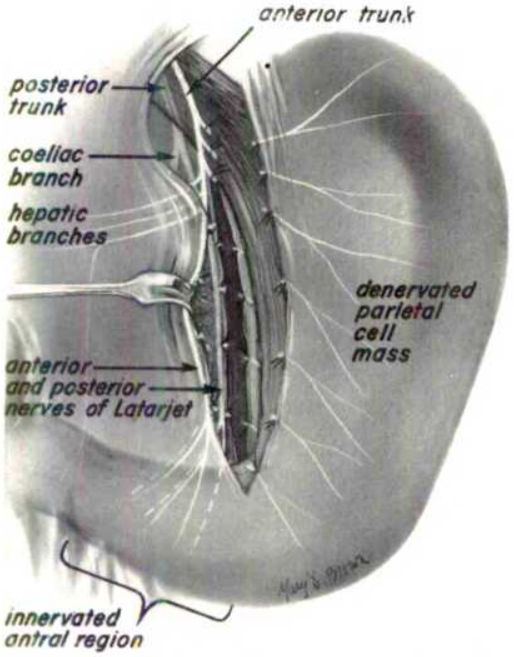

FIG. 1.—Highly selective vagotomy without a drainage procedure. The anterior and posterior vagal nerves of Latarjet to the antral region are preserved in addition to the hepatic and coeliac branches of the vagus. Some artistic licence has been used in order to depict the posterior nerve of Latarjet.

The length of prepyloric stomach left innervated ranged from 5 to 8 cm. Operating time varied from 60 to 150 minutes, with a mean of 110 minutes.

RESULTS

Clinical.—

In Hospital.—The patients' convalescence was without incident and none developed gastric retention. The mean length of stay in hospital after operation was 12 days.

Follow-up.—The patients have fared well since their discharge from hospital. Of the 11 who have been followed up for more than 9 months, 3 are classified as Visick grade 1, 6 as grade 2, and 2 as grade 3. The commonest side-effect is epigastric fullness after meals, which causes almost half the patients to restrict the size of their main meal to about two-thirds of what they ate formerly. Of the 2 patients classified as Visick grade 3, 1 has episodic diarrhoea of moderate severity, and the other experiences epigastric discomfort which is unlike the pain of his ulcer. None of the patients has experienced pain of ulcer type and none has symptoms suggestive of gastric stasis.

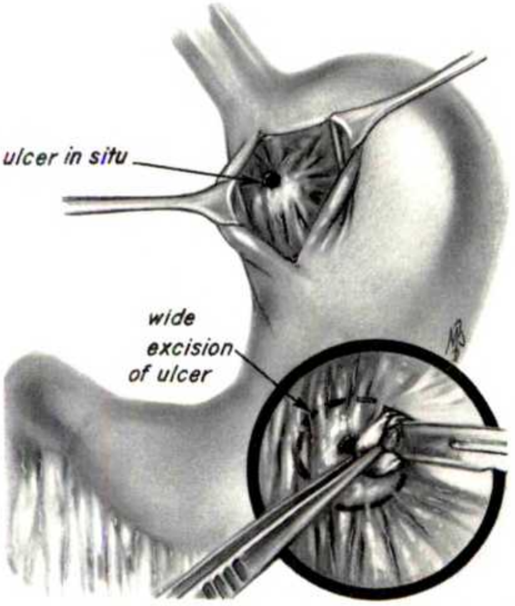

FIG. 2.—Malignancy is excluded by complete excision of the ulcer via a longitudinal gastrotomy followed by immediate frozen-section examination of the specimen.

Barium-meal Examination.—In the 11 patients who had been followed up for at least 9 months barium-meal examination revealed no sign of recurrent ulceration. The volume of resting juice in the stomach was not excessive and gastric emptying was satisfactory.

Gastric Secretion (*Table I*).—

1. *Response to Meat Extract before Operation.*—Mean peak acid output in response to Oxo solution (P.A.O. (Oxo)) was 5·6 mEq. per hour in the 9 patients who were tested. This was, on average, only 20 per cent of their P.A.O.(PG). There was no secretory response to the meat extract in 3 of the 9 patients. (These figures should be compared with the mean P.A.O. (Oxo) before operation in 26 patients with duodenal ulcer of 21·7 mEq. per hour, which was 47·8 per cent of their P.A.O. (PG).)

2. *Spontaneous Acid Output (B.A.O.).*—Only 2 patients were found to be still secreting 'free' acid after operation. B.A.O. (to *p*H 7) decreased from a

mean of 2·2 mEq. per hour before H.S.V. to 0·3 mEq. per hour after H.S.V. in 12 patients with gastric ulcer alone. The mean reduction was only 76 per cent, largely because there was little reduction in B.A.O. in 2 patients who were hyposecretors before operation.

3. *Response to Pentagastrin* (*P.A.O.(PG)*).—Mean P.A.O. (PG) in patients with gastric ulcer alone was 25·1 mEq. per hour before H.S.V. and 8·0 mEq. per hour after H.S.V., a mean reduction of 66 per cent. The mean reduction in 4 patients with combined gastric and duodenal ulcers was 57 per cent.

4. *Insulin Test.*—All 17 tests were negative, signifying that the vagotomies were complete. They were negative by Hollander's criteria and also by all other criteria since there was no response in any test.

DISCUSSION

It should be pointed out that the follow-up of our patients is very brief, only 9 patients having been followed up for more than 1 year and none for longer than 3 years. Hence no claims can be made for the effectiveness of H.S.V. in curing gastric ulcer in the long term. On the other hand, there is good evidence, both clinical and radiological, that gastric emptying is satisfactory, despite the absence of a drainage procedure. If gastric stasis has not become manifest within a year of operation it is unlikely to develop at a later date. Thus, one potential cause of recurrent gastric ulceration appears to be absent.

Truncal or selective vagotomy with a drainage procedure provides a cure in most cases of gastric ulcer (Dragstedt and Woodward, 1951; Hendry and Bahrani, 1965; Burge, 1966; Forrest, 1969; McNeill, McAdam, and Hutchison, 1969; Duthie, Moore, Bardsley, and Clark, 1970; De Miguel, 1970). The incidence of recurrence, however, is somewhat higher than that which follows Billroth-I gastrectomy. This achievement is all the more impressive when one considers that 20 per cent of the vagotomies are likely to have been incomplete (Fawcett, Johnston, and Duthie, 1969). Highly selective vagotomy (selective proximal vagotomy) *with a drainage procedure* also yields good long-term results in the surgical treatment of gastric ulcer (Holle and Hart, 1967). The results of the present study indicate that highly selective vagotomy *without a drainage procedure* (H.S.V.) gives good clinical results in the treatment of patients with benign gastric ulcer, at least in the short term. Particularly encouraging features were the complete relief from ulcer pain experienced by all the patients, and the absence of vomiting and of other symptoms of gastric stasis. The results of postoperative barium-meal examinations were satisfactory although it is recognized that the emptying of barium does not necessarily reflect the emptying of solid food. The results of the secretory tests were also satisfactory, with evidence of completeness of the parietal-cell vagotomy in each case, virtual abolition of spontaneous secretion of 'free' acid, and reduction of the peak response to pentagastrin (P.A.O. (PG)) by 66 per cent.

Certain important objections to the surgical approach which we have adopted will now be considered. It has been suggested, for example, that H.S.V. is illogical, if the Dragstedt (1956, 1971) theory of the aetiology of gastric ulceration is assumed to be correct, that it is dangerous, because of the risk that an ulcer cancer will be missed, and finally that the results of Billroth-I gastrectomy for gastric ulcer are so eminently satisfactory and so clearly better than those of vagotomy with a drainage procedure that any change in surgical management is quite unjustifiable. Let us examine each of these objections in turn.

According to Dragstedt (1956, 1971), gastric ulceration develops as a result of gastric stasis, excessive release of gastrin, and the resulting gastric hypersecretion. Certainly, it is true that anything which causes delayed gastric emptying, such as pyloric stenosis (Burge, 1966) or complete gastric vagotomy (Linares, de la Rosa, Woodward, and Dragstedt, 1964), is liable to lead to gastric ulceration. However, although stasis causes gastric ulceration it does not follow that the gastric ulcers which we see in clinical practice are caused by stasis. Studies of gastric emptying which were performed in patients with gastric ulcer by Buckler (1967) and Griffith, Owen, Campbell, and Shields (1968) suggest that gastric emptying of solid food is within normal limits in most patients with gastric ulcer, although a few individuals do have delayed emptying. In our own patients the following features led us to believe that gastric stasis was not the cause of their ulcer: they did not vomit copiously; they did not have a succussion splash; there was no delay in the emptying of barium before operation; when a nasogastric tube was passed the volume of the resting juice in the stomach was not excessive (less than 150 ml.), and food residues were not found. Spontaneous acid output was low/normal, suggesting that circulating gastrin levels were not unduly high, because the finding of maximal acid outputs within the normal range implied that the parietal cell mass was normal in size. The acid responses to a test meal of meat extract, far from being excessive, as might have been expected if the Dragstedt theory were correct, were in fact small—only 20 per cent of the maximal acid output and about one-quarter of the acid response to meat extract of patients with duodenal ulcer. At operation a finger was passed from the stomach into the second part of the duodenum in each patient. No sign of pyloric obstruction or of duodenal obstruction was found in any of the patients with gastric ulcer alone and only 1 of the 5 patients with combined gastric and duodenal ulcers was found to have pyloroduodenal stenosis (defined by Kirk (1970) as a pyloroduodenal channel which will not admit the distal interphalangeal joint of the index finger or a 14-mm. Hegar dilator).

As to the problem of ulcer cancer, clearly the treatment of a potentially curable lesion by a conservative operation is a tragic error. As many as 5–10 per cent of patients whose gastric ulcer appears to be benign on gross inspection have, in fact, an occult ulcer cancer (Forrest, 1969). If such cancers are treated by radical resection the prognosis is much better than that of gastric cancer in general (Runyeon and Hoerr, 1957; Brown, Cain, and Dockerty, 1961). While all this is beyond dispute, we think that the chances of an ulcer cancer being missed can be reduced to a minimum by the use of clinical methods supplemented by fibrescopic examination of the ulcer, with biopsy and cytological examination. An accuracy rate of 99·3 per cent in differentiating between benign and malignant ulcers of the stomach can be achieved by such means (Arnold, Hampton, Olin, Glass, and Carruth, 1960). Finally, at operation the surgeon has a further opportunity to inspect the ulcer directly and if he still harbours the slightest suspicion that the ulcer is malignant he should perform a gastrectomy. Even if the ulcer appears benign, it should always be exised *in toto*, or at the least its epithelial margin should be excised, and the specimen submitted to immediate frozen-section examination by an experienced pathologist. In our opinion the routine use of these measures will virtually eliminate the possibility that an early carcinoma will be treated in an inappropriate fashion.

It might well be asked what possible advantages H.S.V. could possess compared with the time-honoured Billroth-I gastrectomy for gastric ulcer, which yields good results in 80–90 per cent of patients and has a recurrent ulcer rate of 0–2 per cent (Swynnerton and Tanner, 1953; Duthie and others, 1970). We would answer that an operation which involves neither resection of one-half to two-thirds of the stomach nor an anastomosis is likely to be safer than one which does; statistically significantly safer, not within any individual surgeon's experience but in the global context of the treatment of many thousands of patients. We have now treated 170 patients with duodenal or gastric ulcer by H.S.V. without operative mortality and indeed without any major postoperative complication related to the operative procedure. Secondly, in the case of gastrectomy what is done cannot be undone. Many patients will develop iron-deficiency anaemia and a few will become thin, anaemic, osteoporotic 'gastric cripples'. Their lost stomach cannot be restored to them. Such sequelae should be rare after H.S.V., which preserves the entire gastric reservoir with its emptying still regulated by a normally innervated antropyloroduodenal segment. Dumping has been found to be significantly less common after H.S.V. than after vagotomy with a drainage procedure (Humphrey, Wilkinson, and Johnston, 1972), and will probably also prove to be less common than after gastrectomy. If the ulcer should recur after H.S.V. effective treatment is available in the form of a gastrectomy. Admittedly, Duthie and others (1970) have shown that a Billroth-I gastrectomy yields better results than truncal vagotomy and pyloroplasty in the treatment of benign gastric ulcer. H.S.V., however, is followed by significantly fewer side-effects, such as dumping and diarrhoea, than is vagotomy with drainage (Humphrey, Walker, Pulvertaft, Goligher, and Johnston, 1971; Humphrey and others, 1972) when used in the treatment of duodenal ulcer, and hence it may well prove superior to vagotomy and drainage in the treatment of gastric ulcer also.

In conclusion, it has been shown that patients with gastric ulcer can be treated successfully in the short term by an operation which entails neither gastric resection nor destruction or by-pass of the pylorus. The potential advantages of such a procedure are obvious but its use should probably be confined at present to centres in which complete physiological evaluation and prolonged clinical follow-up of the patients are assured. Longer follow-up of larger numbers of patients and controlled trials are needed to show whether the early promise of H.S.V. in the treatment of gastric ulcer will be fulfilled.

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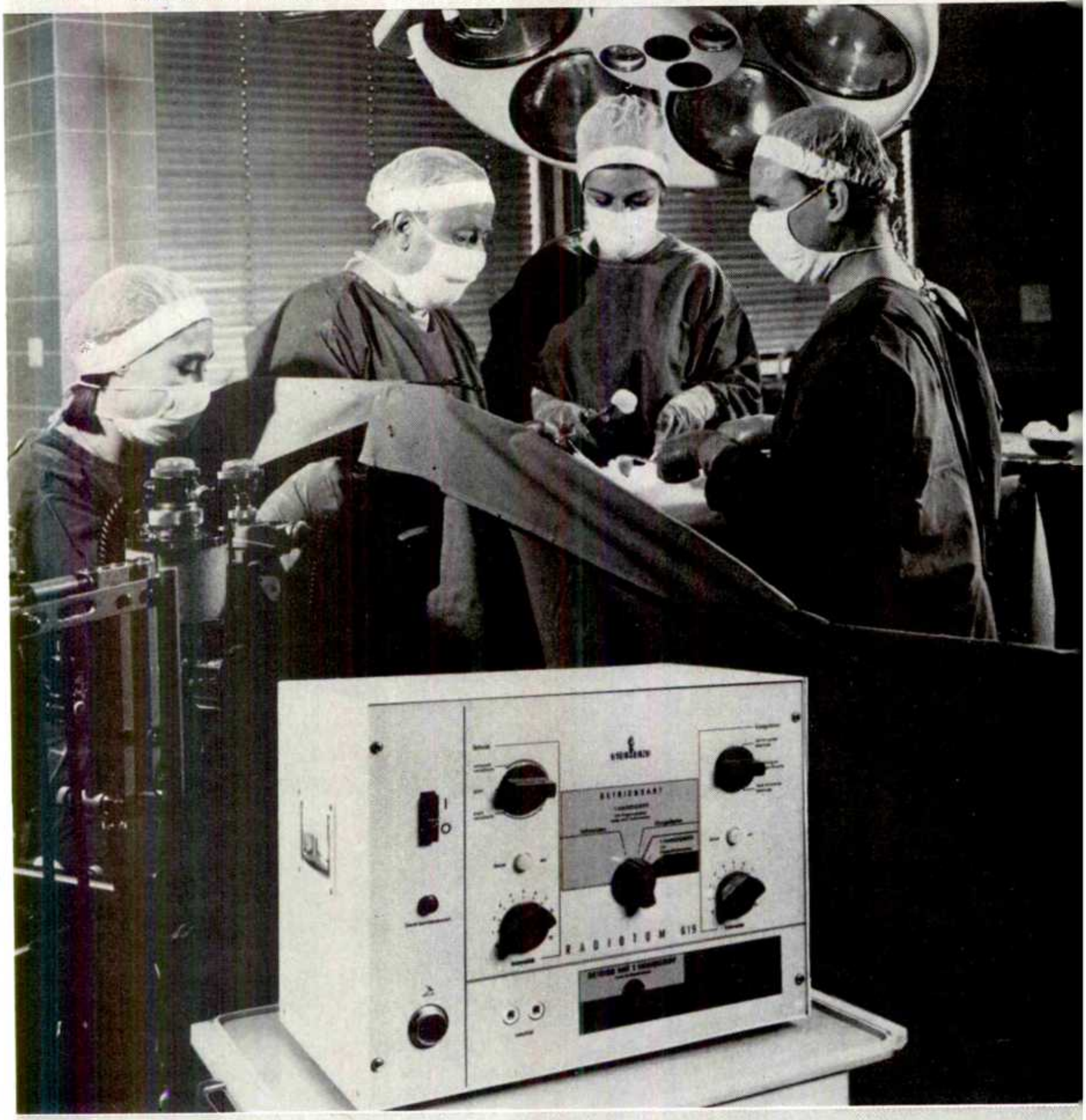

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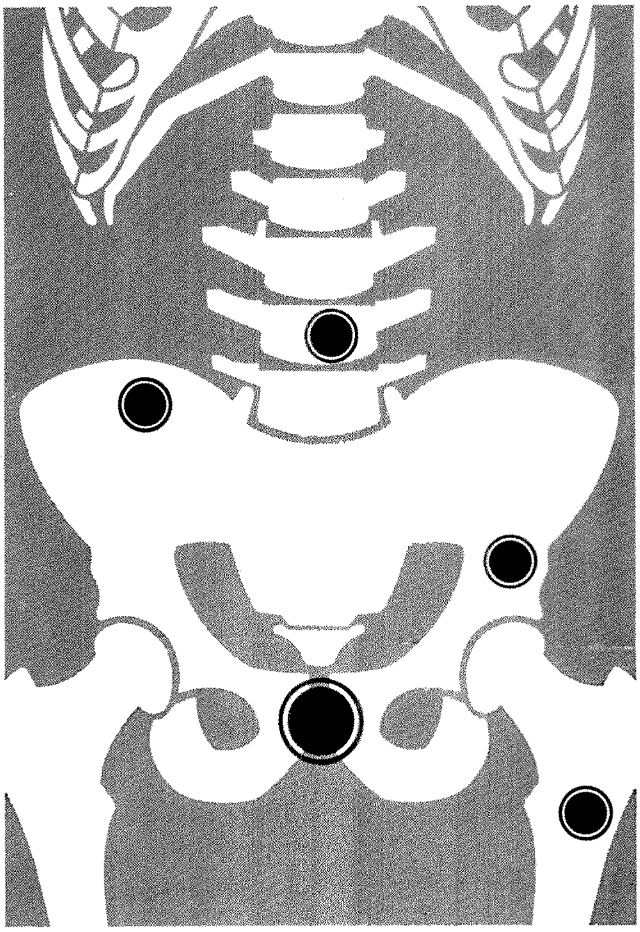

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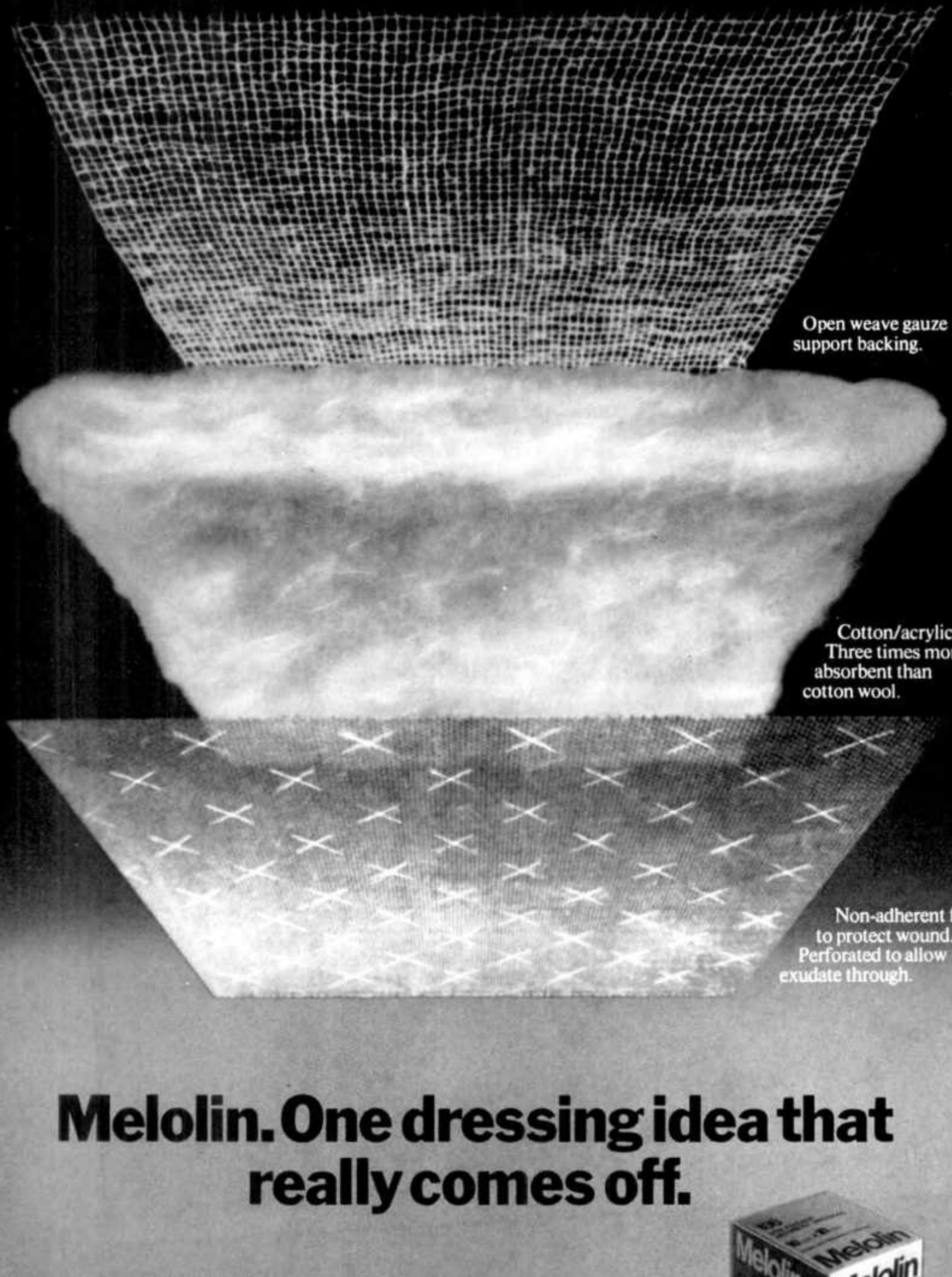
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THE VALUE OF UPPER GASTRO-INTESTINAL FIBRESCOPY

By IAN McCOLL
DEPARTMENT OF SURGERY, GUY'S HOSPITAL, LONDON

SUMMARY

In a series of 330 fibrescopies of the upper gastro-intestinal tract the most useful all-round instrument proved to be a long end-viewing panendoscope. The nature of the radiological errors revealed by endoscopy indicated that the latter is essential before embarking on surgery for antral gastric ulcers, radiographically negative dyspepsia, and further gastric surgery.

ONE of the most important advances in gastro-enterology in recent years has been the introduction of flexible fibrescopes which are much easier and safer to use than the rigid instruments and allow inspection and biopsy of every part of the oesophagus, stomach, and duodenum. The enthusiasm for these instruments has been universal, but Flavell's (1970) description of he fibrescope as 'expensive illuminated spaghetti' prompts the question of how much endoscopy really influences treatment. The present paper attempts to answer this question.

Table I.—TYPES OF FIBRESCOPES USED IN PRESENT SERIES

INSTRUMENT	FIELD	VIEW
Olympus panendoscope G.I.F. A.C.M.I. duodenoscope	Oesophagus Stomach Duodenal bulb	End
Olympus duodenoscope J.F.	Stomach Duodenum	Side
Olympus gastroscope G.F.B. and G.F.B.K.	Stomach only	Side
Olympus oesophagoscope E.F.	Oesophagus Upper stomach	End

MATERIALS AND METHODS

Six different fibrescopes were used in 330 examina-ions. Three were end viewing (Olympus panendo-cope G.I.F., Olympus oesophagoscope E.F., and the A.C.M.I. duodenoscope), and 3 were side viewing Olympus gastroscope G.F.B. and G.F.B.K. and duodenoscope J.F.). All these instruments allow a biopsy to be taken (*Table I*). The indications for ndoscopy are listed in *Table II*. Most of the patients had a barium-meal examination before endoscopy, as here is a risk of perforation of the oesophagus, specially with a side-viewing instrument, in the presence of an abnormality such as a pharyngeal pouch. Patients were examined if possible early in the morning after an 8-hour fast.

Metoclopramide hydrochloride, 20 mg. intra-muscularly, is given 1 hour before endoscopy if there is any likelihood of a full stomach, particularly following haematemesis. Atropine is given 30 minutes before to reduce bronchial secretions and to protect the heart rom vagal effects. A local anaesthetic lozenge is administered 15 minutes before and diazepam, 10–20 mg. intravenously, immediately before the examination. (Rather less than half the cases were conducted under a general anaesthetic with endotracheal intubation and muscle relaxants.) With the patient on his left side the instrument is gently advanced into the oropharynx. He is asked to swallow and although the patient often finds this difficult the attempt usually produces relaxation of the cricopharyngeus and allows the instrument to be passed into the oesophagus, the whole of which can be inspected with the end-viewing instrument, which permits suction rinsing of the lens, air insufflation, and biopsy. Provided that the instrument is advanced only when the way ahead is clear, perforation should be very rare. Fibre-oesophagoscopy is safe even in the presence of marked spinal deformities. The view obtained is incomparably better than that achieved by the rigid oesophagoscope and biopsy is a simple and safe affair. The long end-viewing duodenoscope provides a good view of the oesophagus, stomach, and duodenal bulb, but sometimes a side-viewing instrument is also required to see the antral roof, the fundus, and some aspects of the duodenal bulb and the medial wall of the second part of the duodenum.

Table II.—INDICATIONS FOR FIBRESCOPY IN 330 PATIENTS

Indication	*Percentage of Patients*
Oesophageal	18
Postoperative stomach	11
Haematemesis	8
Barium-negative dyspepsia	15
Additional clarification (duodenal and gastric ulcers and cancer)	48

Table III.—RADIOLOGICAL ERRORS

Lesion	*Percentage of Patients*	
Lesions missed		
Duodenal ulcer	10	36
Cancer	6	
Stomal ulcer	4	
Gastric ulcer	2	
Erosions, polyps	14	
Lesions erroneously reported		
Gastric ulcer	24	64
Duodenal ulcer	16	
Cardiac	14	
Stomal ulcer	10	

Radiology carried out within 3 weeks of fibrescopy.

RESULTS

The results were examined particularly in terms of their influence on treatment. Radiological errors occurred in 34 per cent of the patients (*Table III*), and these consisted of lesions which were seen endoscopically but missed radiologically, and lesions which were reported radiologically but could not be substantiated endoscopically or on subsequent follow-up. Of the radiological errors, 36 per cent were lesions which barium-meal examination had failed to detect.

Understandably the bulk of these consisted of small polyps, superficial erosions, and duodenal ulcers. The cancers were mainly small mucosal lesions, 2 of which could not be identified macroscopically in the excised specimen but which were clearly seen endoscopically and histologically. Of more practical significance were the lesions which had been detected radiologically but which did not actually exist. These comprised 64 per cent of the radiological errors, most of which had been diagnosed as antral gastric ulcers. A misleading radiological appearance was often explicable on endoscopy in terms of mucosal folds.

It is important to stress that the radiological reports were made by radiologists of very differing levels of experience, but when the radiographs were examined by expert gastro-intestinal radiologists who were ignorant of the endoscopic findings the number of errors was reduced by half.

An attempt was made to determine the influence of endoscopy on the treatment of patients (*Table IV*).

Table IV.—CHANGE IN TREATMENT AS A RESULT OF FIBRESCOPY

Change in Treatment	*Percentage of Patients*
Surgery avoided	17
Surgery precipitated	9
Total	26

In 26 per cent there was a change of treatment as a direct result of endoscopy, mainly in preventing unnecessary surgery (17 per cent). Most of these were patients who had been believed to have antral gastric ulcers. In 9 per cent surgery was precipitated by endoscopy, largely on the discovery of small cancers, gastric polyps, and duodenal ulcers. Those patients referred for endoscopy, however, constituted a selected group whose clinical problems had called for further investigation.

DISCUSSION

Endoscopy of the upper intestinal tract is complementary to barium-meal examinations. There is, o course, no question of competition between the tw methods but endoscopy is certainly helping th radiologist to define more precisely his areas c uncertainty. Although radiological errors occurred i 34 per cent of cases, this series does represent a selecte group of patients. In diagnosing oesophageal lesion there is little doubt that the fibre-oesophagoscope wi soon almost completely replace the rigid instrument In a series of 92 patients with barium-negative dyspepsia Cotton and Rosenberg (1971) reached a clinicall significant diagnosis in 34, including 2 cancers and 1 ulcers. As far as acute gastro-intestinal haemorrhag is concerned, endoscopy is proving of great value i that it can be carried out in the patient's bed in th ward under local anaesthesia with little inconvenienc In the series of Cotton and Rosenberg (1971) endoscop established a diagnosis in 86 per cent of the patien whereas radiology succeeded in only 38 per cent.

The radiology of the postoperative stomach notoriously difficult, particularly in the detection recurrent ulcers after pyloroplasty and in demo strating the presence of stomal ulceration. Radiolog is so unreliable that endoscopy is considered to b essential particularly before further surgery embarked upon. The most surprising finding in th present series was the large number of antral gastr ulcers which had been reported radiologically b which were not, in fact, present. In summary the findings would support the contention that fibrescop is essential before surgery is undertaken for antr gastric ulcers, further gastric surgery, and radi graphically negative dyspepsia.

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THE IMPORTANCE OF BILE IN REFLUX OESOPHAGITIS AND THE SUCCESS IN ITS PREVENTION BY SURGICAL MEANS

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SUMMARY

A study was instituted using the Rhesus monkey—an animal which has been found to resemble man both in respect of the anatomy of the gastro-oesophageal region and of the secretion of hydrochloric acid from the stomach—as a model.

Resection of the lower 2 cm. of the oesophagus a upper 1 cm. of the stomach produced reflux into oesophagus in all the monkeys. A bile-diversi procedure protected the monkeys from develop oesophagitis, while bile contamination of the gast juice caused oesophagitis of all grades with xception. Monkeys suffering from such oesophagitis were cured of their disease by Nissen valvulo-plasty even though the stomach was partially in the hest.

THE first record of reflux oesophagitis described as a linical condition was that by Quincke (1879), but it was not universally recognized as a common entity until the past two decades after the publication by Allison (1951). Since that time improved awareness of this disease has come about by better radiology, echniques of *p*H measurement and manometry, and more widespread endoscopy.

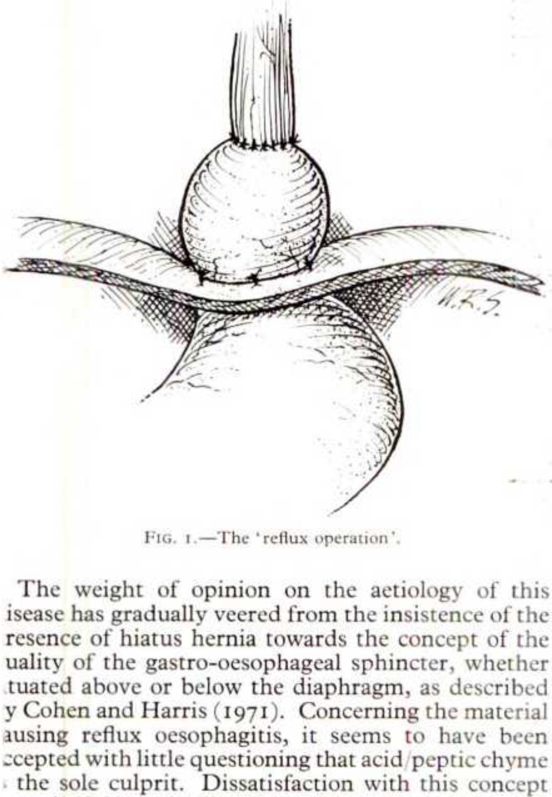

FIG. 1.—The 'reflux operation'.

The weight of opinion on the aetiology of this isease has gradually veered from the insistence of the resence of hiatus hernia towards the concept of the uality of the gastro-oesophageal sphincter, whether tuated above or below the diaphragm, as described y Cohen and Harris (1971). Concerning the material causing reflux oesophagitis, it seems to have been ccepted with little questioning that acid/peptic chyme the sole culprit. Dissatisfaction with this concept as arisen from the knowledge that oesophagitis is by o means rare after total gastrectomy nor in the presence of varying degrees of hypochlorhydria. urthermore, as most of the experimental work has been performed on non-primates it was thought that e Rhesus monkey (*Macacca mulatta*) would be more uitable for study because its maximal acid output and natomy of the oesophagus and stomach are so very lose to those of man.

MATERIALS AND METHOD

Twenty-nine monkeys were used for this experi-ment. Initially they were allocated to four groups y rota but later this was done by randomized election.

The normal monkey does not have radiological eflux demonstrable by barium when this is instilled nto the stomach. Twenty consecutive monkeys failed show reflux even under sedation when the stomach was distended with barium inserted through a naso-gastric tube. Resection of the lower 2 cm. of the oesophagus and upper 1 cm. of the stomach with an end-to-end anastomosis above the diaphragm (*Fig.* 1) caused reflux in 20 animals who were examined radiologically (*Fig.* 2). The above operation is henceforth described as the 'reflux operation'.

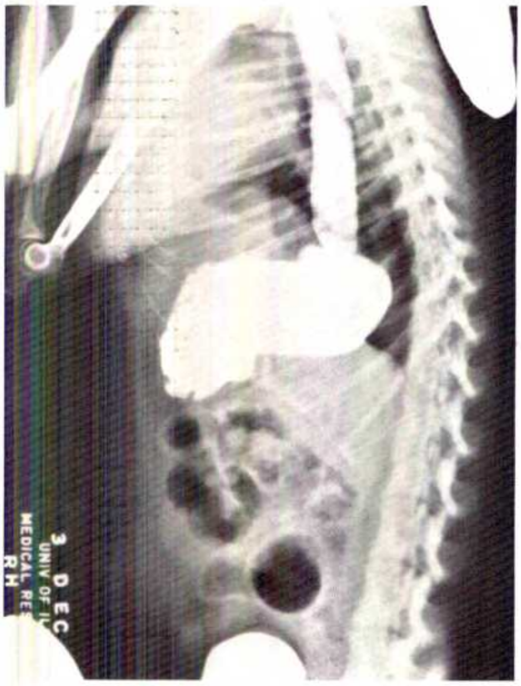

FIG. 2.—Reflux of instilled barium after the reflux operation.

Practical details of the operation are described elsewhere (Gillison, DeCastro, Nyhus, Kusakari, and Bombeck, 1972) but it should be mentioned that the vagal nerve-supply was preserved in every monkey.

Each group of monkeys was examined by an independent endoscopist at 1 and 3 months after undergoing the definitive surgery described below.

Group I.—Six monkeys had the reflux operation alone. They were studied so that the effect of the reflux of unaltered gastric juice could be seen.

Group II.—Seven monkeys had a Roux-en-Y type of diversion of duodenal juice after pylorectomy and closure of the duodenal stump. The open antrum was anastomosed to the efferent jejunum by a two-layered anastomosis (*Fig.* 3). Four weeks later the animals had the reflux operation performed through a left thoracotomy incision.

Group III.—Nine monkeys had a bile-contamination procedure performed (*Fig.* 4) before the reflux operation 4 weeks later. The common bile-duct was ligated to ensure adequate flow through the cystic duct and gall-bladder into the stomach.

Group IV.—Seven monkeys had a similar procedure to those in group III but in addition received daily depot histamine injections (2 mg. per kg.) after the cholecystogastrostomy.

The monkeys were sedated with phencyclidine hydrochloride (0·7 mg. per kg.) before endoscopy, which was done using a 7-mm. rigid bronchoscope by the endoscopist who was completely unaware of what previous surgery, if any, had been performed. His grading of oesophagitis is shown in *Table I.*

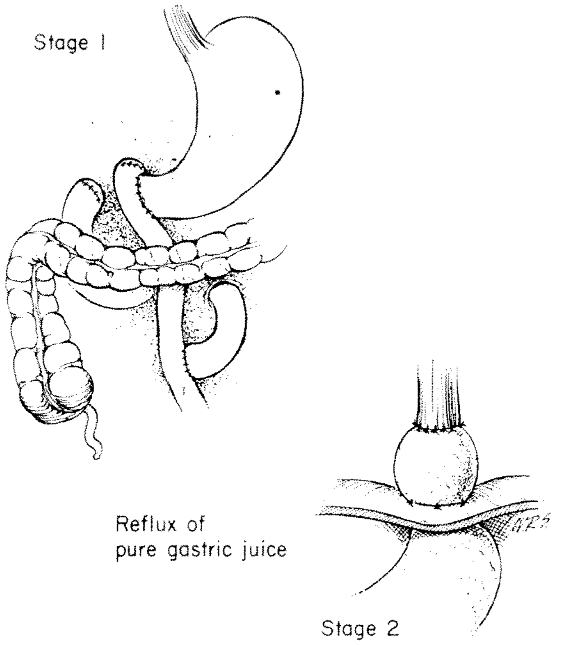

FIG. 3.—The bile-diversion operation carried out in animals in group II.

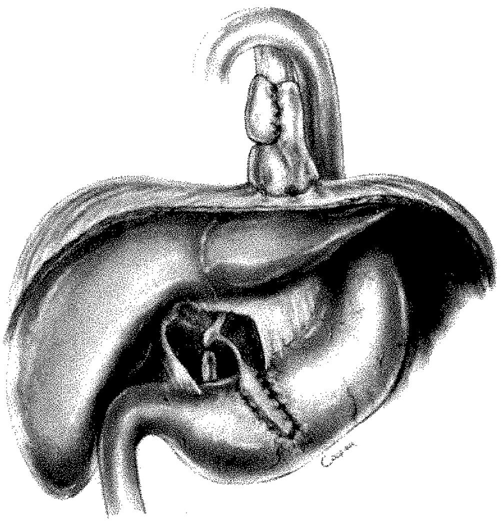

FIG. 5.—Intrathoracic Nissen valvuloplasty and the bile-contamination procedure.

Stricture was defined as a narrowing of the oesophagus as a result of oesophagitis which was sufficient to prevent the bronchoscope entering the lumen of the stomach.

Surgical prevention of oesophagitis was carried out in 5 monkeys with grade-2 oesophagitis. The left thoracotomy incision was reopened, the oesophagogastric junction was mobilized, and a Nissen (1970) fundoplication type of valvuloplasty was constructe (*Fig.* 5).

The progress of the monkeys was assessed by th endoscopist as before.

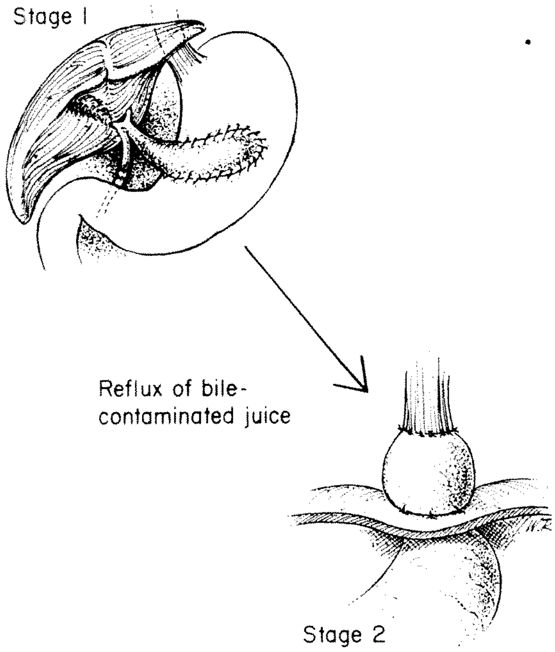

FIG. 4.—Bile-contamination procedure carried out in animals in groups III and IV.

Table I.—GRADING OF OESOPHAGITIS

Type	*Grade*
Normal	0
Erythema	1
Erosive oesophagitis	2
Stricture	3
Death directly due to oesophagitis	4

Table II.—DEGREES OF OESOPHAGITIS 3 MONTHS AFTER REFLUX OPERATION IN GROUP I

Monkey	*Oesophagitis Grade*
31	0
466	2
467	1
519	0
603	0
878	0

Table III.—DEGREES OF OESOPHAGITIS 3 MONTHS AFTE REFLUX OPERATION IN GROUP II

Monkey	*Oesophagitis Grade*
464	0
549	0
574	0
672	0
682	0
554	2

RESULTS

The degrees of oesophagitis are summarized i *Tables II–V.* It can be seen that 23 out of the 2 monkeys studied survived for 3 months. The com monest cause of death was aspiration pneumonit which occurred in 4 monkeys. Some monkeys do n have an adequate cough reflex and this could well be the explanation of death due to aspiration pneumonitis. In group II, 2 monkeys died from a perforated stomal ulcer and a subphrenic abscess due to suture-line leakage.

Table IV.—DEGREES OF OESOPHAGITIS 3 MONTHS AFTER REFLUX OPERATION IN GROUP III

Monkey	*Oesophagitis Grade*
491	2
492	1
564	1
689	2
560	3
430	4

Table V.—DEGREES OF OESOPHAGITIS 3 MONTHS AFTER REFLUX OPERATION IN GROUP IV

Monkey	*Oesophagitis Grade*
598	2
600	2
667	1
700	3
335	3

Group I.—Two out of 6 animals had mild oesophagitis, not only at 3 months but for 6 months after the reflux operation.

Group II.—This group had bile-free gastric juices confirmed by aspiration studies. In the monkey which died as a result of a stomal ulcer, although the jejunum was perforated there was no coexisting oesophagitis. Only 1 of the 6 three-month survivors had oesophagitis, the remainder being normal despite continual reflux of pure acid/peptic chyme.

Group III.—Every animal in this group showed some degree of oesophagitis at all times. *Fig.* 6 shows a complete stricture in the monkey with grade 4 oesophagitis. Using a Wilcoxon (rank) statistical comparison, there was a significant difference between groups III and II ($P < 0.02$) in the degree of oesophagitis.

Group IV.—These animals were found to have a similar incidence of oesophagitis to that occurring in group III. One animal (No. 335) had developed a 'peptic ulcer' just 1 cm. above the gastro-oesophageal anastomosis. Thus, the addition of depot histamine failed to worsen the degree of oesophagitis.

Surgery for Reflux.—Endoscopy was possible 4 weeks after the Nissen (1970) fundoplication in 4 out of the 5 monkeys. The 4 survivors had no oesophagitis at endoscopy and the 1 which died had a lung abscess and grade 1 oesophagitis at post-mortem examination. Despite the valvuloplasty being in the chest it functioned as a barrier against noxious reflux.

DISCUSSION

A brief comment must be made concerning bile rather than pancreatic juice being chosen for mixing with chyme. Previous work by Gillison, Capper, Airth, Gibson, and Bradford (1969) using a radiological test implied that heartburn was associated with the reflux of duodenal juice into the stomach and oesophagus. This symptom, according to Bernstein and Baker (1958), was strongly associated with oesophagitis when using their acid-perfusion test. Lambert (1962) has shown that pancreatic juice has a vital role in the development of oesophagitis in rats, while Moffatt and Berkas (1965) have demonstrated that bile can cause oesophagitis at any pH between 2 and 12 in dogs. We considered that bile was the vital ingredient because of the fact that pancreatic enzymes are inactivated below pH 5. The common bile-duct was ligated in the animals in groups III and IV because the cystic duct has been found to be easily obliterated after cholecystogastrostomy in our experience. Diverting the bile entirely through the gall-bladder prevented this cystic duct obliteration.

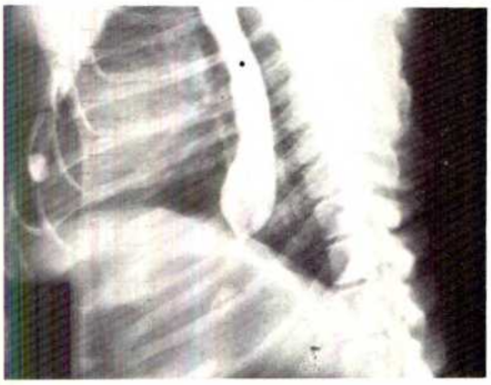

FIG. 6.—The oesophageal stricture in the animal in group III who died.

The monkeys in group IV were given daily injections of depot histamine because we wanted to mimic the state of hypersecretion of gastric juice such as that found in patients with duodenal ulceration. Our clinical experience is in keeping with that of Winkelstein (1935) and Wangensteen and Leven (1949), who found that duodenal ulceration was commonly associated with stricturing oesophagitis. However, despite the histamine we failed to produce a larger parietal cell mass, according to gastric secretion studies, and hence a more serious degree of oesophagitis did not occur in the monkeys in group IV.

Biliary oesophagitis is by no means a new idea owing to the work of Cross and Wangensteen (1951) as well as that of Moffatt and Berkas (1965). However, these workers used intestinal conduits to the oesophagus and preserved the lower oesophageal sphincter. Our experiment was different in two respects: the destruction of the sphincter and the mixing of bile with gastric chyme. These features meant that the mucosa of the oesophagus was exposed to the mixture of bile-contaminated chyme repeatedly over 3 months. To our knowledge, this is the first occasion that a 'peptic ulcer' of the oesophagus has been produced by experimental means.

Davenport (1968) described how bile could cause damage to the gastric mucosal barrier in a similar fashion to salicylates and alcohol. Bile was noted to cause more damage at a lower pH. Ferguson, Sanchez-Palomera, Sako, Clatworthy, Toon, and Wangensteen (1950) demonstrated how much more vulnerable the oesophageal mucosa is compared with other mucosae in the alimentary tract.

We do not refute the importance of acid chyme in reflux oesophagitis, but suggest that in man as well as in the monkey bile has a significant role in the genesis of the disease. The monkeys in group II correspond well with the 8 patients described by Holt and Large (1961), who cured reflux oesophagitis, caused by the long-abandoned cardioplasty operation for achalasia, using the Roux manœuvre.

The Nissen valvuloplasty is not the only way to prevent reflux but has the advantage of being easily performed above or below the diaphragm. The Hill posterior gastropexy is excellent at preventing herniation of the stomach through the diaphragm but, according to DeCastro, Nyhus, Gillison, Nakayoshi, and Bombeck (1971), this procedure does not protect the oesophagus against reflux. The Belsey Mark-IV valvuloplasty (Baue and Belsey, 1967) and the Collis (1968) operation are also effective barriers against reflux but require a thoracotomy for their execution.

Acknowledgements.—We are indebted to the Department of Vetinary Medicine at the Abraham Lincoln School of Medicine for the anaesthesia and animal care, W. Schwartz of the Department of Medical Illustrations at the University of Illinois for *Figs.* 1, 3, and 4, and Mrs. Margot Cooper, medical artist at the University of London, for *Fig.* 5.

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THE CAUSE OF VARICOSITY IN SUPERFICIAL VEINS OF THE LOWER LIMB

BY W. G. FEGAN AND A. L. KLINE

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FOR many years surgeons have been aware of the paradox that some patients can have extremely bad varicose veins and no symptoms of venous insufficiency while other patients have severe symptoms and minimal varices.

We have also been aware that an increase in varicosity is not necessarily paralleled by an increase in symptomatology. In fact, many of us can recall cases of varicose veins of increasing severity over a lifetime in a patient who remained symptom-free. This anomaly has engaged our attention for many years. We have for some time been aware that dilated and tortuous veins in the thigh and sapheno-varices could disappear after treatment of incompetent perforators in the calf. This reversibility suggested to us that the primary defect was unlikely to be in the wall of the thigh vein as we had not in any way altered the wall of the proximal part of the vessel by treating the distal veins (Quill and Fegan, 1971).

We have often observed that when patients with tortuous long saphenous veins assumed the erect position a thrill could be detected by light palpation over the vein. This thrill lasted 15–20 seconds and disappeared when the superficial veins became filled. By clinical methods we were unable to tell whether this thrill was present during walking or if it varied with the rate of walking.

A palpable thrill is produced by vibration and being aware that vibration is one of the results of turbulence we became interested in investigating this phenc menon in more detail, particularly since we wer aware of the association between stenosis, turbu lence, and post-stenotic dilatation in the arteri system.

At present we are approaching this problem (1) b attempting to measure turbulence electronically an (2) by studying histological changes in the veins sites in which turbulence has been detected. We us a specially modified audiofrequency turbulence de tector (Gosling and King, 1969) which measure vibrations transmitted through the vein wall to th skin. At the same time we are doing frequenc analyses of the audio output of the Parks Model 8c Directional Doppler and comparing our tracings wit those found in experimental situations where tu bulence is known to occur. Using the turbulenc detector, we have been able to confirm our clinic findings in symptom-free patients with varicose lon saphenous veins when they assumed the erect positio Also, we have been able to show that turbulenc recommences with walking and synchronizes with th retrograde flow as indicated by the Parks Direction Doppler (*Fig.* 1). There is a reduction in the duratic and intensity of the turbulence with increase in spee of walking. In normal subjects neither retrograc flow down the long saphenous vein nor turbulen could be detected on assuming the erect position after commencing walking (*Fig.* 2). In the patien vith severe post-phlebitic symptoms and signs retrograde flow and turbulence were absent or, if present, vere much reduced when compared with asymptomaic patients (*Fig.* 3).

Turbulence, as detected by the methods described ere, appears to depend on high-velocity retrograde low, which can only occur if the calf pumps are unctioning effectively. In order for the blood to flow lown a dilated long saphenous vein blood in the listal part of the vein must first be drawn into the deep enous system. Clearance of blood into the deep veins nd thence proximally is reduced if the deep veins re blocked following previous thrombosis or if here is significant damage to valves in the deep or erforating veins. This probably explains why we ave been unable to detect turbulence in patients with evere calf-pump dysfunction.

If, as is possible, turbulence is the major factor in he development of prominent superficial varices, our indings help to explain the fact that prominent arices frequently occur in patients with good pumps nd, conversely, that prominent varices are relaively infrequent in patients with severe venous pump lysfunction.

The effects of turbulence on the vein wall have not et been elucidated. In vessels in which turbulence vas detected two histological changes were observed: 1) complete absence of muscle in the media at the art of the circumference closest to the skin (*Fig.* 4), .e., where vibration appeared to be maximal, and (2) hickening of the intima at the same point of the ircumference (*Fig.* 5). When flow in a vessel becomes turbulent there is a greatly increased shear force on the lining of the vessel and it is possible that the intimal thickening seen in veins is a result of this (*Fig.* 6). The effect of shear force is unlikely to be responsible for thinning of the muscle layer. We think that this may possibly be the result of vibration due to turbulence transmitted across the vein wall.

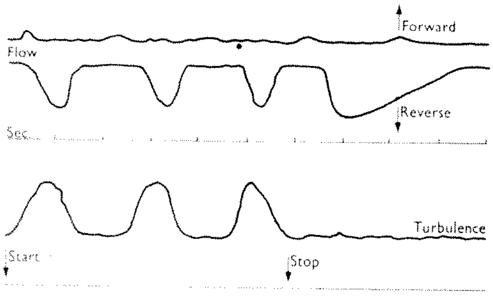


FIG. 1.—Turbulence is present and is synchronized with reverse flow in group I patients on walking.

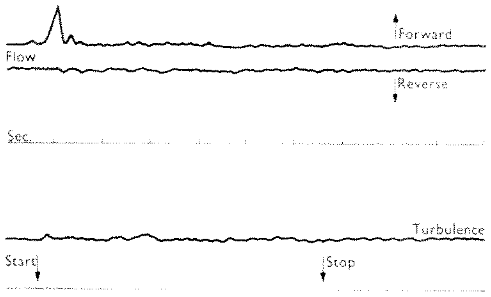


FIG. 2.—Turbulence is absent in normal subjects while walking.

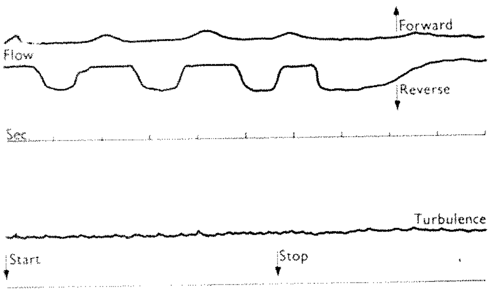


FIG. 3.—Turbulence and reverse flow are absent in group II patients while walking.

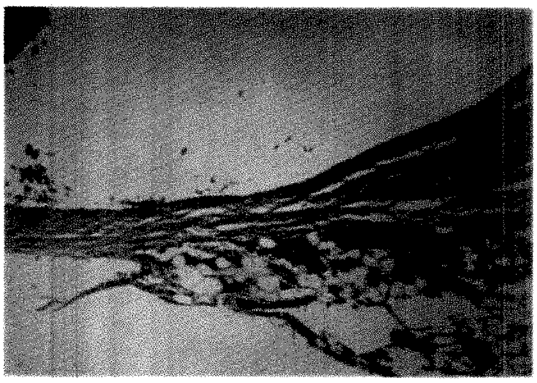


FIG. 4.—Histological section showing absence of muscle in the media at the point of the circumference closest to the skin.

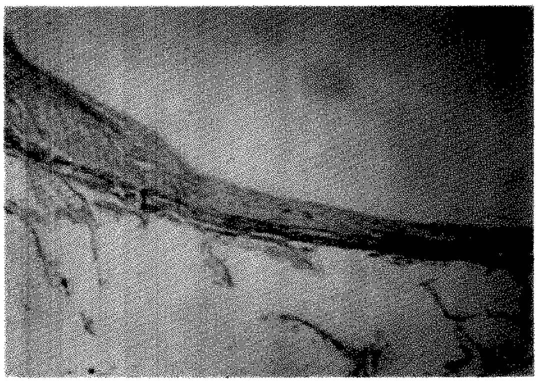


FIG. 5.—Histological section showing thickening of the intima in the media at the point of the circumference closest to the skin.

The understanding of this condition has been made difficult by the frequent superimposition of the effects of turbulent retrograde flow and pump dysfunction. To help to understand the aetiology and to clarify this condition for the sake of therapy it is necessary to divide the patients into three groups:—

Group I.—Those with prominent varices, no symptoms, and good calf pumps.

Group II.—Those with severe symptoms, few varices, and evidence of recanalized thrombosed deep veins with gross calf-pump dysfunction (post-phlebitic syndrome).

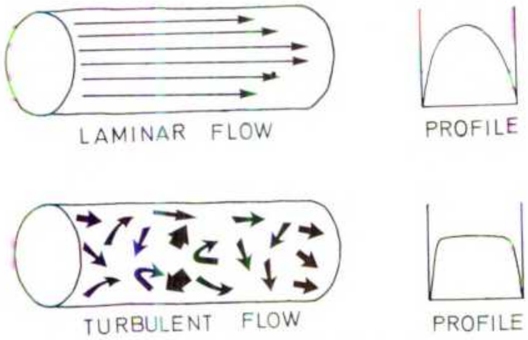
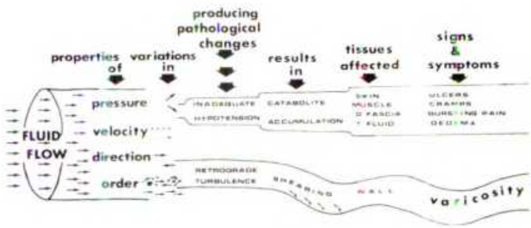


FIG. 6.—Flow profile with turbulence.



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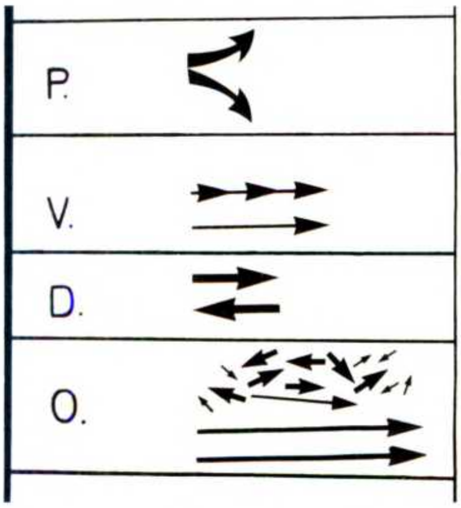

B

FIG. 7.—A, Properties governing flow in a closed system. Pressure: increased or decreased. Velocity: increased or decreased. Direction: forward or retrograde. Order: turbulent or laminar. B, Results of changes in flow patterns on the vein wall and surrounding tissues. P, Pressure. V, Velocity. D, Direction. O, Order.

Group III.—The sometimes confusing patients who have moderately severe varices and also evidence of calf-pump dysfunction.

A simple classification is given in *Table I*.

Table I.—CLASSIFICATION OF VARICOSITY IN SUPERFICIAL VEINS OF THE LOWER LIMBS

Group	*Description*
I	Varicose veins without symptoms are due to turbulence
II	Severe symptoms and minimal varices due to pump dysfunction
III	A combination of groups I and II

Young athletic males with large dilated long saphenous veins are typical of group I patients. Since they are usually asymptomatic, treatment is not always necessary. If one or two incompetent perforating veins can be detected in the calf or foot these should be occluded. A varying degree of regression of superficial proximal varices takes place. At least 3 months should elapse before considering flush ligation. We have found this to be necessary in only a small proportion of cases. We do not feel there is any indication for stripping these patients' veins. The only reason for providing treatment is to avoid the theoretical risk of thrombophlebitis in a dilated superficial vein following trauma.

Group II patients always require treatment, since the underlying pathology always develops from pump decompensation, whether due to damage to the valves in the deep or in perforating veins. Our treatment is to obliterate as many incompetent perforating veins as can be found. As yet there is no effective method of dealing with derangements of the deep venous system and, in our experience, occlusion of incompetent perforating veins usually results in a very considerable improvement in the limb, even in those patients in whom there is associated deep-vein damage (Henry, Fegan, and Pegum, 1971). All of these patients should be followed up because a minority require intermittent advice and additional treatment from time to time. Even in people with proximal pelvic occlusion the symptomatology is considerably improved (Fegan and Doporto, 1967). Some may have to continue to wear elastic stockings for support for the rest of their lives in order to control oedema.

The patients in group III have prominent varices and calf-pump dysfunction. In many, superficial varicose veins precede the development of signs and symptoms of calf-pump dysfunction. In our opinion in order to develop bad varicosity of superficial veins one must have good or adequately compensated pumps. The treatment of this group of patients is the same as that of the patients in group II, namely to seek out and to obliterate incompetent perforating veins. This is necessary to restore pump competence.

Signs and symptoms are evidence of decompensation of the pumps and not of leakage, which can often be completely masked by pump compensation. It is quite possible to have one or two incompetent perforating veins without any symptoms. At the moment we are observing closely a group of young patients in this category. The only effect so far of this incompetence is to give rise to ascending dilatation of superficial veins. At a critical point this dilatation leads to secondary incompetence of valves in the superficial system which is reversible after ambulatory hypotension is restored.

It is possible to attribute groups I and II to alterations in different basic properties governing flow in a closed system. As illustrated in *Fig*. 7, flow in an enclosed system can be either at high or low pressure forward or reverse, fast or slow, turbulent or laminar. When flow is retrograde and turbulent in the superficial system we get varicosity of that system, and then the pumps are unable to develop low pressure in the deep system. After the commencement of walking the tissues are unable to be adequately dialysed. This is due to the failure of the development of a favourable gradient necessary for tissue-fluid clearance. Failure to achieve this is the essential pathological feature of calf-pump dysfunction.

Acknowledgement.—We would like to express our appreciation to Mr. P. J. Byrne for technical assistance and for his considerable work in the development of the technique described in this paper.

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SURGERY FOR CORONARY ARTERY DISEASE

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SUMMARY

Direct distal aortocoronary vein-grafts have been used in 20 patients suffering from ischaemic heart disease. In 16 patients the indication for surgery was severe angina pectoris failing to respond to medical measures. Seven patients had angina decubitus and were Class IV according to the New York Heart Association classification and 9 patients were in Class III. Two patients had recurrent myocardial infarctions and 2 were in cardiac failure. There were 14 good results, 2 failures, and 4 deaths. Post-mortem studies of the hearts confirmed the accuracy of selective angiography in identifying the sites of major coronary obstruction. Findings at surgery showed that the absence or presence of extensive peripheral disease beyond a block could not be reliably assessed in all cases. Histological studies of the veno-arterial anastomoses suggested that rigid atherosclerotic arterial disease is a cause of graft thrombosis and that endarterectomy is a useful procedure though its long-term value is uncertain.

DIRECT surgical by-pass grafts from the aorta to the coronary arteries beyond stenotic atherosclerotic lesions have been widely employed since Favaloro (1969) reported good results with the use of reversed saphenous grafts for ischaemic heart disease.

Johnson, Flemma, Harding, Cooper, and Lepley (1970) showed that the scope of surgery in the management of ischaemic heart disease could be greatly increased by utilizing peripheral grafts in vessels of 1–3 mm. diameter and that multiple grafts were usually required.

Twenty consecutively treated patients suffering from severe ischaemic heart disease have been subjected to direct revascularization in the Thoracic Unit at Edinburgh and the survivors have been clinically assessed during their subsequent course.

PATIENTS SELECTED FOR SURGERY

The majority of the patients suffered from severe incapacitating angina and were classified in Class III or IV according to the functional classification of the New York Heart Association. Class III patients had anginal pain on less than ordinary exertion and Class IV patients had cardiac insufficiency or anginal pain at rest. These patients had failed to obtain relief from the standard drugs, namely nitroglycerin and β-receptor blocking agents. There were also 2 patients who suffered from disabling recurrent attacks of myocardial ischaemia requiring repeated hospitalization and 2 who had gross cardiac failure associated with a ventricular septal defect in 1 patient and severe left ventricular akinesia in the other. These features are summarized in *Tables I and II.*

Table I.—DETAILS OF THE PATIENTS SELECTED FOR SURGERY

INDICATIONS	FUNCTIONAL CLASSIFICATION	NO. OF PATIENTS
Severe angina	III	9
Angina decubitus	IV	7
Recurrent infarction	I	2
Cardiac failure and ventricular septal defect	IV	1
Cardiac failure and akinesia of left ventricle	IV	1

Coronary angiography and left ventriculography were done in all the patients and formed the most important guide to selection for surgery and to the site and number of grafts required.

Sixteen patients had complete obstruction of two main coronary arteries and this was often associated with stenotic areas in the remaining artery jeopardizing the collateral circulation. Two had severe stenosis of one main artery. The 2 patients suffering from recurrent infarctions had total obstruction of the main circumflex or the branches of this vessel.

Left ventricular function was assessed by ventriculography and 15 patients had good contractility. Two patients had severe localized akinesia and 2 had poor general contractility in the distal two-thirds of the left ventricle, whilst 1 patient had almost total

Table II.—DETAILS OF THE CORONARY BY-PASS GRAFT PATIENTS

PATIENT	AGE AND SEX	DURATION (yr.)	ANGINA	INFARCTS	FAILURE	CTR +	E.C.G.				L.V.			CORONARY ANGIO-BLOCKS	BY-PASS GRAFTS	RESULT
							Rhythm	B.B.B.	Q	ST–T	E.D.P. (mm. Hg)	d*p*/d*t* (mm. Hg per sec.)	E.F. (per cent)			
1. H. W.	55 M.	10	+ +	2	0	0	S.	I.R.	0	+	12	1310	73	R., L.A.D., C.	R.*	No pain. Normal exertion tolerance
2. A. F.	60 F.	15	+ + +	1	0	+	S	0	0	+	20	1070		L.A.D., C., R.	L.A.D.*	Less pain; cardiac failure
3. M. R.	53 M.	7	+ +	1	0	0	S	0	0	+	5	1250	82	L.A.D., C.	L.A.D.*	No pain. Good exertion tolerance
4. K. G.	65 M.	7	+ + +	0	0	0	S	0	0	+	15	1100	80	L.A.D., C.	L.A.D.*	No pain. Limited by claudication
5. J. B.	70 M.	2	+	1	+ +	+	S	0	+	+	24	1020	58	R., C.	L.A.D., R.	No pain or failure
6. J. H.	50 M.	2	+ +	4	0	0	S	0	+	+	10	1000	76	R., L.A.D.	L.A.D., R.	No pain. Normal exertion tolerance
7. D. C.	43 M.	4	+ + +	2	0	0	S	0	+	+	25	1100	63	L.A.D., C., R.	L.A.D.*	Not improved
8. J. H.	64 M.	14	+ + +	0	0	0	S	0	0	+	10	1260	70	R., L.A.D.	R.*	No pain. Some effort dyspnoea
9. D. W.	38 M.	2	+ +	1	0	0	S	0	0	+	15	1450	64	L.A.D.	L.A.D.	No pain. Normal exertion tolerance
10. J. U.	55 M.	3	+ +	1	0	0	S	0	0	0	15	1360		L.A.D., C., R.	L.A.D., R.	No pain. Normal exertion tolerance
11. I. M.	49 F.	3	+ +	1	+ +	+	A. fib.	L.	+	+	18	800	43	L.A.D., C., R.	L.A.D., R.	Died.
12. J. T.	47 M.	5	0	2	0	0	S	0	0	0	—	Good contr.		C.	C., R.	Well. No recurrence
13. R. B.	62 M.	1	+ +	0	0	0	S	0	0	+	36	Good contr.		R., L.A.D.	L.A.D., R.	Well. No pain
14. T. M.	41 M.	4	+ +	0	0	0	S	0	0	+	—	Good contr.		R., L.A.D.	L.A.D., R.	Well. No pain
15. A. H.	53 M.	10	+ + +	2	+	0	S	0	+	+	24	Poor contr.		L.A.D., C., R.	L.A.D., R.	Died
16. R. C.	49 M.	5	+ + +	3	0	0	S	0	0	+	15	Poor contr.		R., L.A.D.	L.A.D.	Died
17. W. P.	68 M.	10	+ + +	2	+	+	S	0	+	+	—	Poor contr.		R. L.A.D., C.	R.*	Died
18. G. S.	42 M.	4	+	1	0	+	S	0	+	+	30	Good contr.		C., L.A.D., R.	R.	Well. No pain
19. G. H.	32 M.	1	+	1	0	0	S	0	0	+	0	Good contr.		C.	C.*	Well
20. S. W.	41 M.	3	+ + +	1	0	0	S	0	0	0	5	Good contr.		R.	R.*	Less pain

* With internal mammary implants.

CTR +, Contractility >50 per cent. E.C.G., electrocardiogram; B.B.B., bundle-branch block; Q, pathological Q waves; ST–T, ischaemic ST and/or T changes. L.V., left ventricle; E.D.P., end diastolic pressure; E.F., ejection fraction. Coronary arteries: C, circumflex; L.A.D., left anterior descending; R, right. Contr.: contraction. A. fib., artrial fibrillation; S., sinus rhythm.

akinesia of the left ventricle which was wrongly believed to be a left ventricular aneurysm.

There were 18 men and 2 women aged between 32 and 70 years with a mean age of 50. Sixteen patients had had one or more proved myocardial infarctions. Angina pectoris had been present for over 3 years in the 16 patients presenting with this symptom and it had been present for 5 years or more in 9 of these patients. Two patients were under treatment for hypertension.

The resting electrocardiogram was normal in 3 patients. Seven had pathological Q waves indicating previous myocardial infarction, while 10 others had ST-/ and/or T-wave changes of ischaemia or infarction.

OPERATIVE PROCEDURES

Eleven patients had single grafts and 9 patients had double grafts the details of which are shown in *Table III*. In 9 cases the internal mammary artery was implanted into ischaemic areas of the left ventricle using a modified Vineberg technique. This was usually done into the area of supply of the circumflex artery when diffuse disease of this artery unsuitable for grafting was present. The heart action was supported by cardiopulmonary by-pass during the operation, and a quiet operative field for the distal saphenous vein to coronary artery anastomosis was obtained by the use of moderate hypothermia, ventricular fibrillation, and venting of the left ventricle. Periods of aortic clamping varying from 6 to 36 minutes were used to obtain a bloodless field for accurate anastomosis and to avoid the need for dissection of the tissues surrounding the arteries. Fine 000000 monofilament interrupted sutures with double-ended needles were used.

Table III.—THE SITE AND TYPE OF VEIN-GRAFT EMPLOYED

SITE OF GRAFTS	NO. OF PATIENTS	WITH IMPLANT
Single grafts		
Aorta to right coronary artery	2	1
Aorta to left anterior descending artery	8	5
Aorta to main circumflex artery	1	1
Double grafts		
Aorta to right coronary and left anterior descending arteries	8	1
Aorta to right coronary and circumflex arteries	1	1
Total	20	9

Table IV.—THE SITE OF ENDARTERECTOMY

SITE OF VEIN-GRAFT	NO. OF VEIN-GRAFTS	ENDARTERECTOMY	
		Proximal	Proximal and Distal
Right coronary artery	11	3	3
Left coronary artery	18	3	3
Total	29	6	6

As shown in *Table IV* there were 29 distal vein-grafts employed for 20 patients; proximal endarterectomy was done on 6 occasions with the object of obtaining a free flow of blood from above in the case of short obstructions, improving retrograde flow into proximal unobstructed myocardial arteries, and, more frequently, attaining a pliable unobstructed vessel at the site of anastomosis. Distal endarterectomy was done on 6 occasions usually in association with proximal endarterectomy of small extent for the reasons mentioned. Obstructing pieces of collagenous atherosclerostic material which were cylindrical in shape and up to 4 cm. in length were removed from the distal vessels and their branches where a plane of cleavage could be developed.

Distal endarterectomy from the right coronary artery in its lower third close to the crux extending into the posterior interventricular and right postero-lateral ventricular arteries was done in 3 cases, and from the left anterior descending artery, the diagonal artery, and the circumflex artery on 3 other occasions.

Recently the use of extensive blunt dissection and of a wide incision into the artery at endarterectomy has been avoided by employing carbon-dioxide-gas endarterectomy in the plane of cleavage. This modification was developed by Kuypers (1971) and reported by Vonk, Plum, and Geraedts (1967). It eliminates the use of needle injection of gas as originally described by Sawyer, Kaplitt, and Sobel (1967). There were 2 patients in whom grafts could not be placed at one of the expected sites owing to failure to find a vessel of suitable size, and 1 failure to disobliterate an extensively obstructed right posterior interventricular artery in a patient who died within 72 hours of surgery.

RESULTS

The subjective results of these operations for the relief of pain have been good in that 11 out of 13 survivors operated on primarily for angina pectoris of severe degree have been relieved of pain and have returned to a more active life than before surgery.

Four patients who had extensive distal endarterectomy are amongst those completely relieved of pain at rest and on exertion; in 1 of these the only graft achieved was at the site of endarterectomy.

In 1 patient pain recurred immediately after operation and has persisted since; there is angiographic evidence to suggest that the graft to the left anterior descending artery, which had an extensive distal endarterectomy, is closed; the left circumflex was unsuitable for a by-pass graft so that an internal mammary implant was done without apparent benefit.

One other patient still has cardiac failure and although the pain has been much less it has not been completely relieved.

In 2 patients postoperative selective angiograms to the origin of the graft in the aortic root have shown graft patency at 2 months and 6 months respectively. The 2 patients who had had recurrent infarcts and episodes of severe pain necessitating frequent hospital admissions preoperatively have been improved, but the follow-up period is only 6 and 8 months respectively.

A 70-year-old man in severe cardiac failure with a ventricular septal defect due to a myocardial infarct 3 months preoperatively is well, free of angina, and requires no diuretics in spite of partial recurrence of the septal defect after surgery. There has been no late mortality in those patients surviving the immediate postoperative period in a follow-up of 4–16 months and no serious postoperative complications. There have been 4 early postoperative deaths details, of which are shown in *Table V*.

Two deaths occurred within the 72 hours after surgery from cardiac causes.

Table V.—DETAILS OF THE 4 PATIENTS WHO DIED

PATIENT	AGE AND SEX	INDICATION FOR SURGERY	FUNCTIONAL CLASSIFICATION	LEFT VENTRICULAR FUNCTION	CAUSE OF DEATH	GRAFT PATENCY
R. C.	51 M.	Angina decubitus	IV	Good	Occlusive thrombus	Open
I. M.	49 F.	Cardiac failure	IV	Almost total akinesia	Low cardiac output	Closed
A. H.	60 M.	Angina decubitus	IV	Akinetic distal one-third	Septicaemia with right apical empyema	One open
W. P.	68 M.	Angina decubitus	IV	Akinetic distal one-third	Pulmonary infection	Open

The first patient (R. C.) developed severe retrosternal pain due to recent obstruction of the coronary artery which was totally blocked beyond the first 2 cm. by extensive atherosclerosis. At autopsy all the main coronary arteries were severely narrowed although there was a patent graft into the diseased anterior descending artery.

The second patient (I. M.) died after a long period of hypotension due to low cardiac output with repeated episodes of ventricular fibrillation. At autopsy there was extensive replacement fibrosis in the lateral and anterior walls of the left ventricle presumably from old infarcts. All the branches of the coronary arteries were severely and irregularly narrowed by atherosclerosis and recanalized totally occlusive lesions were identified in the anterior descending and circumflex arteries. The distal anastomosis of each graft was virtually completely closed by the spring-like action of the rigid thickened walls of the diseased arteries.

The 2 other deaths occurred 14 days after surgery which was complicated in 1 patient (A. H.) by intra-abdominal haemorrhage.

At autopsy in patient A. H. severe and ulcerated atherosclerosis was widespread, affecting the aorta and all the major arteries. An atheromatous abdominal aortic aneurysm was present.

Two aorta–coronary artery saphenous vein-grafts were present, the distal anastomoses being fashioned to the left anterior descending and right coronary arteries respectively.

Examination of the myocardium showed extensive areas of hyaline fibrous tissue replacing the myocardium in the inferior wall and extending into the lateral wall. In the inferior wall the myocardial fibres showed some atrophy and there was an increase in the amount of interstitial fibrous tissue.

All the branches of the coronary arteries were severely narrowed by atherosclerosis. Organized mural lesions were present in the circumflex artery.

VEIN-GRAFTS.—The left coronary graft was patent but showed a small amount of mural thrombus related to the sutures of the distal anastomosis. It was also noted that one of these sutures had passed through and had fragmented an atheromatous plaque. The right coronary graft was completely occluded by a mixture of recent thrombus and blood-clot. Typical laminated thrombus was identified in relation to the distal anastomosis which was itself almost completely closed off by the spring-like action of the rigid artery wall. It was interesting that no thrombus was identified in the right coronary artery lumen.

A left subphrenic collection of altered blood was found.

Death was the result of septicaemia complicating a right apical empyema.

At autopsy patient W. P. had a single patent aorta–right-coronary artery saphenous vein-graft; the left internal mammary artery had been mobilized and embedded into the substance of the anterior wall of the left ventricle towards the apex.

The myocardium showed much fibrous tissue in the inferolateral wall of the left ventricle and also in the anterior wall at the apex. In addition, focal ischaemic damage approximately 10–14 days old was noted in the inferolateral wall of the left ventricle.

Localized endarterectomy had been performed in the major coronary arteries which in many instances had left only a relatively small amount of supporting tissue, consisting of the adventitia and small fragments of media. Elsewhere the vessels showed severe irregular narrowing by atherosclerosis. The right coronary artery at a point just proximal to the vein-graft anastomosis was almost completely occluded by two entirely separate portions of recent thrombus. One portion of thrombus was formed on superficially eroded atheromatous plaques, whilst the other formed part of a large piece of mural thrombus related to the anastomotic line between the vein and the coronary artery at a point where the arterial wall was necrotic and thinned following the endarterectomy and suturing. The thrombus, although extensive and almost completely occluding the termination of the proximal part of the right coronary artery, did not significantly encroach upon the lumen of the vein or the distal parts of the right coronary artery.

The vein-graft was otherwise healthy and the internal mammary artery implant showed no abnormality.

The lungs showed chronic airways' disease and were congested with early bronchopneumonia. The airways were plugged with viscid mucopurulent material. A focal mild acute pancreatitis was present.

Death was thought to be primarily the result of respiratory failure.

The 4 deaths occurred in patients who had particularly severe degrees of widespread coronary atherosclerosis and in 3 cases poor left ventricular function. In 1 patient (I. M.) it was mistakenly thought that an aneurysm was present. This patient would not have been subjected to surgery if the left ventricular angiogram had been correctly assessed. It is well-recognized error. In 2 of these patients it was impossible to carry out the projected double vein-graft and only one was accomplished.

DISCUSSION

Though the incidence of asymptomatic ischaemic heart disease in people over the age of 40 is high, patients only present for investigation as the result of the development of stable or unstable angina or myocardial infarction. Unfortunately, unheralded sudden death is not uncommon but it is possible that minor premonitory episodes of unstable angina are often missed. Unstable angina is defined as the onset of fresh angina or the exacerbation of pre-existing angina and it is believed that the prognosis in such patients is much worse than that of stable angina which only carries an average death-rate of 4 per cent during the 5 years following its onset (Weinblatt, Frank, Shapiro, and Sager, 1968).

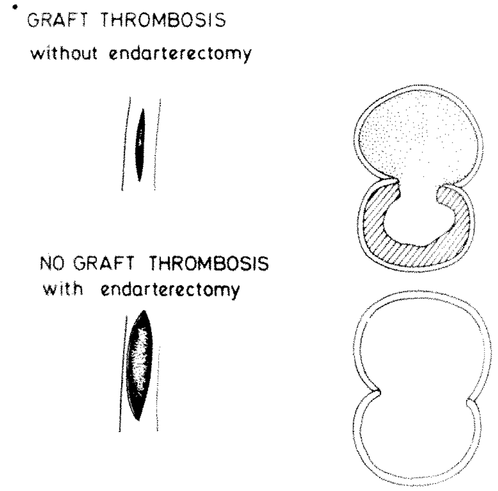

FIG. 1.—Diagrams showing the effect of using endarterectomy at the site of an anastomosis.

Angina in the patient who has had a myocardial infarct carries a death-rate of 8 per cent (Block, Crumpacker, Dry, and Gage, 1952), and in the future, with increasing knowledge, it will be possible to select for surgery patients who are at particular risk. At the present time there is insufficient evidence available to decide whether the mortality of this disease can be reduced by revascularization, though a long-term controlled study is being planned. The majority of the patients in the present series were treated on account of crippling angina and had been in functional Class III or IV with severe triple artery disease; this group is known to carry a higher mortality than the overall mortality for surgically treated patients reported from many centres (Morris, Reul, Howell, Crawford, Chapman, Beazley, Winters, Peterson, and Lewis, 1971).

At autopsy the coronary arteries were dissected from the heart and examined in longitudinal sections according to the method described by Bouch and Montgomery (1970). It was shown that conclusions based on the preoperative coronary angiograms were accurate in respect to the major sites and severity of the stenotic lesions in the major arteries, but were not accurate in indicating the presence of rigid mural atherosclerosis and obstructing lesions in the peripheral vessels.

The pathological evidence on the four hearts studied postoperatively suggests that there are advantages and disadvantages in endarterectomy.

In the absence of endarterectomy the rigidity of the diseased arterial wall may cause spring-like closure of the anastomosis (*Fig.* 1). This was seen in 3 cases and the fact that it was associated with distal vein thrombosis with absence of thrombus in the artery supports this hypothesis.

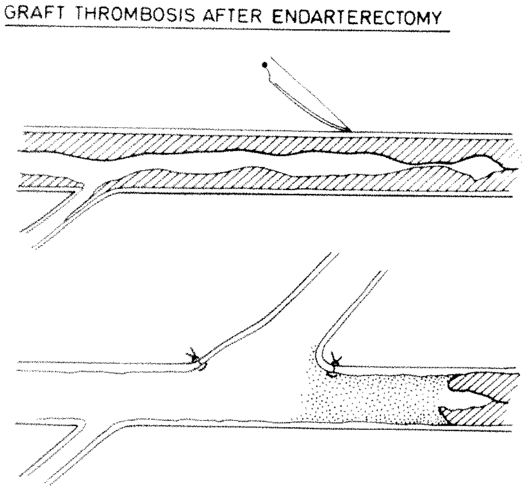

FIG. 2.—Diagrams showing graft thrombosis after endarterectomy.

On the other hand, damage by separation of atherosclerosis at surgery may provide a site for the origin of thrombus formation (*Fig.* 2).

One of the main advantages of placing the saphenous vein by-pass graft distally is that a healthy arterial wall is frequently found beyond the proximal severe disease in the coronary arteries. Unfortunately, in severe long-standing disease the peripheral vessels are often involved as well and coronary angiography has not proved an accurate guide to the presence of a patent healthy vessel beyond a major obstruction. Vonk and others (1971) have pointed out that it is difficult to distinguish between the so-called 'disuse atrophy' beyond complete obstruction and the presence of organic disease. It is impossible to avoid exploration of diseased vessels at surgery, and endarterectomy has been used on these occasions to permit direct revascularization although its long-term value is uncertain.

The value of internal mammary implantation is felt to be doubtful in comparison with direct coronary surgery, so that with increasing experience of multiple vein-grafts and endarterectomy its use should be limited to special cases; the extra operating time and blood-loss involved in adding this procedure to cardiopulmonary by-pass are additional disadvantages.

Acknowledgements.—We are grateful to Mr. A. Logan for his help and advice in this work, and to the Illustrations and Photography Unit, Department of Clinical Surgery, University of Edinburgh.

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[Although not published here, the following paper was also read: **'Starch Granulomatosis of the Peritoneum—Clinical and Experimental Studies'**, Harold Ellis (London).]

SYMPOSIUM ON CROHN'S DISEASE

THE VALUE FOR DIAGNOSIS AND RESEARCH OF SPECIAL INVESTIGATION ON RECTAL BIOPSIES IN CROHN'S DISEASE

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SUMMARY

Proper processing and intelligent use of rectal biopsies and resected material from patients with Crohn's disease allow a wide range of histochemical and immunological, diagnostic and research procedures. Studies of enzyme distribution in biopsies have not fulfilled their early promise, and electron microscopy has not so far proved to be of great value in differential diagnosis. Techniques for determining mucosubstances, however, can be of considerable value in separating Crohn's disease from other conditions. Studies on the distribution of lymphocytes and plasma cells using selective antibodies to human immunoglobulins are practicable and likely to be of value. Close co-operation between the surgeon and the pathologist is essential.

WHENEVER tissues are surgically removed from a patient the surgeon and the pathologist have a dual responsibility. First, an accurate diagnosis, differential diagnosis, and, if possible, a prognosis must be given, and, secondly, any studies on the tissues which may add to the knowledge of the aetiology and pathogenesis of the particular disease diagnosed ought to be undertaken. Resected specimens normally provide ample material for both purposes. Small biopsies are intended primarily for diagnosis, which may be extremely difficult, and research must be subsidiary to this. It is, however, surprising how much additional valuable diagnostic information and research potential there can be in a small biopsy which has been properly preserved and handled because the surgeon and pathologist have discussed the patient together *before* the biopsy was taken. This paper considers the value and scope of special investigations for diagnosis, differential diagnosis, and research on biopsies and surgically resected specimens from patients diagnosed as actually or potentially suffering from Crohn's disease.

THE INITIAL HANDLING OF SPECIMENS

Resected Specimens.—Most unsuccessful histochemical and immunological investigations fail because the material was imperfectly handled when resected. The surgeon should let the pathologist know when resection is being undertaken and the pathologist should, whenever possible, collect the unfixed specimen himself, open it, demonstrate it to the surgeon if he wishes to see it, photograph it himself if facilities exist, and select blocks for appropriate processing immediately. Most specimens can subsequently be photographed satisfactorily if block-taking is carefully done. Appreciable delays before processing interfere not only with the histochemistry but also with the highest quality of histology on which differential diagnosis may depend.

Biopsies.—When a single indivisible piece of tissue only is available, choice of preservation lies between fixation and snap freezing (Dawson, 1972a). In Crohn's disease, where the histochemistry of dehydrogenase enzymes is not likely to be important, fixation is preferable (Dawson, 1972b). The biopsy should be placed, mucosal surface upwards, on a glass cover-slip and fixed in 10 per cent neutral or buffered formol–calcium at 4° C. Supplies of the fixative should always be stored, ready prepared, in the correct-sized bottles in a refrigerator near the theatre in preparation for use; it is advantageous to include two or three cover-slips in each bottle. After taking the biopsy the fixed specimen should either be sent at once to the laboratory or be replaced in the refrigerator—but *not* in the ice compartment—and the laboratory notified. The latter technique is particularly applicable to specimens taken out of normal laboratory hours.

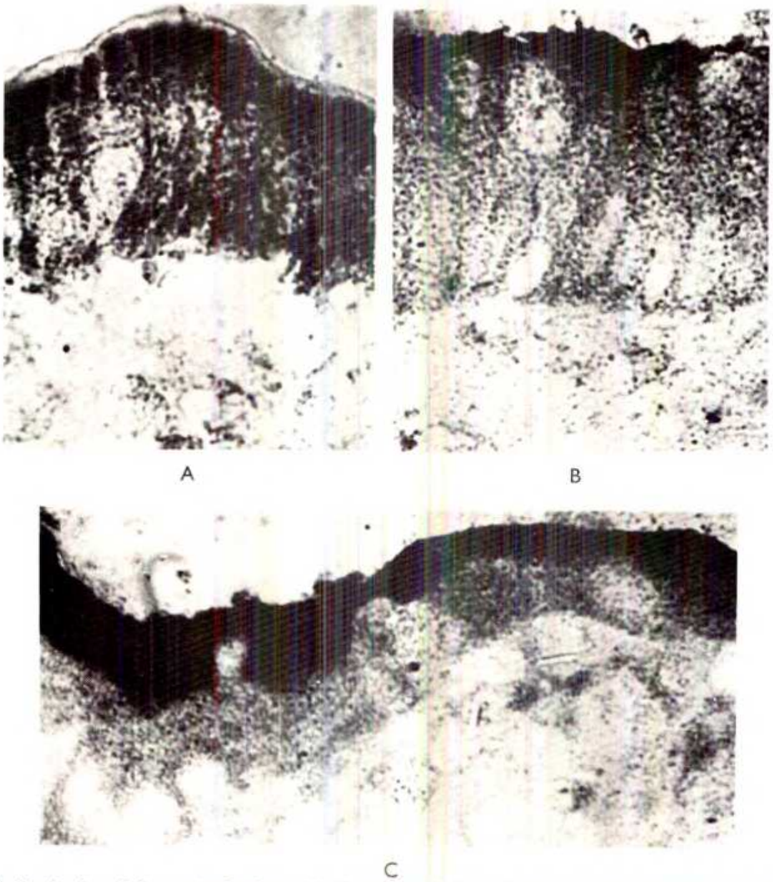

FIG. 1.—A, Normal distribution of glucose-6-phosphate dehydrogenase (G6PD). The finely granular formazan is distributed throughout the cytoplasm of the surface epithelium of rectal mucosa. B, Distribution of G6PD in Crohn's disease. There is a formazan deposit in the upper part of the rectal epithelial cell. C, Distribution of G6PD in ulcerative colitis. The formazan shows as a heavy deposit in the superficial cytoplasm of rectal epithelial cells and there is relatively little in the deeper part. However, the differences between B and C are not great enough to be diagnostic. NADP–tetrazolium technique. (× 200.)

DIAGNOSIS OF CROHN'S DISEASE OF THE LARGE INTESTINE USING RECTAL BIOPSY

Most resected specimens from patients with Crohn's disease have easily recognizable macroscopic and microscopic features and can be diagnosed without difficulty, but problems may arise in rectal biopsies from suspected cases with or without obvious rectal involvement clinically; these fall into four main histological categories:—

1. Biopsies in which the mucosa appears histologically normal. In these one must serially section or step section the block in a search for granulomas; no special investigations are at present of value.

2. An occasional biopsy in which isolated sarcoid-like granulomas are present in an otherwise normal mucosa. Crohn's disease can be strongly suspected but there are no special investigations which will prove it.

3. Biopsies in which sarcoid-like granulomas are present along with mucosal erosion or ulceration, lymphoid aggregates, and other features commonly seen in Crohn's disease. If tuberculosis can be excluded a fairly confident diagnosis can be made.

4. Biopsies in which there is a severe chronic inflammatory reaction in the lamina propria and submucosa, with or without mucosal erosion, ulceration, crypt abscesses, etc., but without a diagnostic sarcoid granulomatous reaction. It is in this group that special investigations can be of diagnostic value; all those which are useful can be undertaken on cold formol–calcium-fixed material.

SPECIAL INVESTIGATIONS FOR DIAGNOSIS

Patients whose biopsies fall into group 4, above, may have Crohn's disease, ulcerative colitis, non-specific proctitis or proctocolitis, or some specific inflammatory disorder. Histochemical techniques for selected enzymes and for mucosubstances have been used in attempts to make a differential diagnosis (Dawson, 1972b).

Enzyme Techniques.—The enzymic pattern in the large intestinal mucosa somewhat resembles that in the basal layer of the small intestine (Dawson and Pryse-Davies, 1963; Melnyk, Braucher, and Kirsner, 1967; Van Noorden, Thayer, Yesner, and Spiro, 1967;

Filipe, 1971). Dehydrogenases and diaphorases with the exception of succinate dehydrogenase are present in a higher concentration in the absorptive cells of the surface epithelium than in the crypts, and the finely granular deposit of formazan which indicates their presence is either diffused throughout the cell or predominantly perinuclear in distribution (*Fig.* 1 A). Various authors, particularly Mendeloff and Monis (1962) and Monis and Mendeloff (1965), described changes in the intracellular distribution of these enzymes in ulcerative colitis, the formazan granules tending to be concentrated immediately beneath the luminal border of each cell (*Fig.* 1 C), and suggested that this could be a useful diagnostic reaction for separating ulcerative colitis from non-specific proctitis and Crohn's disease. Other workers, however, while confirming that such a change in enzyme distribution does take place, believe it to be less specific (Van Noorden and others, 1967). Studies in the present author's laboratory (Filipe, 1971; Dawson, 1972b) show that similar though usually less severe changes can occur in Crohn's disease (*Fig.* 1 B) and in unclassified proctitis and it is believed that they indicate no more than a non-specific reaction in epithelium which is regenerating.

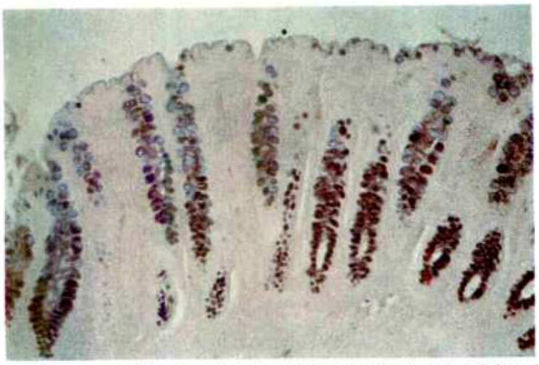

FIG. 2.—Acid non-sulphated (blue staining) and sulphated mucosubstances (brown staining) in normal rectal mucosa. High-iron diamine (HID)–Alcian blue (AB) technique. (× 25.)

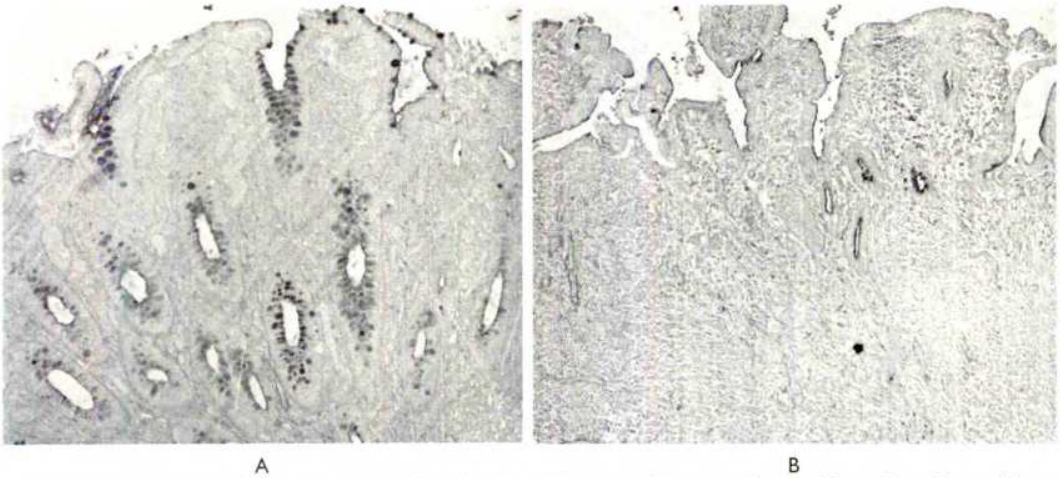

FIG. 3.—A, Rectal mucosa in moderately active ulcerative colitis. There are still some mucin-containing goblet cells remaining. B, Rectal mucosa in severe active ulcerative colitis. Hardly any mucin-containing cells remain. HID–AB. (× 25.)

Techniques for Mucosubstances.—Mucosubstances can be classified histochemically simply, if not entirely accurately, as neutral, acid non-sulphated, and sulphated, using three relatively simple histochemical techniques, namely periodic acid–Schiff (PAS), Alcian blue at pH 2·5, and a high-iron diamine technique, or appropriate combinations. Their normal distribution in the large intestine is well described (Lev and Spicer, 1965; Greco, Lauro, Fabbrini, and Torsoli, 1967; Goldman and Ming, 1968), and most workers, with minor differences, expect to find neutral mucosubstances in the goblet cells of the surface epithelium and the upper one-third of the crypts, acid non-sulphated mucosubstances in the surface epithelium and the upper two-thirds of the crypts, and sulphated mucins in the lower and middle thirds of the crypt rather than on the surface (*Fig.* 2). Studies made on rectal biopsies from patients with ulcerative colitis and Crohn's disease (Greco and others, 1967; Hellstrom and Fischer, 1967; Hradsky, Langr, Nerad, and Skaonic, 1967; Gad, 1969) have shown divergences from the normal pattern in different types of inflammation; in general there is a marked diminution in mucus secretion and goblet-cell

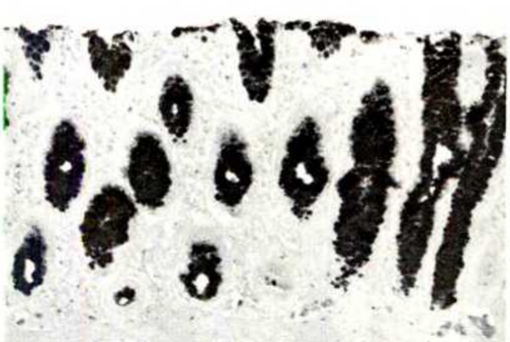

FIG. 4.—Rectal mucosa in Crohn's disease. The mucosubstance pattern is normal. HID–AB. (× 25.)

numbers in ulcerative colitis, a moderate diminution in non-specific proctitis, and little or no diminution in Crohn's disease. Fairly extensive studies by Filipe (1969) and Filipe and Dawson (1970) in general confirm these distributions for rectal mucosa and indicate that the mucosubstances which remain in Crohn's disease are predominantly of the acid non-sulphated type. Far less difference between different inflammatory conditions in colonic mucosa has been found. While I cannot entirely agree with Hellstrom and Fischer (1967) that one can make an accurate differential diagnosis between ulcerative colitis, non-specific proctitis, and Crohn's disease using techniques for mucosubstances, I have found them of definite value in the difficult biopsy.

Electron Microscopy.—The only studies using the electron microscope which I know of in Crohn's disease are those of Aluwihare (1971a, b); these, though of great interest, do not assist in the differentiation of Crohn's disease from ulcerative colitis or proctocolitis. A few incidental unpublished observations made during work done on the value of electron microscopy in detecting precancer in ulcerative colitis (Jenkinson and Dawson, 1971) did not show appreciable differences in individual mucosal cells from different patterns of rectal inflammation.

THE USE OF BIOPSIES AND TISSUES FOR RESEARCH

The aetiology of Crohn's disease remains unknown, but the emphasis in research has shifted towards consideration of it as a manifestation of cell-mediated immunological anergy (Kraft, 1971; Kraft and Kirsner, 1971). Such a suggestion is supported by observations such as those of Mitchell, Cannon, Dyer, Hinson, and Willoughby (1970) that the Kveim test for sarcoidosis, in which disease there is recognized impairment of cell-mediated immunity, is positive or probably positive in 51 per cent of patients with Crohn's disease; that in Crohn's disease there is reduced or absent skin sensitivity to 2-4-dinitrochlorobenzene (Jones, Housley, Ashurst, and Hawkins, 1969); and that lymphocytes from patients with Crohn's disease show a poor *in vitro* transformation response after stimulation with phytohaemagglutinin (Walker and Greaves, 1969; Brown, Taub, Present, and Janowitz, 1970). It is now practicable, using antisera to the human immunoglobulins IgA, IgG, and IgM raised in animals and 'tagged' with either fluorochromes or peroxidase (Petts and Roitt, 1971), to demonstrate in tissue sections of bowel those cells which are synthesizing immunoglobulin, though one cannot reliably distinguish plasma cells which will secrete humoral antibody from lymphocytes which retain cellular antibody in their surface membranes (Pettingale, 1971). Studies have already been made on normal mucosa (Crabbé and Heremans, 1966) and on the mucosa in malabsorption syndromes (Kenrick and Walker-Smith, 1970; Douglas, Crabbé, and Hobbs, 1970) and ulcerative colitis (Hardy Smith and MacPhee, 1971). Similar studies would be practicable on all rectal biopsies which are divisible into two so that fresh-frozen material can be obtained and processed in appropriate ways, and some limited studies might be possible even on formaldehyde-fixed material. These might lead to valuable information, not only as to the aetiology but also in the differential diagnosis of Crohn's disease.

Acknowledgements.—It is a pleasure to thank my colleague, Dr. M. I. Filipe, who did much of the work on mucosubstances; also the technical staff of the Udall Street Laboratories of Westminster Medical School, particularly Mrs. B. Patel and Miss J. Hepple; and Mrs. D. Litinakis for secretarial assistance. Part of the costs of the various investigations were defrayed by the Cancer Research Campaign, the Governors' Discretionary Fund of Westminster Hospital, and a personal research grant from Mr. Maurice Job through the Westminster Hospital Research Trust, all of which I gratefully acknowledge.

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SOME ASPECTS OF THE RADIOLOGY OF CROHN'S DISEASE

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THE clinical diagnosis of Crohn's disease is often difficult, and many of the lesions are not within reach of inspection. Radiology is, therefore, valuable in establishing the diagnosis and defining the site, severity, and extent of disease. A complete review of the varied techniques of radiological investigation and findings in Crohn's disease is beyond the scope of this paper. Various aspects of the barium examination of the gastro-intestinal tract will be considered, with particular reference to several of the less common small-bowel features and to the differential diagnosis of Crohn's colitis.

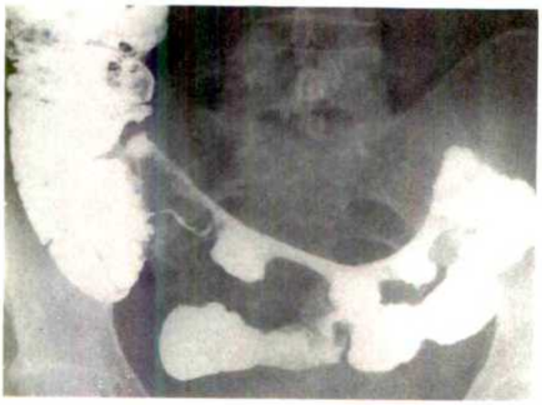

FIG. 1.—Eccentric fibrosis has produced a series of strictures and sacculations resembling a row of hammocks.

SMALL-BOWEL DISEASE

Radiologically, cases may be conveniently divided into either stenotic or non-stenotic types. Strictures which may occur anywhere in the small bowel are often multiple, separated by intervening segments of pre-stenotic dilatation. In the terminal ileum, which is the most frequent site of the disease, narrowing of the lumen by thickening of the wall, or by spasm, produces the classic 'string sign' of Kantor (1934). Occasionally where fibrosis is eccentric and involves a length of one side of the wall a series of 'purse-string' pouches or sacculations is formed along the opposite margin (*Fig.* 1). This feature is not seen in tuberculosis or reticulosis, which in other ways strongly resembles small-bowel Crohn's disease. All these late stenosing lesions are especially liable to be accompanied by fistulae, which occur in about one-third of all the cases of small-bowel disease (Brahme, 1971).

The earliest radiological suspicion of Crohn's disease is irritability of the terminal ileum which is seen on careful screening of the region during the course of a barium-meal examination of the small bowel. Another early sign is a characteristic deformity of the medial wall of the caecum attributable to an oedematous ileocaecal valve, spasm secondary to adjacent ileitis, or extrinsic pressure from enlarged lymph-glands. Although this feature may be the only demonstrable sign of Crohn's disease there are usually associated non-stenotic changes in the terminal ileum consisting of 'cobblestone' mucosa, marginal irregularity, and fissure formation (*Fig.* 2).

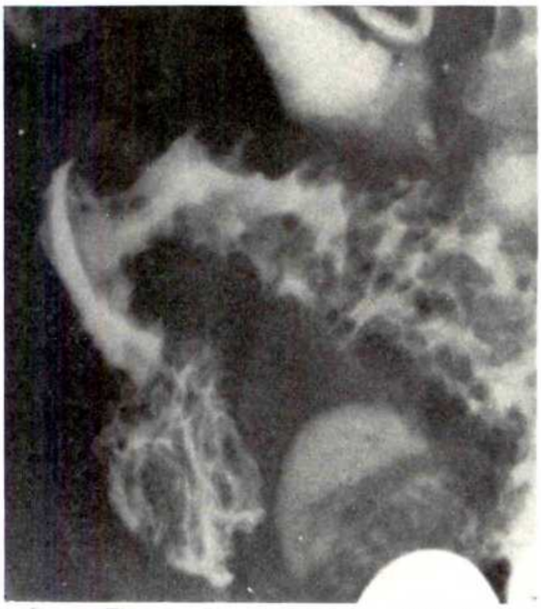

FIG. 2.—There is a curved defect in the medial wall of the caecum at the site of the ileocaecal valve. Non-stenotic changes of Crohn's disease are present in the terminal ileum with 'cobblestone' mucosa and ulceration.

Recurrent disease is a special problem and may occur at an anastomosis following resection of diseased bowel, immediately proximal to an ileostomy, or at a site remote from previous surgery. Radiological investigation is by barium-meal examination of the small bowel, ileal enema through the ileostomy stoma, or barium enema. The features of recurrence are the same as those of the original disease (*Fig.* 3). The radiologist's main problem is becoming familiar with the normal appearances following surgery and there is a strong case for performing base-line barium-meal examinations a few weeks postoperatively on all patients who have had resections for Crohn's disease. Should the patient experience further trouble there is then a previous normal postoperative examination available for comparison.

LARGE-BOWEL DISEASE

The barium-enema diagnosis of colitis, be it ulcerative, Crohn's, ischaemic, or whatever, is usually not difficult. The problem lies in differentiating one type from another, and particularly Crohn's from ulcerative colitis. General features such as narrowing,

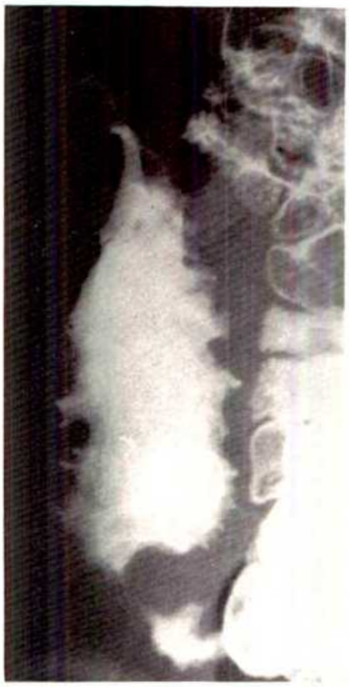

FIG. 3.—A short narrow stricture at the ileostomy stoma (*top left*) and ulceration of the adjacent segment of ileum indicate recurrence of disease.

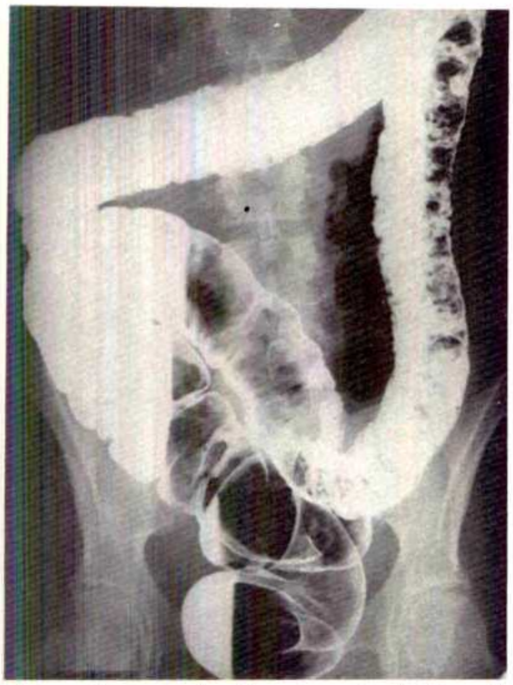

FIG. 4.—Disease involves the colon as far distally as the proximal sigmoid, where there is some eccentric involvement. The rectum and distal sigmoid are normal.

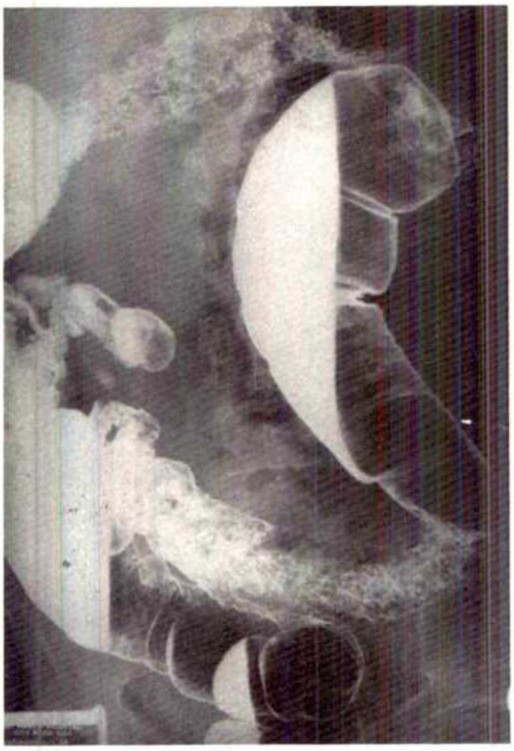

FIG. 5.—Several areas of disease are present, notably in the transverse colon and proximal sigmoid. There is also some eccentric involvement of the distal sigmoid and a patch of ulceration in the mid-descending colon.

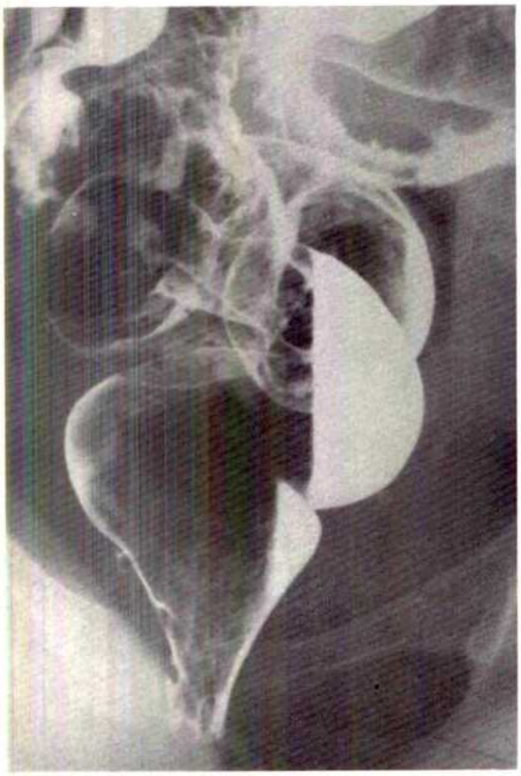

FIG. 6.—A long anorectal ulcer is present and a deep discrete ulcer surrounded by normal mucosa in the right mid-lateral rectal wall. Further disease is seen in the colon.

shortening, and absent or abnormal haustration are sometimes difficult to assess, particularly in borderline cases, and are not helpful in the differential diagnosis. For this purpose the distribution of pathology throughout the colon, rectum, and anus, and the particular features of individual lesions, especially ulcers, are of the greatest assistance in separating Crohn's disease from ulcerative colitis.

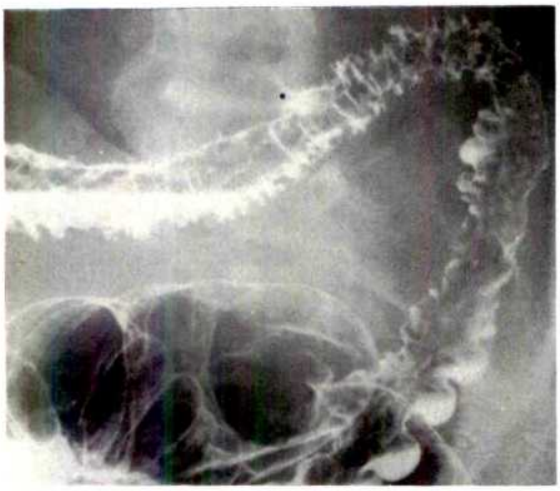

FIG. 7.—There is narrowing of the transverse colon with composite ulcers and fissures. In the proximal descending colon eccentric involvement has produced sacculation of a normal patch of bowel on the medial side. Normal mucosa is seen in the sigmoid.

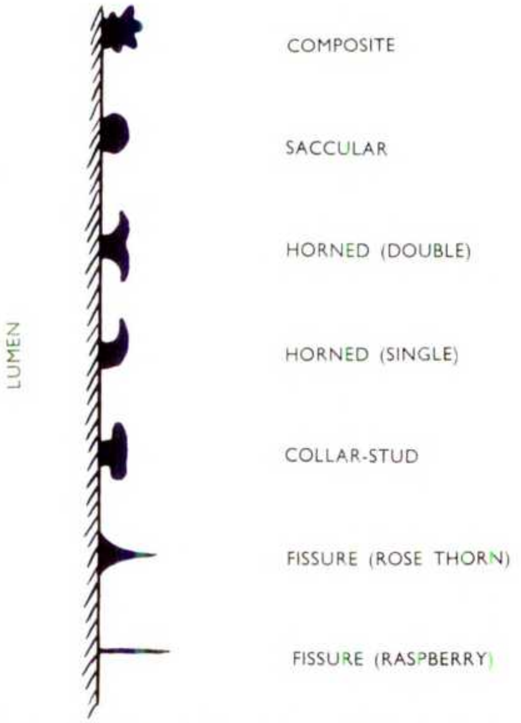

FIG. 9.—Illustrations of the types of ulcer seen in Crohn's colitis.

Distribution of Pathology throughout th Large Bowel.—Crohn's disease involves the rectu in only 50 per cent of cases, has a tendency to b right-sided (*Fig*. 4), and is often discontinuous, wit areas of disease separated by variable lengths of normal bowel ('skip lesions'—*Fig*. 5). In contrast, ulcerative colitis involves the rectum in at least 95 per cent of cases and the disease is in continuity (Lockhart-Mummery and Morson, 1964). In Crohn's disease

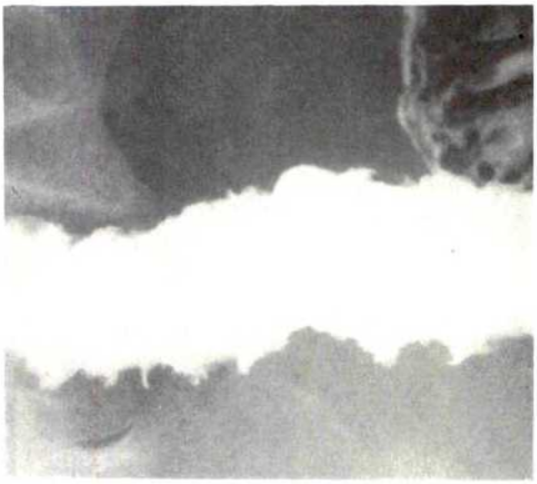

FIG. 8.—A localized view of part of the transverse colon showing several of the characteristic types of Crohn's ulceration, i.e. fissure, horned, and composite.

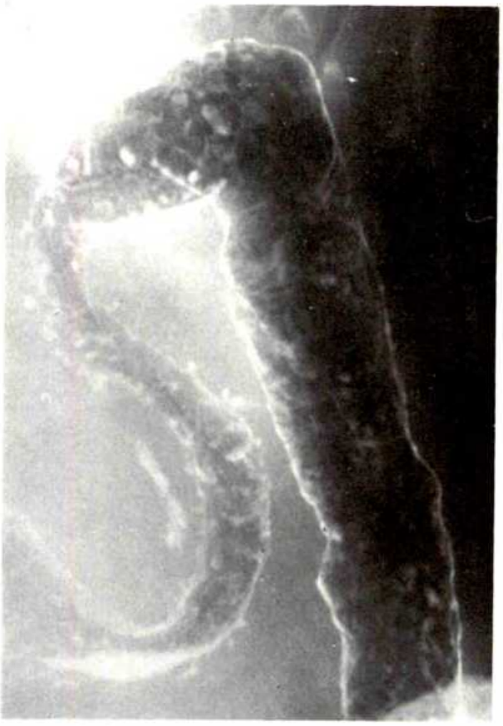

FIG. 10.—Confluent intramural ulceration is present together with narrowing and deep ulceration.

ormal patches of mucosa may be present in the nidst of diseased areas and vice versa, or discrete lcers may be surrounded by an area of normal mucosa (*Fig.* 6). Involvement may be eccentric, sometimes with sacculations of the normal bowel wall produced by contraction of areas of severe disease on the opposite wall (*Fig.* 7). Similar appearances are seen in ischaemic strictures (Marston, Pheils, Lea-Thomas, and Morson, 1966) and scleroderma (Kemp Harper and Jackson, 1965). Rarely, localized scarring

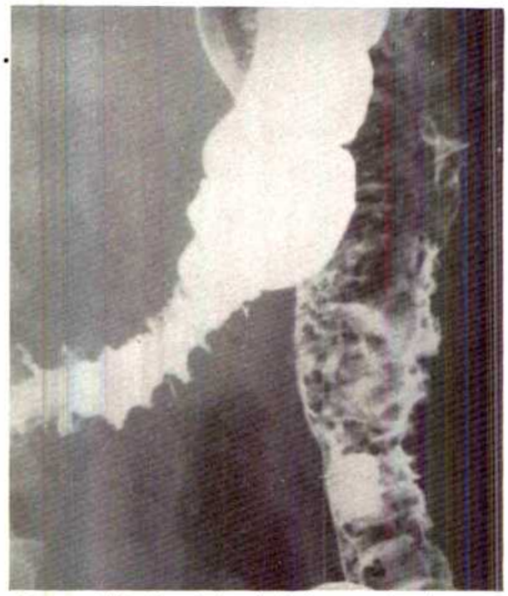

FIG. 11.—This view of the splenic flexure region shows many of the characteristic features of Crohn's colitis. The transverse colon is narrowed with deep fissures and composite and horned ulcers. Similar ulceration is seen in the descending colon together with 'cobblestone' mucosa. The mucosa of the splenic flexure itself looks normal.

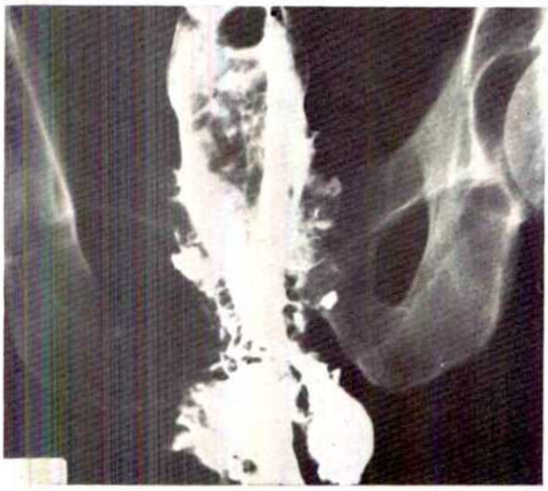

FIG. 12.—Gross anorectal disease is present with fistula and abscess formation. Rectal ulceration is mainly of the fissure variety, both rose-thorn and raspberry-thorn.

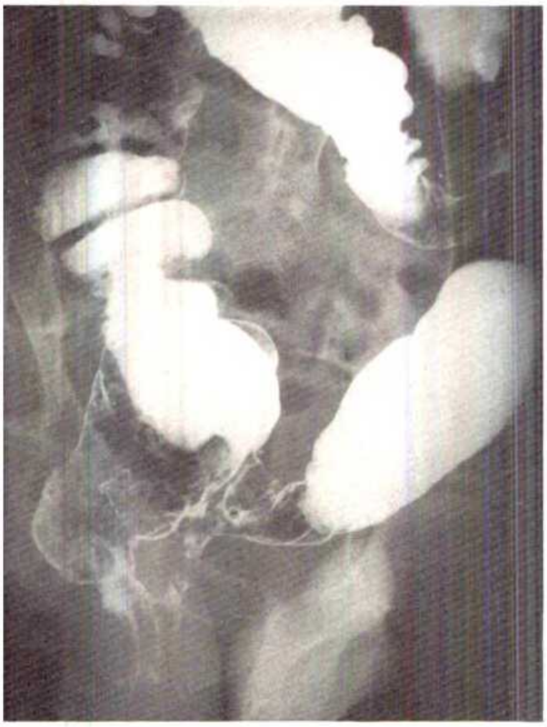

FIG. 13.—There are irregularity and narrowing of the anal canal and lower rectum with a fistula extending from the lower rectum to the sigmoid. A rectocolic fistula is one of the least common varieties in Crohn's disease. A stricture is present at the splenic flexure.

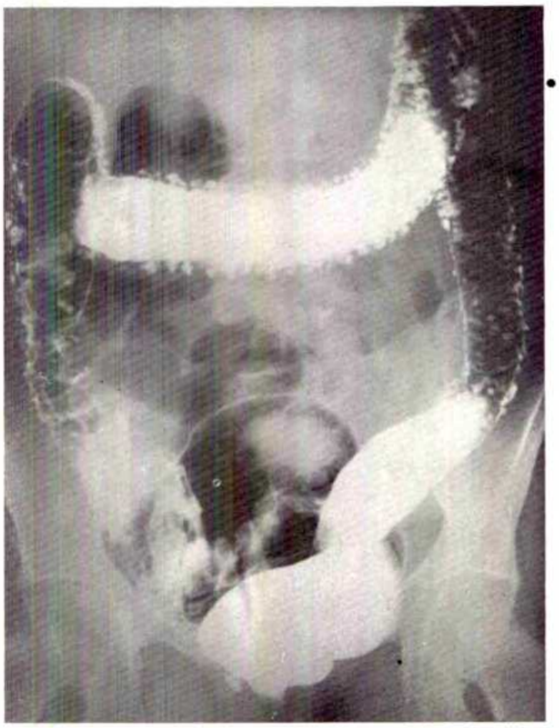

FIG. 14.—Many of the characteristic features of Crohn's colitis are present such as a pararectal abscess, a normal-looking sigmoid with gross changes in the rest of the colon, and deep composite ulceration in the transverse colon. The caecum is contracted and there is probable disease of the terminal ileum.

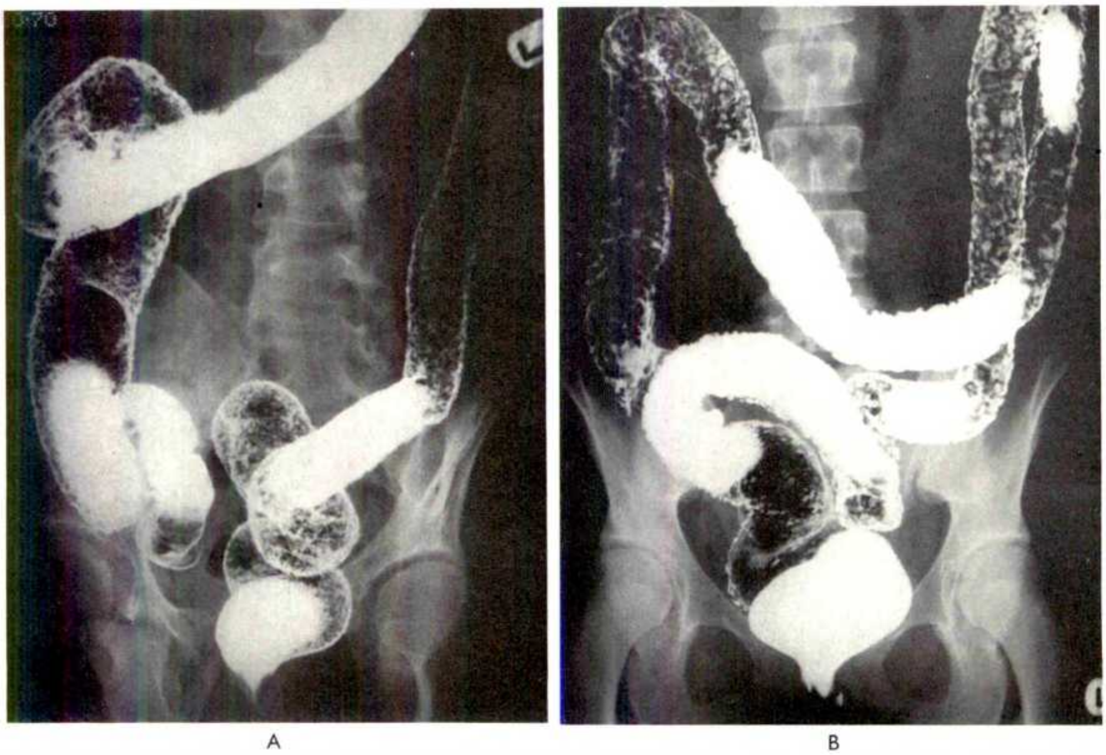

FIG. 15.—A, Shallow ulceration, pseudopolyposis, dilated terminal ileum, and absence of an anal lesion indicate ulcerative colitis. B, Deep pleomorphic ulceration, 'cobblestone' mucosa, and a perianal abscess indicate Crohn's colitis. The ileum was also diseased. There is a strong resemblance between these two examples of total ulcerative colitis and Crohn's disease respectively.

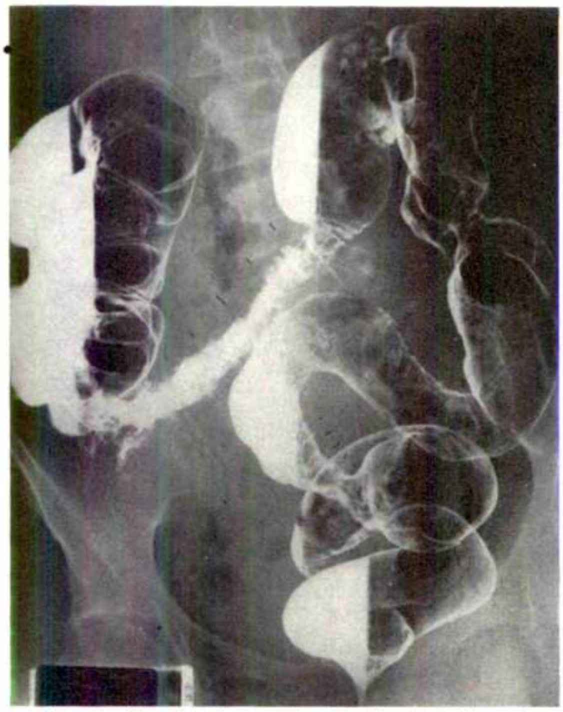

FIG. 16.—Several strictures of various lengths and severity, some with ulceration, are present. An eccentric patch of mucosal disease is seen in the proximal sigmoid and there is a deep discrete ulcer in the right lateral wall of the rectum.

and narrowing of the colon lead to the formation o large false diverticula (Berridge, 1971). Haustratio may be retained in the presence of severe ulceration or eccentric incomplete loss of haustration may occur All these features are at variance with the mor uniform changes of ulcerative colitis.

Features of Individual Lesions.—Of the individual features of Crohn's colitis, the most importan is ulceration because some of the forms that the ulcer may take are characteristic and assist in differentiatio from ulcerative colitis. Occasionally only one type o ulcer is present in an individual case, but usuall ulceration is pleomorphic (*Fig.* 8), unlike ulcerativ colitis where all the ulcers in an individual case ten to be of similar size and shape. Some of the differen types of ulcer are illustrated in *Fig.* 9. Deep ulceratio of more than 3 mm. depth is very strong evidence o Crohn's disease, as are fissures, composite or horne ulcers, and linear intramural confluent ulceratio (*Fig.* 10). A fissure is a deep spicular ulcer, eithe broad-based triangular and rose-thorn, or narro linear and raspberry-thorn in shape, extending int the bowel wall at right-angles to the lumen (Young 1970). A composite ulcer consists of a large saccula ulcer with short finger-like projections resembling sea-mine or cow's udder.

The 'cobblestone' appearance of Crohn's diseas owing to the high-lighting of surviving islands o oedematous mucosa by a network of linear ulceratio and the pseudopolypoid inflammatory changes o ulcerative colitis bear a strong resemblance and ar sometimes indistinguishable (*Fig.* 11).

Anal lesions consisting of anal and perianal swelling, ulceration, abscesses, and fistulae are present at some tage in 75 per cent of the cases of large-bowel Crohn's disease, particularly in those with severe colonic nvolvement and in one-quarter of those cases with mall-gut disease only (Gray, Lockhart-Mummery, nd Morson, 1965). The radiological demonstration of n anal or perianal lesion may be a vital clue to the iagnosis of Crohn's disease as not all of these lesions re previously detected clinically (*Figs.* 6 and 12). imilar changes in ulcerative colitis are considerably ss common and are always accompanied by proctitis. olitis with a normal rectum and an anal lesion is iagnostic of Crohn's disease as the anal pathology an be counted as a skip lesion.

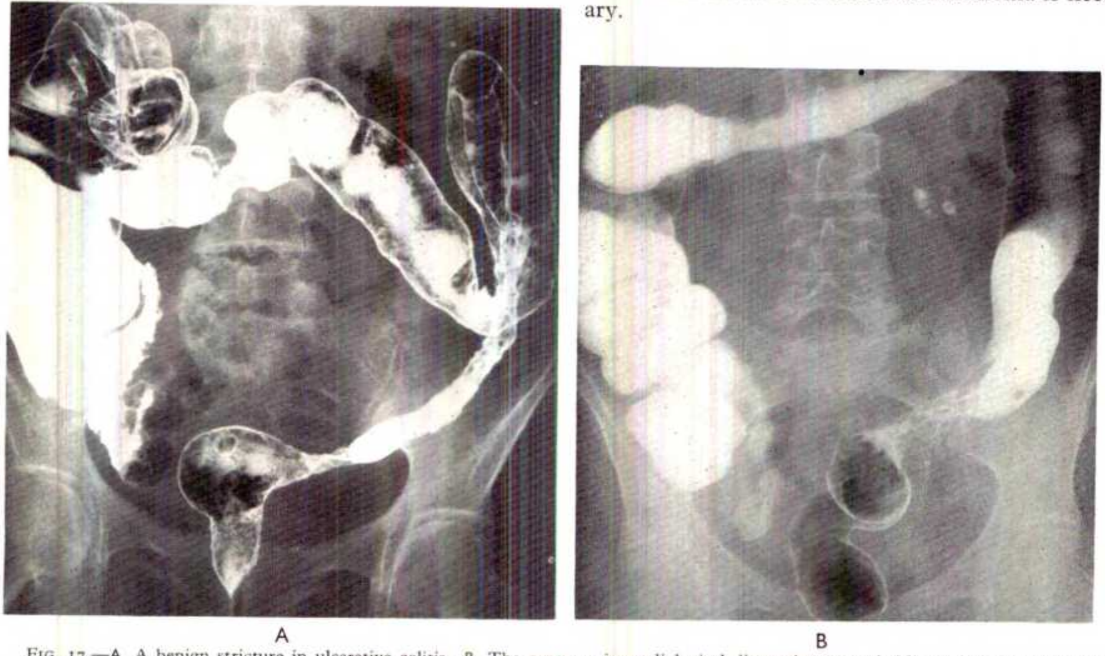

FIG. 17.—A, A benign stricture in ulcerative colitis. B, The preoperative radiological diagnosis was probable carcinoma in ulcerative colitis because irregular intraluminal filling defects are present in the stricture and just proximal to it. However, pathological examination of the colectomy specimen was characteristic of Crohn's disease and there were also some features to suggest additional diverticulitis. There is a strong resemblance between these two examples of extensive long-standing colitis with sigmoid stricture.

able I.—THE LIKELIHOOD OF CROHN'S COLITIS RELATED O ANORECTAL DISEASE AND DISTRIBUTION SEEN ON BARIUM-ENEMA EXAMINATION

DISTRIBUTION			LIKELIHOOD OF CROHN'S COLITIS
Anal Lesion	Proctitis	Colitis	
+	−	+	***
−	−	+	**
+	+	+	*
−	+	+	
−	+	−	
+	+	−	*
iscontinuous disease (skip lesions)			***
ccentric involvement			**
leal lesion			***

* = Possible Crohn's colitis. ** = Likely Crohn's colitis. *** = ery likely Crohn's colitis. The presence of more than one feature om *Tables I* and *II* increases the likelihood of Crohn's disease.

Fistulae are more often a feature of small- than of large-bowel disease. Communication may occur between the gut lumen and the skin or lumen of another viscus (*Fig.* 13). In the pelvis differentiation from diverticulitis and carcinoma is necessary.

Table II.—THE LIKELIHOOD OF CROHN'S COLITIS RELATED TO A VARIETY OF INDIVIDUAL LESIONS SEEN ON BARIUM-ENEMA EXAMINATION

INDIVIDUAL LESIONS	LIKELIHOOD OF CROHN'S COLITIS
Deep ulcers of any form	*
Deep ulcers in the rectum	**
Saccular ulcers	*
Composite or horned ulcers	***
Fissures, either rose-thorn or raspberry-thorn	***
Linear intramural confluent ulceration	***
Discrete ulcers surrounded by an area of normal mucosa	***
Retained haustration in ulcerated bowel	**
'Cobblestone' mucosa	**
Fistula	**

See Table I for key.

SOME DIAGNOSTIC PROBLEMS OF LARGE-BOWEL DISEASE

In the majority of cases assessment of all the available radiological signs allows a confident diagnosis to be made (*Fig.* 14). There are, however, a minority of cases, perhaps of the order of about 5 per cent, where the diagnostic features are uncertain and occasionally frankly misleading. This situation arises if insufficient diagnostic signs are demonstrated, either because they are not present or because radiological examination is not of the necessary quality. Alternatively, clear diagnostic signs may be demonstrated, but are conflicting, favouring different diagnoses. Under these circumstances the problem is knowing to which signs to afford the greatest weighting. An attempt at this has been made in *Tables I* and *II*.

Total Colitis.—This situation removes several of the most helpful signs of Crohn's disease, such as a right-sided distribution with sparing of the rectum and discontinuous, eccentric, or patchy disease. Clues to diagnosis may be found at the two ends of the large bowel, i.e., the ileum and the anus. Involvement of the terminal ileum occurs in about half the cases of Crohn's colitis (Morson, 1971) and is seen as narrowing, often with strictures elsewhere in the small bowel. In ulcerative colitis if the ileum is involved it is dilated ('backwash' ileitis). In the presence of total Crohn's colitis an anal lesion is to be expected and most of them will be seen on barium-enema examination. Study of individual colonic lesions, especially ulcers, and the recognition of other features such as 'cobblestoning' and fistula formation enable the correct diagnosis to be reached in the majority of cases, but there is a small residuum in which differentiation is not possible (*Fig.* 15).

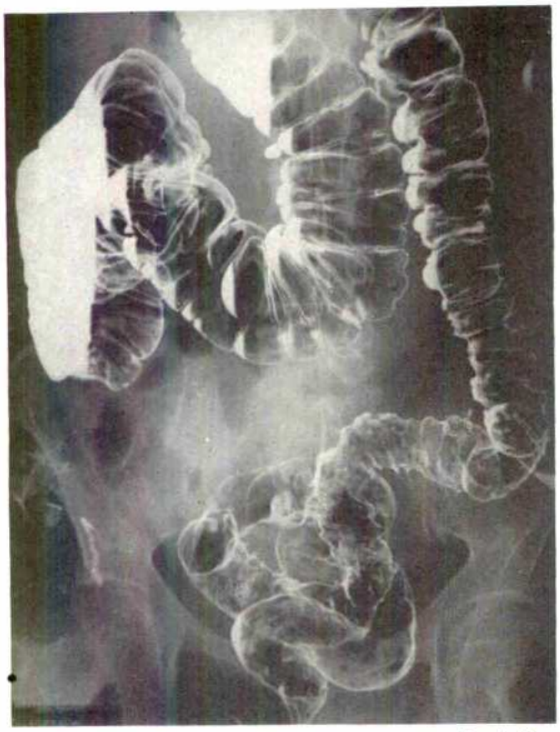

FIG. 18.—At first glance the appearances suggest diverticular disease, but on closer observation not all the barium-filled projections are diverticula. Some of them are deep and spicular, and along the medial wall of the distal descending colon ulceration is of the 'collar-stud' variety. There is therefore coexistent diverticular and Crohn's disease.

Strictures.—These are seen in about one-quarter of cases of Crohn's colitis, being multiple in half of them (Lockhart-Mummery and Morson, 1964). The length, site, and degree of narrowing are variable (*Fig.* 16) (Young, 1970). In most cases the ends are tapered or funnelled. The walls of the stricture may be studded with ulcers, but these are usually absent from long-standing narrow strictures. Many of the strictures of Crohn's disease and ulcerative colitis are indistinguishable so that differentiation is made by assessment of the changes in the remainder of the bowel. Of particular difficulty is the stricture occurring in quiescent or 'burnt-out' colitis (*Fig.* 17). Shouldered ends, ragged channels, and irregular intraluminal filling defects indicate carcinoma and a likely diagnosis of ulcerative colitis. Other conditions which must be included in the differential diagnosis are diverticulitis, ischaemia, irradiation, various extrinsic lesions such as metastasis and abscess tuberculosis, and a variety of tropical diseases (Simpkins and Young, 1971).

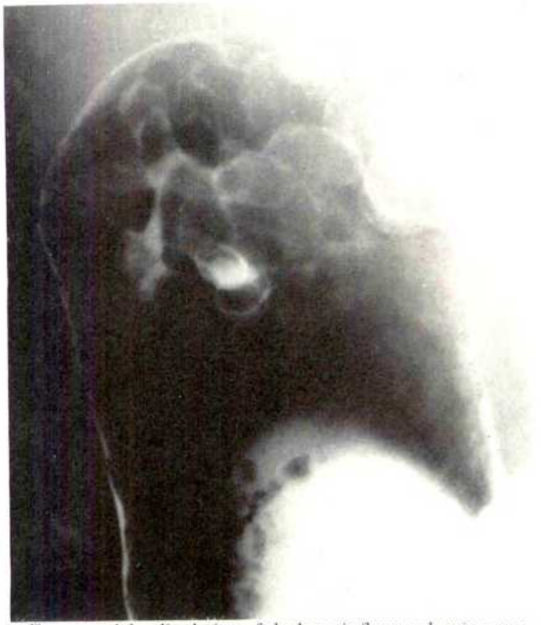

FIG. 19.—A localized view of the hepatic flexure showing complete obstruction by a polypoidal mass of Crohn's granuloma simulating carcinoma.

Coexistent Diverticular Disease.—Schmidt Lennard-Jones, Morson, and Young (1968) have drawn attention to the difficulty in diagnosing Crohn' disease in the presence of diverticular disease and th importance of detecting this combination because o the high incidence of postoperative complications Radiologically, Crohn's disease in the presence o diverticula is suggested by deep narrow fissuring ulceration involving the rectum or colon away fron the area of diverticular disease, linear confluen intramural ulceration, or fistula (*Fig.* 18).

Complete Obstruction.—The granulomatou changes of Crohn's disease may be so prominent tha they produce complete obstruction to the flow o barium on enema examination and simulate th presence of a polypoidal carcinoma (*Fig.* 19). Th demonstration of other changes of Crohn's disease i the colon or small intestine will assist diagnosis, but i their absence differentiation from carcinoma may nc be possible. Similar filling defects in the medial wa of the caecum resembling carcinoma have bee described by Berridge (1971).

Acknowledgements.—I am grateful to the surgeons under whose care the patients were examined. I also wish to thank the Department of Medical Photography of Leeds General Infirmary for preparing the illustrations.

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NUTRITIONAL DISTURBANCES IN CROHN'S DISEASE

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NUTRITIONAL disturbances are common in Crohn's disease (Cooke, 1955; Pimparker, Mourhan, and Bockus, 1960; Krause, Bergman, and Norlen, 1971). The main manifestations of malnutrition in such patients are weight-loss, anaemia, hypoproteinaemia, electrolyte depletion, and vitamin deficiencies. Furthermore, there are a variety of mechanisms whereby such malnutrition may take place. Thus, there may be a low intake of food because of simple anorexia or fear of aggravating abdominal pain by eating; malabsorption due to either loss of gut surface from inflammation, resection, or surgical by-pass, or the presence of a stagnant loop syndrome caused by strictures, fistulas, or a surgical side-to-side anastomosis. The situation may also be aggravated by excessive loss of protein, blood, electrolytes, and bile-salts from the bowel lumen and also the toxic effect of the inflamed bowel. An analysis of the relative importance of these various factors in 63 patients with Crohn's disease has been published fully elsewhere. There it was concluded that the importance of malabsorption had been overstressed in the past (Dyer and Dawson, 1972a).

WEIGHT-LOSS

Weight-loss is frequent and in childhood may be the cause of a perplexing diagnostic problem, for occasionally adolescent girls may present with weight-loss while the gastro-intestinal symptoms are minimal. On occasion it is difficult to determine whether the weight-loss is in fact due to anorexia nervosa or to an occult intestinal disease (Silverman, 1966). *Fig.* 1 shows the weight chart of such a patient with known Crohn's disease who had minimal symptoms of her disorder and loss of weight. This responded to anti-inflammatory drugs which, of course, would not occur in true anorexia nervosa.

ANAEMIA

The anaemia may theoretically be due to (1) a lack of iron resulting from either impaired intake or excessive loss from the bowel, (2) a lack of vitamin B_{12} caused by resection of inflammation of the ileum or the presence of a stagnant-loop syndrome, and (3) the presence of folate deficiency due to an inadequate intake or increased requirements. In a recent survey (Dyer, Child, Mollin, and Dawson, 1971) of 63 hospitalized patients four-fifths of the men and half of the women were found to be anaemic. Iron deficiency, as determined by bone-marrow examination, was found in 40 per cent of the patients but would have been spuriously diagnosed more frequently if the serum iron and presence of hypochromic cells in the blood-film had been relied on. Vitamin-B_{12} deficiency occurred in 16 per cent of the patients, usually in those who had undergone ileal resection or had extensive ileal disease. Although a stagnant-loop syndrome (Tabaqchali and Booth, 1970) might theoretically be expected to occur frequently, in fact this is a rare mechanism for the genesis of vitamin-B_{12} deficiency (Vince, Dyer, O'Grady, and Dawson, 1972). Folate deficiency is extremely common (Hoffbrand, Stewart, Booth, and Mollin, 1968), as reflected by both a low red-cell count and serum

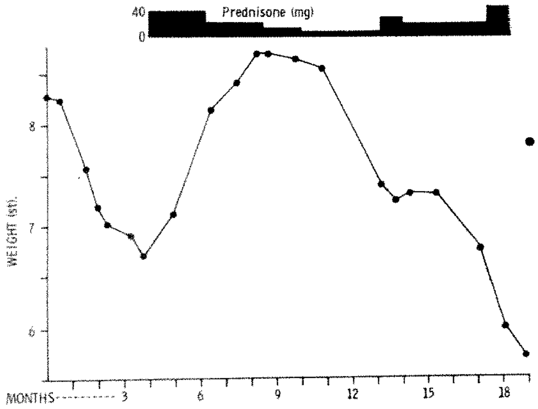

FIG. 1.—Weight-chart of a patient with Crohn's disease who presented initially with weight-loss. The initial response to steroids with subsequent relapse is shown.

folate. It occurs equally in patients who have colonic or small-bowel disease and is far more likely to be due to an impaired intake combined with an increased requirement than to actual malabsorption (Dyer and others, 1972). Occasionally patients have been described whose anaemia responds to oral folate but this has been a rarity.

It would seem that by far the commonest cause of anaemia in patients with Crohn's disease is toxic depression of the marrow.

HYPOPROTEINAEMIA

Fig. 2 shows that patients with Crohn's disease have a far greater depression of the serum albumin than patients with coeliac disease who have an abnormal jejunal mucosa and frequent malabsorption. These results are similar to those reported by Cooke in 1955. If one considers that approximately only 35 g. of protein are needed each day and that most patients are eating much more than this amount, then another mechanism must be invoked to explain the hypoproteinaemia. Furthermore, the serum albumin is reduced whether the patients have ileocolic or diffuse small intestinal disease (*Fig.* 3). These two facts strengthen the view that the commonest cause of hypoproteinaemia is loss of protein from the inflamed bowel into the lumen. This may be digested and reabsorbed but the liver has only a limited capacity to synthesize albumin so that hypoproteinaemia ensues—protein-losing enteropathy (Steinfeld, Davidson, and Gordon, 1960; Waldman, 1970). However, in some patients with profound anorexia true protein deficiency with depletion of all the body stores may be present.

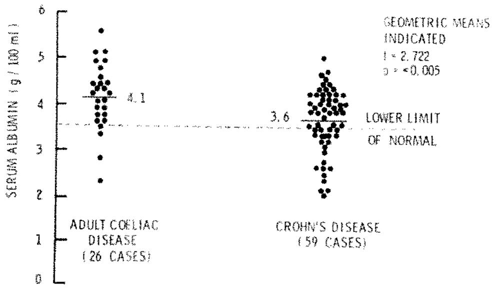

FIG. 2.—Serum albumin in patients with coeliac disease and in those with Crohn's disease (Dyer, 1971).

ELECTROLYTE DEPLETION

Electrolyte depletion occurs as a result of diarrhoea and sometimes steatorrhoea, for the faecal fat is frequently raised in small-bowel Crohn's disease. Its occurrence is most likely due to a disturbance of the bile-salt metabolism. Normally the conjugated bile-salts are not absorbed in the jejunum, in this way maintaining a high concentration of these detergent substances in the lumen of the jejunum from where fat and other lipids are usually absorbed, but these bile-salts are actively absorbed by the ileum, thus preserving the bile-salt pool. This recirculates many times a day and usually only a small amount escapes into the faeces. When the ileum is resected bile-salts are inadequately preserved and an excess escapes into the large bowel where it is degraded into the unconjugated bile-salts and various metabolites (Heaton 1969). These have a cathartic action (Mekhjian Phillips, and Hofmann, 1971). If the resection is large enough and the loss of bile-salts great enough there is an inability of the liver to synthesize adequate replacement and therefore there is a fall in the bile-salt pool with a subsequent decrease in the bile-salt concentration in the lumen of the bowel; steatorrhoea subsequently ensues (Dawson, 1971).

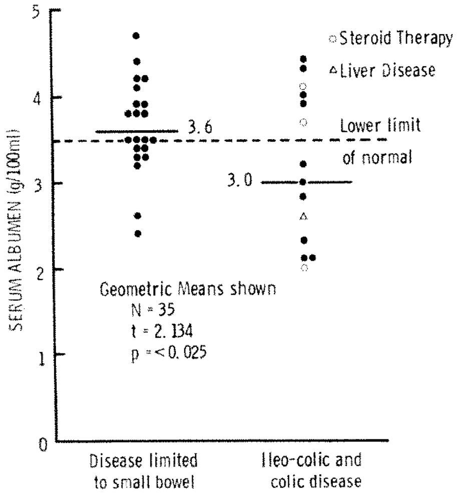

FIG. 3.—Serum albumin in patients with small-bowel disease and in those with ileocolic disease (Dyer, 1971).

The stagnant-loop syndrome occasionally occurs in Crohn's disease but only rarely accounts for the steatorrhoea (Vince and others, 1972). It is of some interest that the steatorrhoea, in spite of being due to bile-salt deficiency, is rarely accompanied by osteomalacia (vitamin-D deficiency) or a prolonged prothrombin time. In fact, when a high alkaline phosphatase is found in patients with Crohn's disease it usually represents impaired liver function (Dyer and Dawson, 1972b) rather than bone disease.

THE MANAGEMENT OF NUTRITIONAL DISTURBANCES

The most important factor is to control the degree of inflammation present either by resection or by suppression of the inflammatory reaction with steroids or possibly azathioprine (*see* article by Rhodes, p. 819). This leads to an improved appetite and a decrease in the nutritional requirement.

Anaemia.—If vitamin-B_{12} deficiency has been demonstrated and malabsorption confirmed by, for example, the Schilling test, monthly injections of vitamin B_{12} will be needed. It is rare that folate supplements will be indicated, for once the appetite returns and the inflammation is removed the serum folate returns to normal. Occasionally iron supplements are of importance, but the presence of a slightly hypochromic film and a low-iron-binding capacity may give a misleading impression that the patient is suffering from iron deficiency when, in fact, he is suffering from a depressed iron uptake by cells in the marrow.

Hypoproteinaemia.—The very nature of the hypoproteinaemia means that a high-protein diet will usually be of little help in such patients if the dominant cause of the hypoproteinaemia is loss of protein into the bowel with inability of the liver to resynthesize. However, in the few patients who are truly protein-depleted an adequate protein intake is important. Furthermore, protein malabsorption may be aggravated by gross steatorrhoea (Pinter, McClaken, Lamar, and Goldsmith, 1964), and control of the steatorrhoea often helps the protein status of the patient.

Very occasionally intravenous salt-poor albumin or amino-acid mixtures and calories may be needed to improve the nutritional status of the patient, but this type of régime is probably being used excessively at the moment.

Steatorrhoea and Diarrhoea.—These are best controlled by a low-fat diet (less than 40 g.), and only rarely are antibiotics of help if a stagnant-loop syndrome should have been demonstrated. Diarrhoea may be helped by the control of steatorrhoea, the use of simple anti-diarrhoeal agents, such as codeine phosphate, or the administration of Lomotil. If the diarrhoea is due to irritation of the colon from unabsorbed bile-salts then cholestyramine (Questran), up to 4 g. q.i.d., can occasionally give impressively helpful results. Unabsorbed bile-salts are less likely to be present if gross steatorrhoea is also a factor (Hofmann and Poley, 1969). If the diarrhoea is severe potassium supplements may be needed.

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AZATHIOPRINE IN THE TREATMENT OF CROHN'S DISEASE

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As long as the cause of Crohn's disease remains obscure, treatment must be given on an empirical basis. Recently, attempts have been made to explain the disease in immunological terms, and there have been reports of abnormalities in both cellular and humoral immunity (Kraft, 1971; Kraft and Kirsner, 1971). Because of these findings, together with the all too frequent failure of current therapy to control the disease, immunosuppressive drugs, usually azathioprine, have been tried. There have been 14 published studies, which include about 160 patients, in the past 3 years (Avery Jones, Brown, Lennard-Jones, Hywel Jones, and Milton-Thompson, 1969; Brooke, Hoffmann, and Swarbrick, 1969; Brooke, Javett, and Davison, 1970; Brown and Achkar, 1970; Drucker and Jeejeebhoy, 1970; Arden Jones, 1971; Fausa and Gjone, 1971; Rhodes, Bainton, Beck, and Campbell, 1971; Willoughby, Kumar, Beckett, and Dawson, 1971). The possible clinical indications for treatment with azathioprine have included ill patients (some severely ill and others with abdominal fistulae), patients receiving prednisone where an attempt has been made either to reduce or to withdraw the steroid and patients before and after surgery, in the hope of reducing operative complications and recurrence of the disease. Most of these studies have been uncontrolled and for this reason may give a biased account in favour of the treatment.

There are only two controlled trials of therapy in Crohn's disease, both of them with azathioprine. The lack of previous trials in this condition is perhaps a reflection of the difficulties inherent in such a study.

AZATHIOPRINE IN PATIENTS WITH ACTIVE DISEASE

In a double-blind cross-over trial patients were given azathioprine (4 mg. per kg. for 10 days and 2 mg. per kg. thereafter) for 2 months and a placebo for 2 months, the sequence of the treatment periods being made on a random basis (Rhodes and others, 1971). Activity was based on clinical and biochemical features, while progress during the trial was based on the patient's assessment of symptoms together with several laboratory measurements. Changes in the body-weight were noted and patients recorded on a diary card the frequency of stools and colic.

Sixteen patients were admitted to the trial. Six had fistulae (4 on to the abdominal wall, 1 vesicocolic, and 1 perianal). Two patients were dwarfs with recurrent colic. One patient had severe rectal disease with a stricture, and the remaining 7 patients had weight-loss with diarrhoea as a prominent feature. Eight of the patients could be described as 'quite unwell' during the trial.

Fourteen patients completed the trial and a further patient had treatment in both periods. If the progress during the period of azathioprine is compared with that during the placebo period, in 6 patients there was no difference between the periods, 7 patients were better with the placebo, while 2 were better with azathioprine. If the periods are considered separately, with azathioprine 7 patients showed no change in symptoms, 6 deteriorated, and 2 improved. The corresponding figures for the placebo period were 11, 1, and 2 (possibly 3) respectively. In no patient did azathioprine cause a striking improvement, but 2 patients showed a marked deterioration (1 was the result of an allergic arthritis and the other was caused by severe colic which resolved when the drug was withdrawn).

AZATHIOPRINE FOR PATIENTS DURING A STEROID-INDUCED REMISSION

In another double-blind controlled trial patients were treated on a random basis with either azathioprine or placebo for up to 24 weeks (Willoughby and others, 1971). All the patients were in remission and receiving prednisone. One group of 12 patients had recently had an acute illness which had responded to prednisone; the second group of 10 out-patients were on maintenance therapy with up to 15 mg. of prednisone daily. Progress of the patients was assessed clinically and confirmed by a 'disease-activity score' based on the clinical and laboratory data.

Azathioprine in a daily dose of 4 mg. per kg. was given for 10 days and 2 mg. per kg. thereafter. In the first group of patients who were recovering from an acute illness the dose of prednisone was reduced when a remission had been obtained. Azathioprine was started and an attempt was made to discontinue the steroids about 4 weeks later. The second group of patients who appeared to require maintenance treatment with prednisone had this drug discontinued after 4 weeks of azathioprine. If deterioration in the symptoms occured and it was considered necessary to change the treatment the patient was withdrawn from the trial. Ten out of the 11 patients receiving azathioprine completed the 24-week period of the trial compared with only 3 out of the 11 on a placebo, a highly significant advantage in favour of azathioprine. This difference applied to both groups, for the improvement brought about by steroids in those who had recently had an acute illness was maintained by azathioprine.

EARLY AND POSSIBLE LATE COMPLICATIONS OF AZATHIOPRINE THERAPY

The incidence of the short-term complications of leucopenia and thrombocytopenia is probably related to the dosage and seems to occur more commonly with 4 mg. per kg. per day than with 2 mg. Leucopenia is seldom a problem in clinical management when blood-counts are made regularly. However, septicaemia and intra-abdominal abscesses have been reported for treatment with azathioprine (Brooke and others, 1970; Northfield and Roberts, 1972). Although these complications may have occurred without azathioprine therapy, it is difficult to exonerate azathioprine and the associated leucopenia from having played a contributory role.

A severe polyarthralgia and fever have been reported in several patients after about 10 days of therapy We encountered this complication in 2 out of 2 patients while others have not recorded the problem with larger series. The complication appears to be due to a sensitivity reaction and we were unable to resume the drug.

Azathioprine may cause a deterioration in some patients. One of our patients had to discontinue treatment because of very severe small intestinal colic while a second patient complained that the fistulous discharge from his abdominal wall was worse than i had ever been previously.

The long-term consequences of immunosuppression in Crohn's disease are unknown. Even without azathioprine therapy, malignancy has been reported as a complication in both small and large intestinal disease. One must ask whether the risk o malignancy is increased by long-term azathioprine and if so whether the risk is justifiable in view of the possible benefit from the drug. Malignancies, particularly lymphoma, have been reported in recipients of renal transplants on immunosuppressive régimes (Penn and Starzl, 1970). There are only 4 reports o malignancy associated with azathioprine therapy in clinical situations other than in patients who have had transplantations. Experimental work on New Zealand black mice has shown that the incidence of lymphoma in these lymphoma-prone mice is significantly increased by azathioprine, possibly due to depression of the cellular reactivity (Krueger, Malmgren, and Berard, 1971). The *in vivo* cell reactivity, particularly of 'T' lymphocytes, is thought to be of importance in immunological surveillance and control of potentially malignant-cell lines; azathioprine probably depresses these 'T' cells and steroids have a similar effect Patients with Crohn's disease already have impaired *in vitro* 'T'-cell reactivity and *in vivo* depressed delayed hypersensitivity reactions. In Crohn's disease therefore, there is an increased risk of malignancy associated with impaired cellular immunity; both azathioprine and steroids may further depress the cellular response. We have no measure of this cumulative effect but should be aware of its existence

THE POSSIBLE PLACE OF AZATHIOPRINE

In view of the complications which have been associated with azathioprine it is perhaps better reserved for patients who are resistant to other therapy. It may be safer to use only 2 mg. per kg. per day and in combination with a small dose of steroids. I am reluctant to use the compound as the first drug of choice in ill patients. There is no way of predicting those patients (a minority) who may show a favourable response. Steroids appear to help most of the patients in this clinical situation without carrying the special hazards associated with azathioprine.

However, once a clinical remission has been obtained with steroids a special group of patients appears to be delineated who may benefit from the drug. In this situation azathioprine appears to be effective and may be used either to reduce or to discontinue the steroid therapy. At present I should not readily recommend its use as the sole drug in other clinical situations However, there are reports of a favourable response in many other groups of patients: those with extensive inoperable disease, those with fistulae (both abdominal and perianal), those with recurrent disease after previous surgery, and those with systemic manifestations such as pyoderma gangraenosum.

The use of immunosuppressive therapy in Crohn's disease is a situation which is not unique in clinical medicine, although one must feel a little uncomfortable about it. The cause of the disease and the action of the agents that are used in its treatment are both unknown. The response of patients is unpredictable and the long-term hazards are, as yet, undefined. In spite of these obstacles there may well be a place for immunosuppressive therapy in the treatment of Crohn's disease—a place which must be further defined by careful, long-term clinical trials.

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SURGICAL TREATMENT OF CROHN'S DISEASE OF THE SMALL INTESTINE

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The most common site for Crohn's disease is in the distal part of the small intestine. In a typical case the ileal wall is thickened over a distance of 10–20 cm. Sometimes there are short skip lesions which are within a few centimetres of the main mass and which, surgically, may be considered as part of it. A remote skip lesion in the proximal ileum or jejunum occurs in 12 per cent of cases. In the majority of patients the transmural inflammation extends distally as far as the ileocaecal valve. Frequently the caecum and the adjacent ascending colon are healthy, but in some patients their walls are also involved by the granulomatous process.

The onset of Crohn's disease is gradual in most cases, with increasing diarrhoea, abdominal colic, and weight-loss. Ten per cent of cases begin acutely and the presentation may closely simulate that of acute appendicitis. Undoubtedly there are other forms of acute ileitis which are distinct from Crohn's disease and which resolve spontaneously.

Modern medical treatment with corticosteroids and azathioprine can often induce a remission in the chronic inflammatory process, but there is no convincing evidence that it ever produces a permanent cure. Drug treatment may well be required for the remainder of the patient's life if he is to be kept free of symptoms. There are dangers inherent in this course and many people will not accept it. Elective surgical resection is safer and more certain but it is not a guarantee of cure in Crohn's disease.

ACUTE ONSET OF CROHN'S DISEASE

When a short history and clear signs of inflammation in the right iliac fossa make a diagnosis of suppurative appendicitis seem probable, laparotomy is essential. An inexperienced operator may have some difficulty in determining the true nature of the ileal lesion. In most cases the inflammatory mass is simply returned to the abdomen. No attempt should be made to take a biopsy specimen from it, and examination of segments from enlarged mesenteric lymph-nodes is not often rewarding. It is advisable to remove the appendix provided that the caecal wall is healthy. During the years that follow the patient will possibly suffer further attacks of abdominal pain; in these circumstances it is reassuring to know that the appendix is no longer present. The risk of a fistula developing after an appendicectomy performed according to the above criterion is virtually nil (Atwell, Duthie, and Goligher, 1965).

A marked degree of intestinal obstruction is rare in a first attack. Short-circuit with exclusion (*see below*) is probably the treatment of choice.

INDICATIONS FOR OPERATION IN CHRONIC CROHN'S DISEASE

The principal indications for elective operation are set out in *Table I*. The ideal lesion for resection is one that is well localized, which has not progressed, and which has remained quiescent for many months. Any previous complication greatly strengthens the argument in favour of operation. When more than 50 per cent of the small intestine is seen to be diseased, the remaining portion must be suspect. This type of case is generally unsuitable for resection and should be treated medically.

In children and young adults retardation of growth and sexual development and inability really to enjoy life are important considerations. Patients who have had Crohn's disease have a right to expect to be able to indulge in (almost) all normal activities. Recurrent bouts of subacute obstruction strongly suggest that operation is necessary. Continuous loss of blood and protein from ulcerated mucosa may only be stopped by resecting the affected segment. A mass may simulate an appendix abscess or a carcinoma and most patients would wish to be rid of it. External fistulae on the abdominal wall are a nuisance, and while some respond to azathioprine many require resection of the underlying diseased bowel. Remote toxic manifestation in skin, eyes, and joints may likewise fail to respond until all the inflamed intestine has been excised.

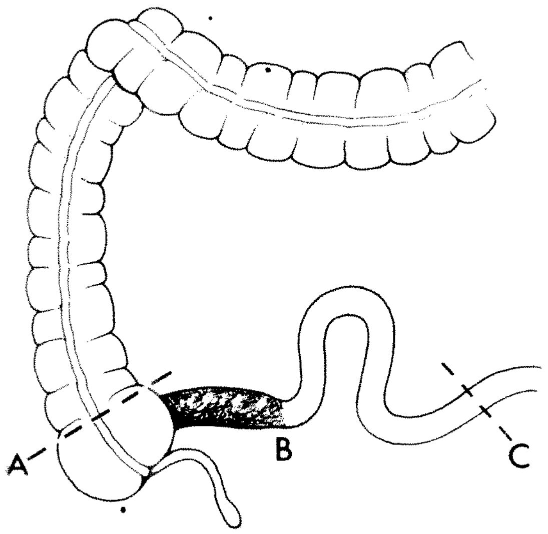

FIG. 1.—Resection of Crohn's disease of the terminal ileum. The colon is transected at A. The upper limit of disease (B) is 20 cm. beyond the point C where healthy ileum is divided obliquely.

Table I.—INDICATIONS FOR ELECTIVE RESECTION IN CHRONIC CROHN'S DISEASE OF THE ILEUM

1. Localized, quiescent disease
2. Failure of adequate medical therapy
3. Inability to enjoy life, retardation of growth
4. Sub-acute intestinal obstruction
5. Persistent anaemia, hypoproteinaemia
6. Abdominal mass
7. External abdominal fistulae
8. Complications in the skin, eyes, and joints

ELECTIVE RESECTION OF ILEUM

The abdomen is opened through a lower right paramedian incision. A careful inspection is made of the entire length of the gastro-intestinal tract and the distribution of any enlarged mesenteric nodes is noted. With disease confined to the lower ileum the aim is to conserve as much of the water-absorbing mucosa of the colon as possible, while removing at least 20 cm. of what looks like healthy ileum proximal to the upper limit of the disease (*Fig.* 1). Leakage may be the immediate result of any attempt to incorporate inflamed intestine in an anastomosis. Even if such an anastomosis remains watertight, reactivation of the disease process soon leads to the reappearance c troublesome symptoms.

A suitable point on the ileum about 20 cm. abov the thickened, red segment (or a closely related ski lesion) is marked with a Babcock's forceps. The ileocaecal part of the intestine is mobilized so that the resection and anastomosis are performed outside the abdominal wall. The line of division of the mesentery is then selected. With a thin mesentery it passes straight from the marked point on the ileum to the start of the ascending colon immediately beyond the ileocaecal valve. If the caecal or adjacent colonic wall is unhealthy a formal right hemicolectomy is necessary With a grossly thickened mesentery and large lymph-nodes it is much safer to keep close to the ileum leaving the nodes behind. When thick, oedematous bites of tissue are held in Mayo's artery forceps it is advisable to transfix them before tying them off.

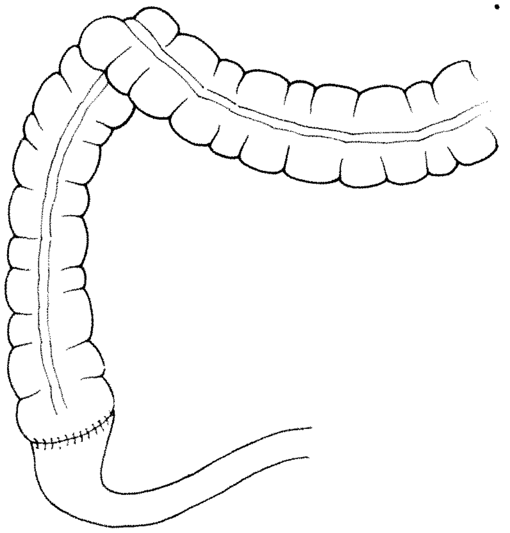

FIG. 2.—The completed anastomosis of healthy ileum to ascending colon.

At least 1 cm. of the circumference of both healthy ileum and ascending colon are cleared of fat mesentery, etc., so that muscle suitable for holding the stitches of the anastomosis is clearly seen. A fine-bladed Schoemaker crushing clamp is placed obliquely across the cleared ileum so that more of the anti-mesenteric wall will be removed; another clamp is applied distally and straight across the ileum. The triangular, uncrushed piece of ileum between the pairs of clamps is sent for histological examination to ascertain if it is free from disease. The commencement of the ascending colon is divided transversely between further pairs of Schoemaker clamps and the specimen is removed.

A few interrupted silk stitches are inserted between the posterior outer surfaces of the obliquely cut ileum and ascending colon. The medial and lateral stitches act as stays and those between help to approximate the somewhat unequal ends of the intestines. Soft occlusion clamps are applied to the two parts of the intestine several centimetres clear of the anastomosis. The Schoemaker clamps are removed and the ends are gently prised open and swabbed clean. A careful search is made for any evidence of aphthoid ulcers on the mucosa surfaces. If any are found an additional 5 cm. of intestine should be removed and the inspection repeated.

A two-layer anastomosis is then made, using outer interrupted silk stitches with an inner continuous locked catgut stitch (*Fig*. 2). It is important to see exactly where every stitch goes and to make sure that the ends of each layer are carefully infolded. The stitches should be 3–4 mm. apart. The silk stay stitches may be used to rotate the anastomosis through 180° to enable the outer posterior layer to be completed before the gap in the mesentery is closed.

SHORT-CIRCUIT WITH EXCLUSION

This operation is performed when resection seems indicated but the findings in the abdominal cavity and pelvis suggest that radical surgery would be unduly hazardous. There may be a large inflammatory mass stuck down in the pelvis against the iliac blood-vessels and ureter, or there may be dense adhesions from a previous operation. Staying well over to the left, out of harm's way, may be a less heroic but is probably a safer course of action in a poor-risk patient. The surgeon who is confronted by acute, complete intestinal obstruction, with inflamed terminal ileum, may also consider it advisable to divide and close the ileum 20 cm. above the diseased segment and then restore intestinal continuity with an ileotransverse anastomosis.

SKIP LESIONS

Skip lesions close to the main mass are resected along with it. One remote skip lesion may be resected or by-passed. There is rarely justification for having more than two anastomoses in series. When several skip lesions are present it is wiser to regard the whole of the small intestine as being diseased and to treat the case medically. A protein-losing or stenotic segment may still merit resection, the other lesions being controlled by drugs.

EXTERNAL FISTULAE

External fistulae nearly always follow a previous abdominal operation or drainage of an abscess. Care is required in opening the peritoneum so as not to damage adherent intestine. Often the inflamed mass can be pinched off the parietes, the track through the abdominal muscles being simply curetted. Sometimes there is a fine fibrous strand running backwards towards the diseased ileum; this is easily divided.

A broken-down anastomosis is a much more serious problem and acts like an uncontrollable ileostomy. It requires, as a matter of urgency, either a re-resection or establishment of a proper, perhaps temporary, ileostomy. Intravenous feeding may be required.

PROGNOSIS

The operative mortality should be less than 2 per cent. On following up those at risk the true recurrence rate at 5 years is 18 per cent following primary resection for ileal disease (Kyle, 1971). At 10 years the rate is 33 per cent. Recurrences may take place 10–20 years after operation. Females under 30 years of age and with short histories tend to fare worse. The erythrocyte sedimentation rate and the presence of lymph-node enlargement, or of a granulomatous reaction in the bowel wall, do not appear to affect the prognosis.

Short-circuit with exclusion produces less satisfactory results. However, an ill patient who had a technically dangerous lesion is still alive. The recurrence rate is more than 50 per cent greater than that with resection, and various types of anaemia may develop. There has been no trouble with 'blown stumps' and resection at a later date is always possible.

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CROHN'S DISEASE OF THE LARGE BOWEL

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IN trying to discuss some aspects of Crohn's disease as it affects the large bowel I have naturally sought help from the collective experience at St. Mark's Hospital. In the past 20 years 371 new cases of Crohn's disease have been treated at St. Mark's Hospital, but as the cases referred there are predominantly large-bowel problems the distribution of the disease seen is not representative of the pattern of Crohn's disease in the country as a whole. The figures from the Birmingham series compiled by Cooke and quoted by Morson (1971) suggested that about 17 per cent of patients with Crohn's disease had involvement of the large bowel only, and a further 17 per cent had involvement of the small and large bowels, so that in about a third of all cases the large bowel was affected. Classification of the sites of involvement in Crohn's disease is very difficult, but an attempt to do this in 371 new patients seen at St. Mark's Hospital in the past 20 years is shown in *Table I*. The patients were new in the sense that no excisional or by-pass surgery had been undertaken before referral and the sites of involvement were those found at the time of the initial investigation. Fifty-one patients had involvement of the small bowel only, in 86 cases there was disease in the small and large bowels, while in 213 patients the disease was apparently confined to the large bowel, a percentage of 57 per cent compared with Cooke's figure of 17 per cent (Morson, 1971).

Analysis of the age distribution of these cases according to the sites of involvement has produced some rather interesting figures (*Fig.* 1). It will be seen that the patients with small-bowel involvement or with disease involving the small bowel and any part of the large bowel are mainly in the younger age-groups, those with extensive colonic disease but no small-bowel disease show a fairly uniform spread over all the age-groups, whereas those with disease confined to the distal colon and rectum are mainly in the older age-groups, although we have seen some young patients with this rather unusual form of the disease. These figures can perhaps be put more succinctly by saying that in the first group (small intestine ± colon) 85 per cent of the patients were under 45 years of age, whereas in the third group (rectum ± sigmoid and localized colon) more than 70 per cent were over 45 years of age.

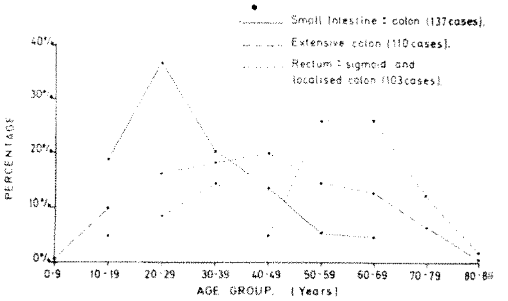

FIG. 1.—Age distribution and sites of involvement in 350 cases of Crohn's disease.

Table I.—SITES OF INVOLVEMENT AT INITIAL PRESENTATION

Site	*No. of Patients*	*Percentage*
Small intestine only	51	13·7
Small intestine and colon	86	23·2
Extensive disease of colon	110	29·7
Localized disease of colon	18	4·8
Rectum ± sigmoid colon	85	22·9
Anus only	21	5·7
Total	371	100·0

To turn now to a few points in the diagnosis of large-bowel Crohn's disease. The many points of difference between large-bowel Crohn's disease and ulcerative colitis have been stated frequently and do not need to be repeated here. In the majority of cases the distinction can be made fairly confidently on clinical and/or radiological grounds, even before pathological confirmation is forthcoming. However, this differentiation is not always possible and the clinician may sometimes be in doubt. It is particularly in cases with an acute clinical presentation that diagnosis may be difficult, even with the help of radiology and biopsy. Goligher (1971) has stated that about 10 per.cent of all patients with acute 'colitis' coming to surgery are found to have Crohn's disease on final analysis, though my experience would put the figure somewhat lower. However, there is no doubt that Crohn's disease of the large bowel may present acutely, may perforate, may cause a toxic dilatation of the colon, and may require emergency colectomy; and that the handling of these acute cases of Crohn's disease can be just as difficult and hazardous as the management of acute cases of ulcerative colitis. About 3 per cent of the St. Mark's Hospital cases have been regarded as 'unclassified', that is, those which cannot histologically be diagnosed with certainty, even on pathological examination of the whole specimen. Perhaps in a few years' time, in the light of further knowledge, it may be possible to look back and to classify these cases, or it may be found that there is yet another type of large-bowel inflammatory disease which at present is unknown.

The tendency of Crohn's disease to present with strictures of the bowel is so familiar that other possible causes of stricture may be forgotten. I have seen 2 cases with multiple colonic strictures closely resembling Crohn's disease which at laparotomy have proved to be secondary deposits from an occult primary undifferentiated carcinoma of the stomach, and a primary anaplastic carcinoma of the colon in a young patient also led to great difficulty in diagnosis. Ischaemic colitis leads to strictures in the colon, most commonly at the splenic flexure; there is usually a history of an acute attack of pain with rectal bleeding and this makes the diagnosis fairly definite. However, occasionally a stricture may be found in the colon without such a history, or in a less usual part of the colon, and then the diagnosis between ischaemic disease and Crohn's disease may be impossible. Tuberculous disease of the ileocaecal region still occurs, although in my experience it is far less common than Crohn's disease in this country at the present time. Surgical tuberculosis now is usually seen in immigrants from Asia, but recently a doctor from one of the Common Market countries was referred to St. Mark's Hospital with a diagnosis of Crohn's disease of the ileocaecal region, but after resection this proved to be a classic ileocaecal tuberculosis.

Crohn's disease may arise in, and be confined to, the sigmoid colon in some elderly patients. These are also the commonest site and age for diverticular disease so that there may be difficulties with differential diagnosis between the two conditions, which may in fact coexist. In such cases the radiological appearances may be very difficult to interpret (*Fig.* 2). Fortunately in most patients with Crohn's disease of the sigmoid colon there are inflammatory changes which can be seen on sigmoidoscopy, and anal lesions are present in about 80 per cent of cases. One should always be suspicious of any case of apparent diverticulitis associated with an anal lesion, with much oedema and granularity on sigmoidoscopy, or with much pus in the lumen of the bowel. A mucosal biopsy may be of value in such cases as it is important to make the diagnosis before undertaking surgery; patients with Crohn's disease have a greater tendency to leak at anastomoses, and a one-stage resection, as undertaken for most cases of diverticulitis, may not be suitable for a case of sigmoid Crohn's disease.

Finally on the question of diagnosis I should stress that Crohn's disease of the large bowel is very easily missed unless the possibility is constantly considered. I have in mind particularly 2 patients seen in the past year. One of these was a very neurotic lady with abdominal symptoms in whom both a barium-meal and follow-through examination and sigmoidoscopy had been quite normal. At that time she refused a barium enema and was regarded by her general practitioner as an 'irritable bowel syndrome' until a rising erythrocyte sedimentation rate and falling plasma proteins made her medical consultant insist upon a barium enema. This showed gross and extensive Crohn's disease of the large bowel. The other patient, a woman in her fifties, gave a history of vague pains in the right iliac fossa for some years, this symptom being ascribed to adhesions following a difficult appendicectomy some years previously. Recently, investigation by a rheumatologist, whom she consulted for recurrent joint pains, showed a persistently high erythrocyte sedimentation rate and a seronegative arthropathy, suggesting that her joint troubles might be secondary to a 'colitis'. Again sigmoidoscopy and a barium-meal examination were negative, but a barium enema showed two strictures in the transverse colon which proved to be typical Crohn's disease after resection (*Fig.* 3). Such cases, with little in their symptomatology or signs to suggest a lesion in the large bowel, are not uncommon, and a barium-meal and follow-through examination is a very inaccurate and inadequate procedure for diagnosing colonic disorders.

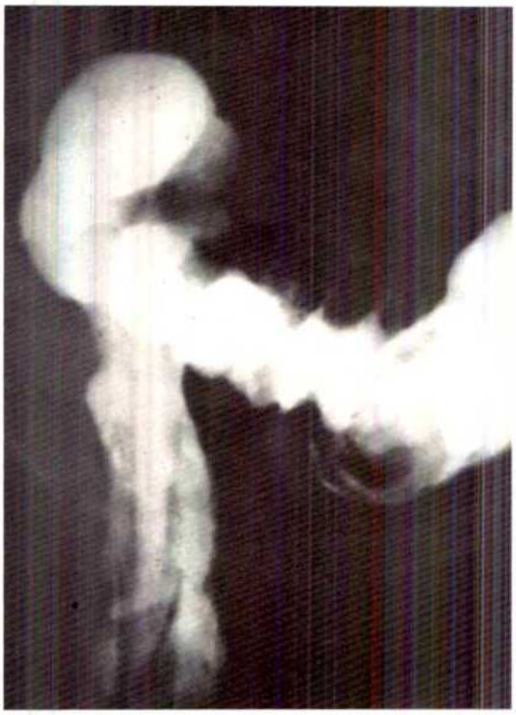

FIG. 2.—Barium-enema radiograph of the sigmoid colon affected by localized Crohn's disease. The 'spiking' shown is similar to appearances sometimes seen in diverticulitis.

Turning now to the management of patients with large-bowel Crohn's disease, I would stress that medical treatment should be attempted first unless there is a very definite indication for surgery such as marked stenosis. It is not my place to discuss medical treatment in any detail but I would like to mention the value of sulphonamides in some patients, particularly in the older age-group and those with less severe forms of the disease. Sulphathalidine alone has frequently been successful in procuring a remission lasting for some years. The value of sulphonamides, Salazopyrin, steroids, or azathioprine in the prevention of recurrence following resection for this disease is still unknown. Such information would be very valuable and controlled trials are, I believe, already under way.

In presenting some of the results of surgical treatment I would like to mention four groups of patients. First, there has been a small group with localized disease of the colon, usually presenting with a stricture in the sigmoid colon. Some of these cases have resembled or been associated with diverticular disease and have already been mentioned as presenting diagnostic difficulties. Seventeen patients with localized disease of this sort have been treated by resection and anastomosis. Many of them were elderly and some have since died of unrelated causes but 10 are alive and only 3 have had evidence of further disease, all of them with local recurrence near the site of the anastomosis. In these the operation was probably ill-chosen and the disease was more extensive than was realized at the time. However, limited surgery has been moderately successful in this group and a permanent artificial stoma has been avoided.

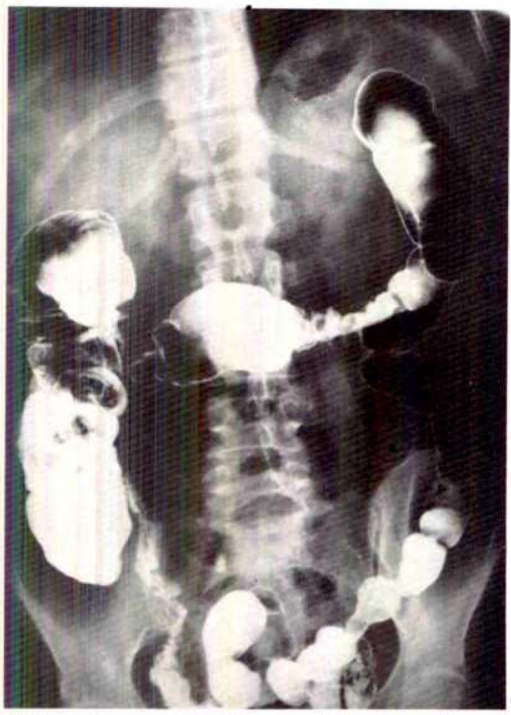

FIG. 3.—Barium-enema radiograph, showing two strictures in the transverse colon caused by Crohn's disease.

Twenty-six patients with disease apparently confined to the distal sigmoid and rectum have been treated by excision of the rectum with a terminal sigmoid colostomy. Only 1 patient has had evidence of further disease, in this case involving the rest of the colon and the terminal ileum. This distal form of the disease is rather unusual and is nearly always associated with distressing anal lesions; many of the patients have had a diverting colostomy, with very little benefit, before being referred to St. Mark's Hospital. However, this group seems to have done well after excisional surgery and they have been most rewarding patients to treat.

Total colectomy with ileorectal anastomosis has been used for patients with extensive colonic disease and a normal rectum on sigmoidoscopy and biopsy. In half of these patients the disease was confined to the large bowel, but in 13 cases there was some involvement of the terminal ileum also. Twenty-seven patients have been treated by this operation and the results are set out in *Table II*, from which it can be seen that the operation has proved somewhat disappointing. Twelve patients are well and symptom-free, 5 have active disease at the moment, which is controlled medically, 5 have required excision of the rectum for recurrence, and 5 have died, 3 of the deaths being related to surgery. All the recurrences were seen within 6 years of the operation. The success rate of the operation, therefore, is only about 50 per cent, a figure similar to those from Birmingham and Leeds (Burman, Cooke, and Williams, 1971; de Dombal, Burton, and Goligher, 1971). An analysis of the St. Mark's Hospital cases published by Baker (1971) showed that recurrence occurred both above and below the anastomosis and equally in those with or without small-bowel disease preoperatively.

Table II.—RESULTS OF COLECTOMY AND ILEORECTAL ANASTOMOSIS

Result		*No. of Patients*
Dead		5
Alive		22
Recurrent disease (excision of rectum 5, medical treatment 5)	10	
	Total	27

Table III.—RESULTS OF TOTAL PROCTOCOLECTOMY

Result		*No. of Patients*
Dead		8
Alive		56
Recurrent disease	4	
	Total	64

Between 1952 and 1971 the operation of total proctocolectomy, leaving the patient with a permanent ileostomy, has been carried out in 64 patients at St. Mark's Hospital; this figure includes only those in whom all the excisional surgery was carried out there. The operation was done in one stage in 27 patients and in more than one stage in 37 patients. The results are set out in *Table III*. Eight of these patients have died: 3 as a result of surgery, 1 following persistent perineal disease, and the other 4 from unrelated causes. Of the remaining 56 patients, only 4 have had recurrent disease, that is, about 7 per cent. The shortest interval between surgery and recurrence was 10 years and the longest 17 years. It is perhaps of interest that there has been no recurrence so far in any patient treated by a one-stage proctocolectomy, but as this operation has been done mainly in the past 10 years it is not yet known if this is a significant finding. All the 4 recurrences have occurred in the terminal ileum, either at or immediately proximal to the ileostomy and there has been no case of extensive small-bowel recurrence or of a proximal skip lesion.

Comparison of the results of these two operations shows that for patients treated by total proctocolectomy the recurrence rate was less than 10 per cent, and the interval between surgery and recurrence was 10 years or more in each of the 4 cases. By contrast a recurrence rate of almost 50 per cent was seen in patients undergoing colectomy and ileorectal anastomosis, and in each of the 10 cases of recurrence the disease reappeared within 6 years of surgery. The only difference between the patients preoperatively was that those selected for ileorectal anastomosis had an apparently normal rectum on sigmoidoscopy and biopsy. There were no significant differences between the two groups in age, sex, or preoperative duration of disease. The reason for the different incidence and patterns of recurrent disease following these two procedures is not known but is obviously a field for further research and observation.

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THE RESULTS OF SURGICAL TREATMENT FOR CROHN'S DISEASE

BY F. T. DE DOMBAL
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ANY surgeon who sets out to assess the results of his surgical intervention, whatever the disease and whatever the operative treatment, must first answer two questions. These concern the nature of the patient population under study and the nature of the assessment which the surgeon will make; in other words, which cases are to be included for assessment, and by what criteria can success and failure best be adjudged?

In Crohn's disease there are special problems involved in the assessment of results, and reference to studies in Leeds (de Dombal, Burton, and Goligher, 1971a, b) serves to illustrate both aspects. Thus, 382 patients are alleged to have been seen and treated for Crohn's disease at the General Infirmary, Leeds, yet in some 50 instances it was impossible to substantiate the diagnosis, and in only 244 of the 382 cases was it certain that the patient had undergone primary surgery in the General Infirmary. Therefore a selected (albeit well-defined) group of 244 patients was chosen for study, but it should be noted that in doing so no less than 36 per cent of the patients originally made available had to be rejected from consideration.

The criteria by which the patients were chosen for assessment have been set out elsewhere and will be discussed in detail later. However, at this juncture two points are worth making. First, the early and late results of surgery are quite different from one another, and any assessment must clearly separate these two aspects. Secondly, 'obvious' criteria for assessment (such as recurrence of disease) may not in the event be those which most reflect the patient's satisfaction with his ultimate outcome, and this point too will be dealt with in more detail in due course.

EARLY RESULTS OF SURGERY

Mortality.—There can be little doubt that the most disturbing aspect of the results of surgery for Crohn's disease is the proportion of patients who fail to survive during the early postoperative period. In the Leeds series 415 operations were performed, with a total of 24 deaths prior to the patients' discharge from hospital, an overall early mortality rate of 5·8 per cent. When one considers that many of the patients had more than one operation, the overall proportion of Leeds patients who died in the early postoperative period is no less than 7·2 per cent. Moreover, this must be seen in context of an 11·3 per cent overall related mortality for the Leeds series (which itself seems to be fairly representative in this respect, as indicated in *Fig.* 1). Thus, the majority of deaths related to Crohn's disease, its consequences, and its therapy are undoubtedly concentrated in the early postoperative period. However, as shown in *Fig.* 2, this risk is not constant, being higher after reoperations than after primary surgery and being significantly raised in elderly patients. Fortunately, as *Fig.* 2 also indicates, the overall risk is dropping (from 10 per cent in the 1940's to 3 per cent in the past decade).

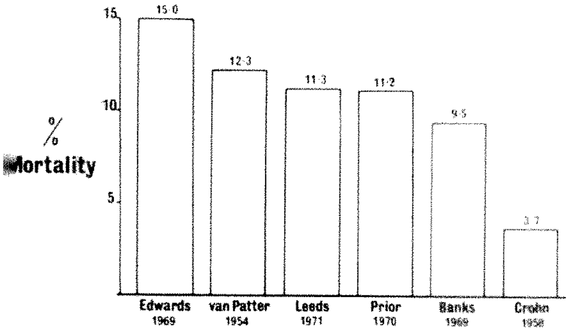

FIG. 1.—Overall mortality due to Crohn's disease in several large series.

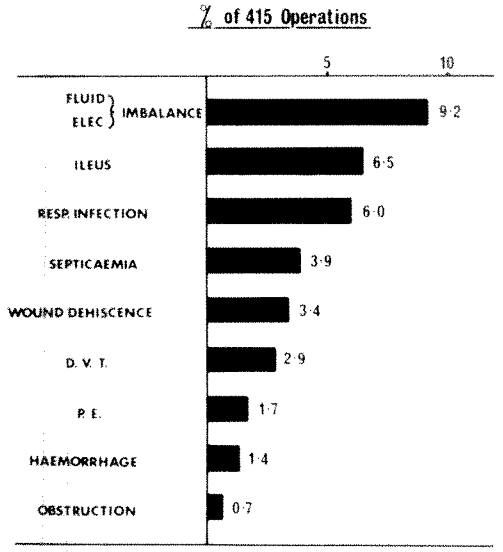

FIG. 3.—Complications in the early postoperative period.

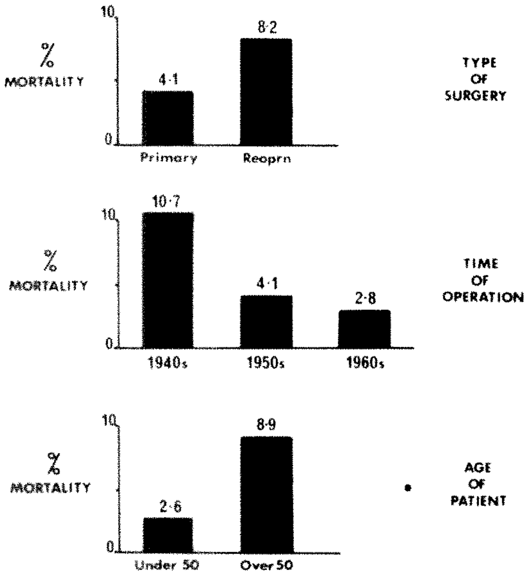

FIG. 2.—Factors affecting the overall postoperative mortality in the Leeds series.

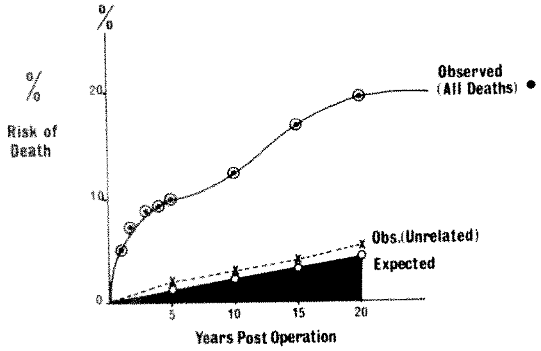

FIG. 4.—Long-term mortality after surgery for Crohn's disease.

Morbidity.—As regards the early postoperative morbidity and its various causes, the experience in Leeds is unremarkable. The various complications which may arise are listed briefly in *Fig.* 3; it is perhaps worth re-emphasizing that the patient with Crohn's disease frequently presents difficult problems in the management of fluid and electrolyte imbalance, particularly after reoperations, and that prolonged ileus is a very real risk in a proportion of patients.

LATE RESULTS OF SURGERY

Mortality.—Consideration of the long-term results of therapy for Crohn's disease must also begin with an analysis of the overall cumulative mortality, and this is shown for the Leeds series in *Fig*. 4. Quite clearly there is a small but definite mortality attributable to the disease and its therapy, since the overall death rate is greater than that which might be expected amongst the general population, yet the *unrelated* mortality is strictly comparable with that predictable from the Registrar General's (1964 figures.

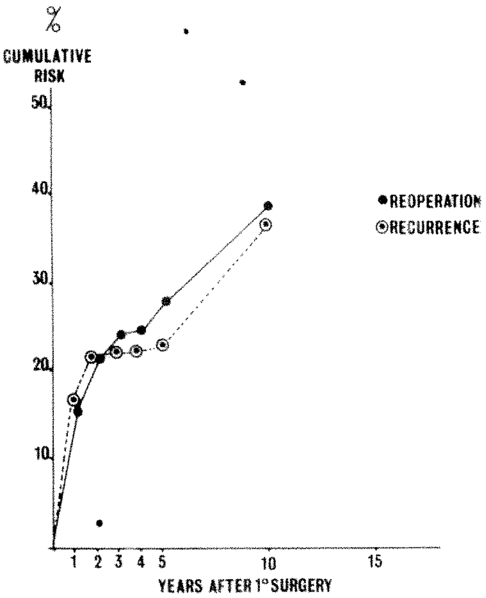

FIG. 5.—Recurrence and reoperation rates after primary surgery for Crohn's disease.

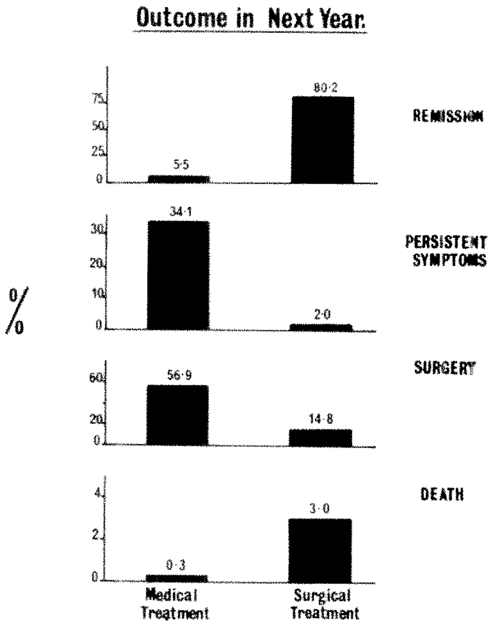

FIG. 7.—Comparison of the short-term response to conservative and operative treatments.

Reoperation and Recurrent Disease.—Thes aspects of the long-term follow-up of patients wit Crohn's disease have been dealt with at length elsewhere (de Dombal and others, 1971a, b), but it ma be helpful to make one or two additional point First, reoperation and recurrent disease are undoubtedly related in that most reoperations ar performed on account of recurrent disease, as show in *Fig*. 5. Secondly, both the curves in *Fig*. 5 ar biphasic, and this points to the possibility of mor than one type of recurrence—a hypothesis which ha already been developed elsewhere at some lengt Finally, the Leeds experience is probably reasonabl representative, as demonstrated by consideration c the overall recurrence rates from a number of larg series (*Fig*. 6).

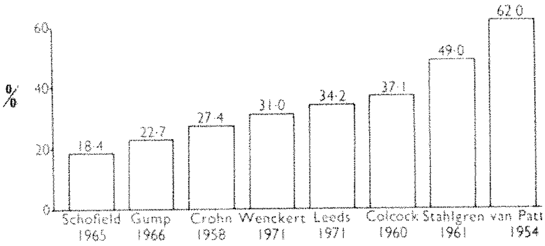

FIG. 6.—Overall recurrence rates from a number of large series.

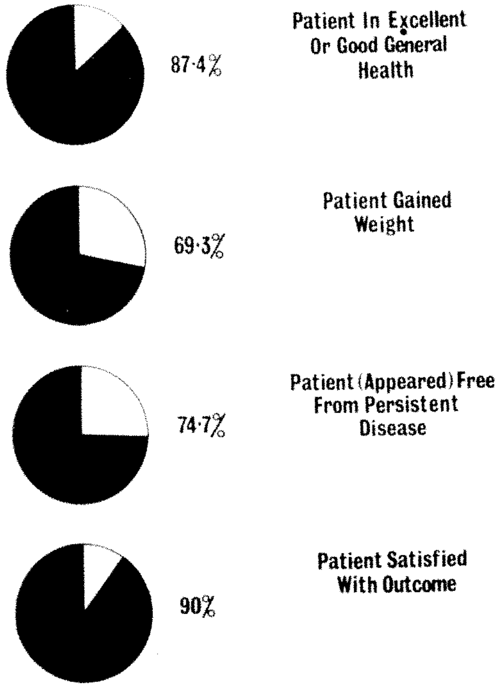

FIG. 8.—Overall status of the surviving patients at the time of the review.

Symptomatic Course.—This can only proper be assessed if one compares the symptomatic cour following surgery with that of patients on long-ter conservative therapy. An assessment of the course he initial year is shown in *Fig.* 7, which illustrates two main features. First, the mortality after surgical treatment is much higher than that on conservative management alone (3·0 versus 0·3 per cent). This presumably reflects a situation in which the more severe the symptoms are, the more likely the patient is to undergo surgical treatment. Secondly, as regards the symptomatic outcome, *Fig.* 7 emphasizes the paucity of response to conservative management, so that only 5 per cent of patients on continuous onservative management actually achieved a full emission of symptoms. Conversely, no less than 80 per cent of the patients operated upon during their initial attack of Crohn's disease spent at least the next year in full clinical remission. Moreover, as has been shown elsewhere (de Dombal and others, 1971b), hese general trends persist throughout the course of he patients' illness, in that years on conservative management alone are vastly more likely to be marred by symptoms of Crohn's disease than are years following surgical intervention.

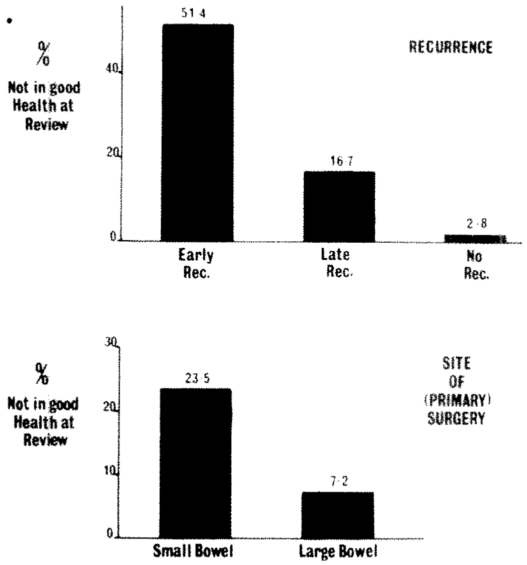

FIG. 9.—Factors modifying the status of the survivors at review.

STATUS OF PATIENTS AT REVIEW

The status of the patients at the time of their review in Leeds was really very much better than had been imagined. As indicated in *Fig.* 8, the vast majority of surviving patients were in acceptable general health, had maintained or gained weight, were apparently free from persistent disease, and were broadly satisfied with their treatment and its outcome. Two factors modify this picture (*Fig.* 9), namely whether or not the patient had a recurrence and if so the timing of that recurrence), and also the primary site of surgical intervention. Surprisingly, he length of follow-up between the time of primary surgery and the review in 1968 did not seem to affect he status at review in any major way (*Fig.* 10). This would seem to give grounds for hope that the reasonably good short-term results obtained so far will not deteriorate too much with the passage of time.

CONCLUSIONS AND SUMMARY

Thus, what might be termed the 'central equation' or the 'central dilemma' in the management of Crohn's disease and in the consideration of the role of surgery within that management is arrived at. On the one hand, conservative management is relatively safe, whereas surgery in the 1960's has been followed by an immediate risk to life of approximately 3 per cent (higher in old people and after multiple operations). On the other hand, long-term conservative management does little to alleviate symptoms and surgery is notably successful in this respect. Are the individual patient's symptoms sufficiently disabling to warrant acceptance of an immediate risk to life of around 3 per cent? On the answer to that question must depend the decision to offer or to withhold operative treatment.

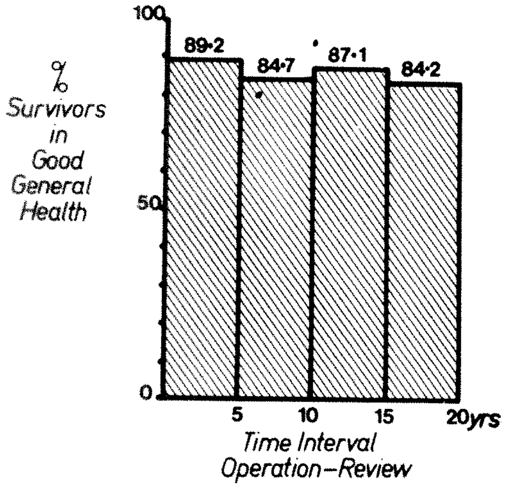

FIG. 10.—Relationship between the duration of follow-up and the status of the survivors at review. (*Reproduced from de Dombal, F. T.* (1972), '*Clinics in Gastroenterology: Crohn's Disease*'. *London: Saunders.*)

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SYMPOSIUM ON THROMBO-EMBOLISM—CURRENT MANAGEMENT

THE DIAGNOSIS OF DEEP-VEIN THROMBOSIS

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DEEP-VEIN thrombosis is a common complication of surgical operation (Sevitt and Gallagher, 1959; Flanc, Kakkar, and Clarke, 1968; Negus, Pinto, LeQuesne, Brown, and Chapman, 1968) and of major illness (Maurer, Wray, and Shillingford, 1971), and pulmonary embolism is responsible for many deaths each year (Kemble, 1971). It is well recognized that many small calf-vein thromboses give rise to no symptoms or signs (Kakkar, 1969; Negus, Pinto, and Brown, 1969b). More importantly, extensive femoral or iliac thromboses are also frequently 'silent' (Mavor and Galloway, 1969; Evans, 1971).

The importance of early and accurate diagnosis of this potentially dangerous condition is reflected in the number of ingenious attempts which have been devised to improve the situation (*Table I*). Some of these, such as the measurement of platelet adhesiveness, have proved unreliable, and others, for example the measurement of fibrin-degradation products, are at present too complicated for daily clinical use.

Table I.—METHODS OF DIAGNOSING DEEP-VEIN THROMBOSIS

AUTHOR	METHOD	RELIABILITY
Bauer (1940)	Phlebography	Reliable
Atkins and Hawkins (1965)	^{125}I-fibrinogen	Reliable
Bygdeman, Eliasson, and Johnson (1966) Hume (1966) Negus, Pinto, and Brown (1969a)	Platelet adhesiveness	Unreliable
Lane (1967)	Infra-red thermography	Unproved
Sigel and others (1968)	Doppler ultrasound	Reliable
Mullick and others (1970)	Limb impedance	Unproved
Fletcher, Alkjaersig, O'Brien, and Tulevski (1970)	Fibrin-degradation products	Reliable, complex

Impedance phlebography is a recent development with encouraging possibilities (Mullick, Wheeler, and Songster, 1970). The method depends on the patient's ability to take a deep breath and to hold it for 5 seconds; this changes the venous volume and electrical conductivity of the limb, and the difficulty some patients may find in doing this perhaps accounts for the poor accuracy of the method (53·5 per cent) in one series (Dmochowski, Adams, and Couch, 1972). Impedance phlebography can only detect thromboses in the major veins of the leg and pelvis (Wheeler, Pearson, O'Connell, and Mullick, 1972), and at present would appear to have no advantages over the Doppler ultrasound technique.

The present paper is confined to a description of the three proved methods currently available for the diagnosis of deep-vein thrombosis: phlebography, Doppler ultrasound, and ^{125}I-fibrinogen uptake. Th details of these techniques have been reported s often recently that there is no need to repeat then and I will concentrate on describing the advantag and limitations of each and on their relative values i clinical practice and research.

PHLEBOGRAPHY

Phlebography is the most useful single diagnosti method for the investigation of suspected deep-vei

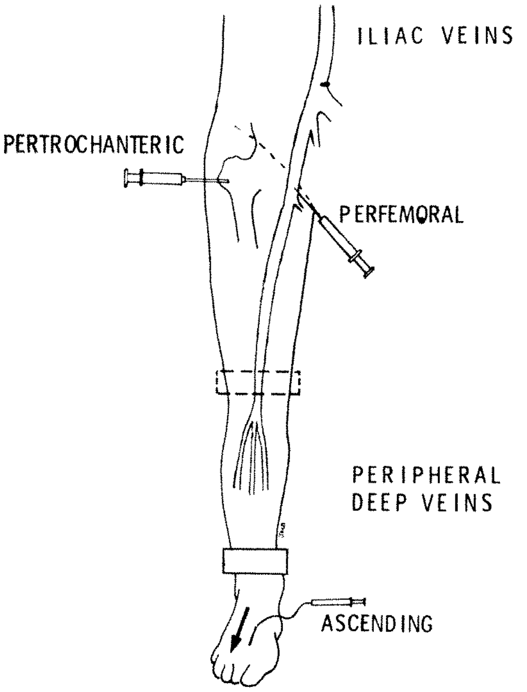


FIG. 1.—Phlebography in the diagnosis of deep-vein thrombosis. The above-knee cuff is removed for delineation of the femoral and iliac veins.

thrombosis. Delineation of the peripheral deep vei is performed by retrograde injection of contra medium into a dorsal foot vein, the superficial vei being occluded by an ankle cuff. The investigation most satisfactorily performed with help from an imag intensifier. With the exception of some of th intermuscular veins, good views of the deep veins an of the calf and thigh are easily obtained, and wit suitable patient tilting and calf compression the ilia veins can also be examined by this technique (L

Thomas, 1971). More precise delineation of the iliac veins and inferior vena cava is achieved by iliac phlebography, usually by the pertrochanteric route (Lea Thomas, 1969), as direct femoral puncture is often impossible in the presence of thrombus (*Fig.* 1).

A phlebogram not only shows the extent of thrombus formation but also indicates its fixity to the vein wall—a point of extreme importance in the management of pulmonary embolism or where surgical thrombectomy or fibrinolytic therapy is being considered. Loose, potentially removable thrombus produces a 'ground-glass' type of shadow and contrast medium can be seen between the thrombus and the vein wall (*Fig.* 2). Older, fixed thrombus results in radiological disappearance of the affected vein, and this is usually accompanied by the presence of dilated collateral veins (*Fig.* 3).

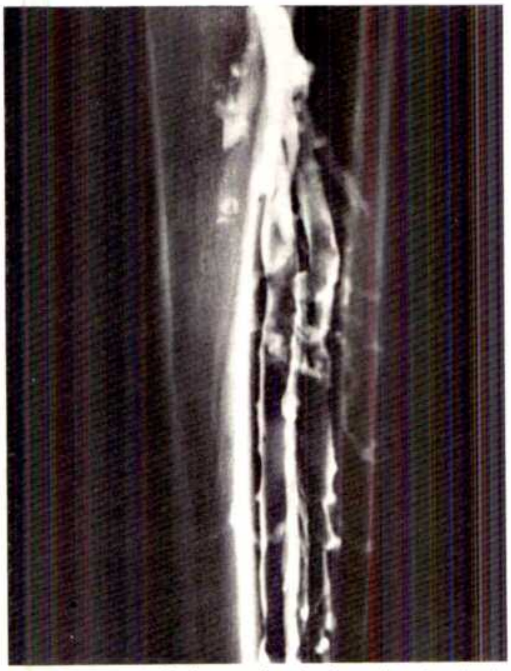


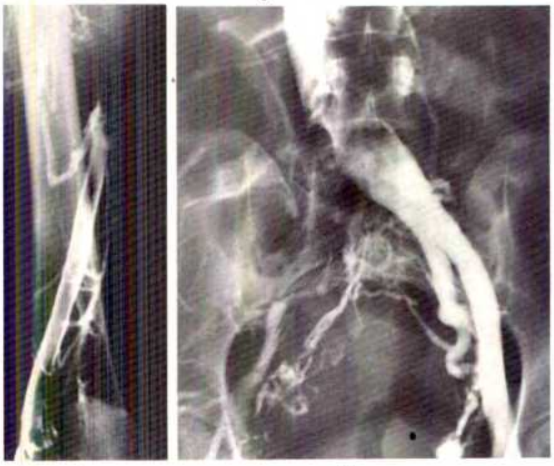
FIG. 2.—Peripheral phlebogram showing loose thrombus in the calf veins.

Phlebography demands no more than the normal resources of an average radiological department with, in addition, the interest and time of a radiologist. Of these simple requirements, time is usually the least readily obtainable.

The disadvantage of phlebography is that there must be some indication for its use, and, as is well known, many deep-vein thromboses are completely 'silent'. Some sort of screening technique is therefore advisable, and the two such techniques presently available are Doppler ultrasound (Strandness, Schultz, Sumner, and Rushmer, 1967; Sigel, Popsky, Wagner, Boland, Mapp, and Feigl, 1968) and the ^{125}I-fibrinogen technique (Hobbs and Davies, 1960; Atkins and Hawkins, 1965). Both methods have been established as accurate by comparison with phlebography (Flanc and others, 1968; Negus and others, 1968; Evans and Cockett, 1969; Yao, Gourmos, and Hobbs, 1972) and the technical details of each have recently been described (Evans and Negus, 1971).

DOPPLER ULTRASOUND TECHNIQUE

Doppler ultrasound, or, more properly, the transcutaneous Doppler ultrasound flow-detection method,* detects changes in flow velocity, such changes being electronically converted either into sound or into a graphic record. Patency of a vein is indicated by a change in flow velocity being produced under the flow probe by a distant stimulus. With the probe placed over the common femoral vein the necessary increase in flow velocity is effected either by squeezing the leg distal to the probe, which increases femoral vein flow and produces a loud noise from the apparatus, or by changes in respiration, such as the Valsalva manœuvre, which alter flow velocity in the inferior vena cava and iliac veins and result in a wind-like roaring. Venous obstruction prevents the transmission of flow changes and therefore no noise is produced by the apparatus (*Fig.* 4).



A B

FIG. 3.—A, Peripheral phlebogram of a 23-year-old woman. The lower third of the superficial femoral vein contains loose thrombus and above this the lumen is occluded by adherent thrombus. B, Pertrochanteric iliac phlebogram of the same patient showing occlusive thrombus in the right external and common iliac vein.

Doppler ultrasound has the great merits of simplicity, speed, and inexpensiveness, and with a little training and experience can be safely and usefully employed by medical students and technicians. The technique is not capable of detecting thromboses confined to the calf, but this disadvantage is less serious than it may first seem as calf thrombi, though by far the most common of all deep-vein thromboses, are unlikely to produce emboli of significant size unless they propagate to the popliteal vein (Evans, 1971).

Doppler ultrasound is used at St. Thomas's Hospital for twice-weekly examinations of the legs and iliac veins of patients recovering from major surgery until the patient is fully ambulant. The results of similar ward surveys have been reported (Evans, 1971; McIlroy, 1972).

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* The apparatus in most general use is the Sonicaid D. 205.

The method is also useful for the rapid investigation of patients with suspected deep-vein thrombosis and it can be used to decide on the necessity for phlebography. For instance, when there are unequivocal signs of calf-vein thrombosis and Doppler ultrasound shows no evidence of propagation to the popliteal vein and no femoral or iliac vein obstruction, treatment with anticoagulants can be started without further investigation by phlebography. Monitoring by Doppler ultrasound must be continued in the early stages of such treatment.

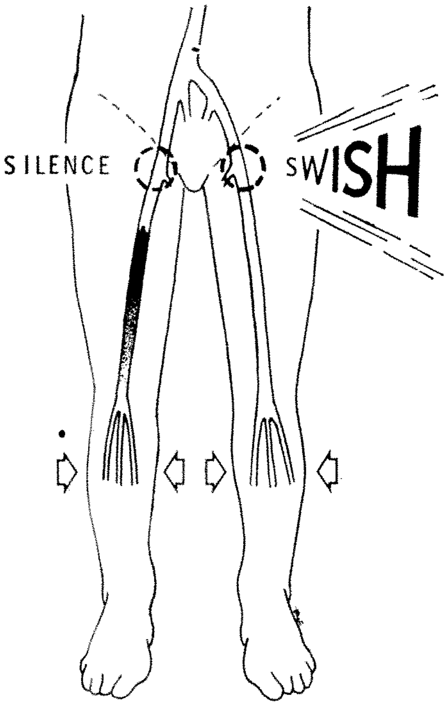
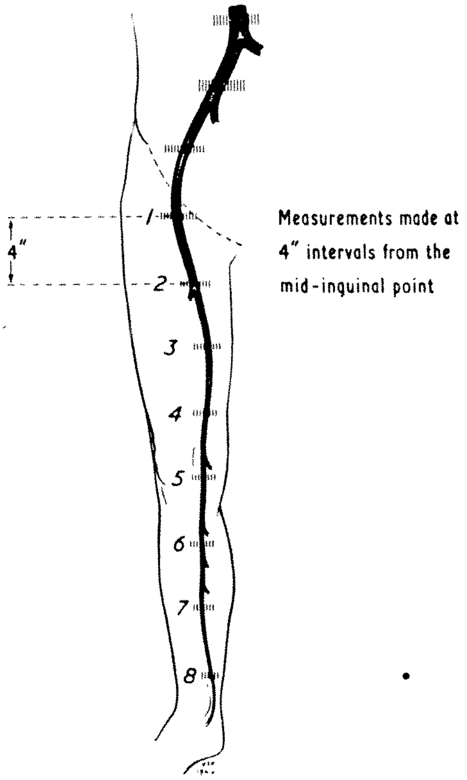


FIG. 4.—Diagram showing the principle of Doppler ultrasound detection of venous obstruction.

^{125}I-FIBRINOGEN-UPTAKE TECHNIQUE

The ^{125}I-fibrinogen-uptake technique depends on the incorporation of human-serum fibrinogen, obtained from a small pool of hepatitis-free donors and labelled with ^{125}Iodine,* into a forming thrombus, where it can subsequently be detected by an external scintillation counter. ^{125}I-fibrinogen, 50–100 µc., is injected intravenously after blocking thyroid uptake with oral inorganic iodide, and the measurement of radioactivity is subsequently made either with a scaler or with a ratemeter.† Details of the technique and of the criteria for the diagnosis of thrombosis have previously been reported (Negus and others, 1968; Evans and Negus, 1971) (*Figs.* 5 and 6). The method will accurately detect small thrombi in the lower leg and thigh, but it cannot be used in the presence of healing wounds or in the groin or abdomen where thrombus formation not infrequently occurs independently of the calf veins (Evans and Negus, 1971).


4"
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Measurements made at 4" intervals from the mid-inguinal point

FIG. 5.—Diagram showing the points over which scintillation counts are made.

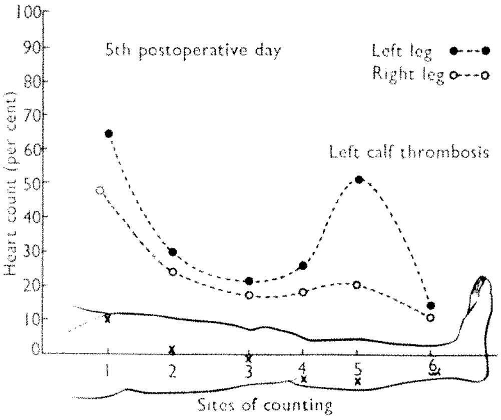

FIG. 6.—^{125}I-labelled fibrinogen detection of venous thrombosis in the left leg of a 63-year-old woman.

Fibrinogen uptake is primarily a method for the prospective detection of forming thrombi and is very suitable for patient screening and for research. The method has produced much information about the natural history of lower-leg deep-vein thromboses which are common, occurring in about 28 per cent of middle-aged and elderly patients undergoing major surgical operation (Browse and Negus, 1970), and which are now known to appear early in the post-operative period (Flanc and others, 1968; Negus and others, 1968; Kakkar, 1969; Negus and others, 1969b). Many trials of means of preventing deep-vein thrombosis have used fibrinogen uptake as the method of detection (*Table II*).

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* Obtainable from the Radiochemical Centre, U.K. Atomic Energy Authority, Amersham, Bucks.

† A scaler is preferable for research; a ratemeter is suitable for routine clinical use. A suitable portable ratemeter is the Isotope Localization Monitor, 235, D. A. Pitman Ltd.

Fibrinogen uptake also has a useful place in routine clinical practice, being an accurate method of screening high-risk patients undergoing major surgical operation. The precise definition of high risk is difficult, but it may broadly be said that the risk of thrombosis increases with age; other conditions carrying a high risk include a past history of deep-vein thrombosis, obesity, malignant disease, thoracotomy, splenectomy, hip operation, and retropubic as opposed to transurethral prostatectomy.

The method is inadvisable in young or pregnant patients. It cannot detect groin or iliac thromboses and should therefore always be used in conjunction with Doppler ultrasound. The combination of the ^{125}I-fibrinogen and Doppler ultrasound techniques can also be used for the diagnosis of the suspected case if phlebography is not available. It takes at least 6 hours from the intravenous injection to obtain a result (Nanson, Palko, Dick, and Fedoruk, 1965). Thrombi more than 6 or 7 days old may be undetectable and the method is unreliable in the presence of much oedema (Browse, Clapham, Croft, Jones, Lea Thomas, and Williams, 1971). These disadvantages make phlebography preferable in most patients with suspected deep-vein thrombosis.

Table II.—THE PROPHYLAXIS OF DEEP-VEIN THROMBOSIS: TRIALS USING ^{125}I-FIBRINOGEN

AUTHOR	METHOD	EFFECTIVENESS
Rosengarten and Laird (1971)	Leg elevation	Ineffective
Rosengarten, Laird, Jeyasingh, and Martin (1970)	Elastic stocking	Ineffective
Browse and Negus (1970)	Galvanic calf stimulation	Effective
Sabri, Roberts, and Cotton (1971a)	Foot pedal	Effective
Hills, Pflug, Jeyasingh, Boardman, and Calnan (1972)	Intermittent calf compression	Effective
Sabri, Roberts, and Cotton (1971b)	Intermittent calf compression	Effective
Lambie, Barber, Dhall, and Matherson (1970)	Dextran	Effective
Kakkar, Field, Nicolaides, Flute, Wessler, and Yen (1971)	Heparin (low doses)	Effective
Williams (1971)	Heparin (low doses)	Effective

Table III.—THE DIAGNOSIS OF DEEP-VEIN THROMBOSIS

Subject	*Investigation*	
Routine ward screening	Doppler ultrasound	
Selected patient screening and research	^{125}I-fibrinogen + Doppler ultrasound	
The suspected case Presentation:—	*Rapid preliminary*	*Final*
Calf tenderness ± swelling	Doppler ultrasound	Phlebography or ^{125}I-fibrinogen
Acute white leg	—	Phlebography
Chronic leg swelling	Doppler ultrasound	Phlebography Lymphography
Pulmonary embolism	Doppler ultrasound	Phlebography
Collapse ? massive pulmonary embolism ? myocardial infarct	Doppler ultrasound	Electrocardiogram and chest radiograph then phlebography

CONCLUSIONS

These are the methods of detecting deep-vein thrombosis presently available. The indications for each are summarized in *Table III*, where it will be seen that Doppler ultrasound is generally used for rapid preliminary investigation and for routine ward screening to indicate the presence or absence of femoral or iliac thrombus. Phlebography is generally used for definitive diagnosis. ^{125}I-fibrinogen is useful in research and in screening high-risk patients, and in the diagnosis of suspected calf or femoral thrombosis it can be substituted for phlebography if the latter is unavailable, provided that its limitations when used in this way are clearly understood (*Fig*. 7). It should be used in conjunction with Doppler ultrasound.

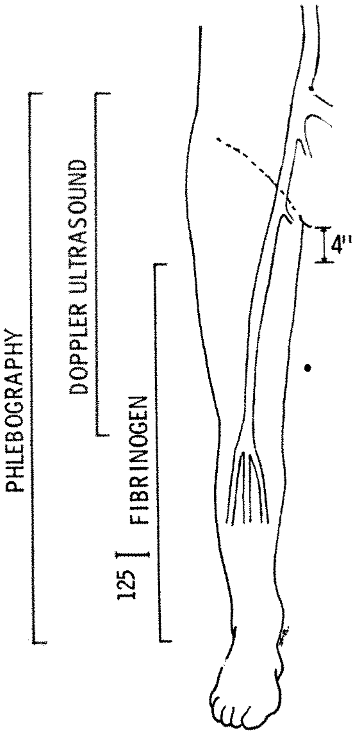

FIG. 7.—The venous drainage of the lower limb showing the segments in which each method of diagnosis is accurate.

In the establishment of diagnostic facilities for a clinical unit the order of priority should be:—

1. Phlebography.
2. Doppler ultrasound.
3. If there are then sufficient funds and personnel available the means of performing the ^{125}I-fibrinogen uptake technique should be obtained.

The research worker would do well to put his priorities in the reverse order.

Acknowledgements.—I am grateful to Dr. M. Lea Thomas for allowing me to reproduce radiographs, and to Mrs. E. K. H. Miles for her secretarial help. The illustrations have been provided by Mr. J. Bamfield, Medical Chartist, and the photographs by Mr. T. Brandon, Department of Clinical Photography, St. Thomas's Hospital.

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CONSERVATIVE MANAGEMENT OF THROMBO-EMBOLISM

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THIS communication is concerned with the use of drugs for the treatment of established thrombosis of the deep veins of the leg. Other well-tried principles of conservative management, such as firm external support to the legs, active leg exercises, elevation of the foot of the bed, and early ambulation, should not, however, be neglected.

The use of anticoagulant or thrombolytic drugs, at any level of therapeutic effect, entails a risk of bleeding. This risk rises sharply if the patient's vascular system is damaged, if there is any other reason for impaired haemostasis, for example renal failure or liver failure, or if the administration of the drug departs from the accepted standards of control. Close clinical supervision of the patient is the most important form of control. Overt bleeding can sometimes be tolerated, but any suspicion of concealed bleeding, for example retroperitoneal haemorrhage, indicates the need for modification of the treatment whatever the results of laboratory tests.

With the exception of massive thrombosis, phlegmasia caerulea dolens or phelgmasia alba dolens, which is not amenable to any form of conservative treatment, clinical diagnosis is unreliable. The usual signs of thrombosis may be absent, and even when they are elicited the presence of a thrombus cannot be assumed with any confidence (Nicolaides, Kakkar, Field, and Renney, 1971). In a study of 247 patients believed to have deep-vein thrombosis ascending phlebography showed that 35 per cent had normal radiographic appearances of the whole venous drainage of both legs, including the iliac veins (Kakkar, 1972). Dependence on clinical signs alone must mean that some patients who need treatment will not receive it, while for others it will be superfluous. Fortunately, this dilemma is resolved by the known prophylactic effect of the oral anticoagulants (Sevitt and Gallagher, 959). For patients in whom there are suggestive clinical signs at least a high risk of thrombosis may be assumed, and this is enough to justify the use of these drugs until the risk is thought to have passed. The oral anticoagulants are selected for this purpose in preference to other prophylactic agents since clinical experience suggests that they may hasten the resolution of established thrombi and reduce the incidence of complications, pulmonary embolism, and the post-phlebitic syndrome. However, this belief has never been satisfactorily tested by a controlled trial.

There are many patients in whom oral anticoagulants will fail to prevent extension of a thrombus or the occurrence of pulmonary embolism. Whenever possible, objective diagnosis of the thrombosis should be obtained, as has already been discussed by Mr. Negus (*see* p. 830). When the age, site, and the size of the thrombus are known it is possible to formulate a more ambitious policy of treatment, knowing that the greater risks of bleeding are acceptable for those patients whose life is imperilled by a thrombus in the veins above the knee. Considerable evidence now shows that a thrombus in the popliteal or any proximal vein is the type which gives rise to massive pulmonary embolism (Sevitt and Gallagher, 1961; Kakkar, Howe, Flanc, and Clarke, 1969; Mavor and Galloway, 1969). The alternatives to be considered here (to be used only with such objective diagnosis) are a continuous infusion of heparin, ancrod (Arvin, Twyford Laboratories Ltd.), or streptokinase. Treatment can be continued until objective assessment shows that the maximum benefit has been obtained; new streptokinase antibodies are likely to prevent its use for longer than 7 days. Urokinase is not yet generally available for the treatment of deep-vein thrombosis.

Oral Anticoagulants.—The risk of bleeding has been reduced by recent advances in the study of the pharmacology and control of the oral anticoagulants, which decrease the liver synthesis of the vitamin-K-dependent clotting factors. The risks of hypersensitivity to indanediones, including phenindione, are now recognized, and the coumarin derivatives such as Warfarin are therefore preferred (Douglas, 1971). There is a greater awareness of the possibility of interaction with a multiplicity of other drugs (Koch-Weser and Sellers, 1971). Those interactions which occur in hospital are usually evident from laboratory control. Out-patients must be warned against self-medication and alcoholic intoxication. It is also necessary to guard against the more insidious risk of withdrawal of certain drugs, especially the barbiturates, with the consequent decay of the new enzymes which these drugs have induced in the liver. These enzymes increase drug metabolism and as they decay (often 2–3 weeks after stopping the sedatives when leaving hospital) the metabolism of Warfarin slows down. Consequently there is an increased anticoagulant effect and a real risk of bleeding. This can be anticipated by a reduction of the anticoagulant dose or, preferably, by avoiding the known enzyme-inducing drugs in patients treated with anticoagulants.

The great variations in laboratory control as practised in different hospitals have been eliminated by the introduction of the British Comparative Thromboplastin Reagent (Poller, 1969) for the one-stage prothrombin time. All hospitals can now refer their results to a British Comparative Ratio of patient-to-control prothrombin time. When this ratio lies between 1·8 and 3·0 an effect has been achieved which corresponds to a value for the Thrombotest, the alternative standardized reagent, of 6–10 per cent. Sevitt and Innes (1964) showed the latter value to be more effective in prophylaxis than values of 10–20 per cent. Since any lower level frequently causes bleeding this is a relatively well-defined therapeutic range for laboratory control.

Heparin.—This acidic mucopolysaccharide directly inhibits the formation and action of thrombin. Many clotting tests, including the clotting time, partial thromboplastin time, and thrombin time, are prolonged by heparin, but there is little correlation between them (Pitney, Pettit, and Armstrong, 1970). It is also possible to express the results as the amount of protamine needed to return the test to normal (O'Shea, Flute, and Pannell, 1971). No therapeutic range has been defined. Empirically, it seems desirable to modify the dose of heparin to produce a change in the test chosen by the laboratory. Bleeding may occur at any level but seems more common if the ratio of patients-to-control thrombin time exceeds 10. Immediate neutralization of the heparin effect is achieved by intravenous protamine.

Ancrod.—This fraction of the venom of the Malayan pit viper removes A-fibrinopeptides from fibrinogen without directly affecting coagulation enzymes or platelets. The resulting molecules spontaneously polymerize to form 'micro-clots' which are rapidly removed from the circulation by reticulo-endothelial cells, leaving a low-plasma fibrinogen. This novel anticoagulant action has the additional merit of reducing plasma viscosity. Control is by measurement of the plasma fibrinogen or by a simple clot-observation test (Pitney, Bray, Holt, and Bolton, 1969). The effects can be reversed by an anti-venom, which unfortunately carries a risk of hypersensitivity reactions since it is prepared in animals, and by the transfusion of fibrinogen concentrates, which may transfer virus hepatitis.

Streptokinase.—This purified exotoxin of haemolytic streptococci combines with human plasminogen to form an activator which converts additional plasminogen to plasmin. This enzyme has a direct thrombolytic effect and the fibrinogen/fibrin degradation products (F.D.P.) resulting from its action have complex anticoagulant properties (Kowalski, 1968). Among the drugs considered, only streptokinase has this combined thrombolytic and anticoagulant effect.

An initial dose of 250,000–500,000 U. is given intravenously in the first 30 minutes. This is sufficient to neutralize circulating anti-streptokinase antibodies — a legacy of previous streptococcal infections—in the majority of patients and to leave an excess of streptokinase which will convert much of the circulating plasminogen to plasmin (Verstraete, Vermylen, Amery, and Vermylen, 1966; Kakkar, Flanc, Howe, O'Shea, and Flute 1969; Amery, Deloof, Vermylen, and Verstraete, 1970). Before the plasmin is fully neutralized by circulating antiplasmins it will begin to digest many of the plasma proteins. Bleeding may follow the resulting decrease of clotting factors, especially fibrinogen, and the consequent liberation of F.D.P. However, if a continuous maintenance infusion of 100,000–150,000 U. hourly immediately follows the initial dose of streptokinase the only source of plasminogen is that which is freshly synthesized and since this is a slow process the greatest danger is limited to the first few hours when significant amounts of plasminogen are available. Laboratory control is carried out by using the thrombin time, which is prolonged either by a decrease in the fibrinogen or an increase in the F.D.P. A very long time is to be expected in the first few hours and indicates that the initial dose has been effective; after 6–12 hours it should return to normal. After this, a ratio of patient-to-control thrombin time of 3·0 or more suggests that blood-plasminogen levels are increasing with resulting formation of plasmin and F.D.P. in excess, and a renewed risk of bleeding. This indicates the need to check the delivery of the maintenance dose of streptokinase; it will usually be found that this has decreased, often for technical reasons, for example obstruction of the intravenous drip. The drug is best given by a reliable mechanical delivery device.

It is important that circulating antibody is neutralized by the initial dose. Patients with recent streptococcal infection or those who have received streptokinase previously should have the level of antibody measured before infusion (Flute, 1964). Safety depends on maintaining a low concentration of blood-plasminogen. It may become necessary to reverse the effects of streptokinase rapidly because of bleeding or because urgent surgery is required. An inhibitor of fibrinolysis, for example epsilon aminocaproic acid, should be given before the transfusion of blood or blood-products containing plasminogen. With this proviso even major thoracic surgery is possible within an hour of ending a streptokinase infusion. Streptokinase is rapidly cleared from the blood and no inhibitor is needed at the end of a successful infusion, although this should be followed by oral anticoagulants for 6–8 weeks to prevent rethrombosis. Heparin can be used, beginning 6 hours after the end of infusion, to cover the period while oral anticoagulants develop their effect.

THE CHOICE OF THERAPY

When a thrombus is extending or is in the popliteal or a proximal vein the risk to life justifies active treatment unless one of the well-known contra-indications makes any form of drug therapy unacceptable. Of the alternatives mentioned, only streptokinase has the direct thrombolytic effect which offers the greatest chance of rapid dissolution of thrombus, perhaps with preservation of function of the venous values (Kakkar, Howe, Laws, and Flanc, 1969). Streptokinase is more likely to be completely effectiv if the thrombus is less than 96 hours' duration Against this must be set the risk of bleeding and o allergic reactions. Older thrombi completely occludin the lumen in limbs where there is a well-develope collateral circulation are less likely to achieve complet dissolution with streptokinase, and perhaps are bes treated by continuous heparin infusion for 3–4 day and oral anticoagulants for 6 months, until th maximum possible recanalization of the vein obtained. The response to any form of treatmen should be measured objectively, usually by repeate phlebograms.

CONCLUSION

Any policy must be tentative and will requir modification as knowledge of the natural history o thrombosis advances. At present clinical suspicion o deep-vein thrombosis may be held to justify only ora anticoagulants and local measures to relieve symptom If a precise anatomical diagnosis shows a thrombu in the popliteal vein or above a difficult choice mus be made between treatment with heparin, ancrod streptokinase, or surgery.

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THE DIAGNOSIS AND MANAGEMENT OF MASSIVE PULMONARY EMBOLISM

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N a group of more than 50 patients seen at the Brompton Hospital, London, all of whom had isolated acute massive pulmonary embolism, it has been possible to define the haemodynamic disturbance, and hence the presenting symptoms and signs, resulting from acute obstruction to right ventriular outflow occurring as an isolated disturbance. Patients are included only if the embolism was of less than 48 hours' duration and its presence and severity were proved by pulmonary arteriography, embolectomy, or both. No patient is included in whom there was pre-existing cardiorespiratory disease.

DIAGNOSIS

The symptoms and signs of isolated, acute, massive, pulmonary embolism are (1) a sudden reduction in the cardiac output, (2) acute right entricular failure, and (3) disturbance of pulmonary entilation and perfusion (Gorham, 1961; Paneth, 966; Dalen and Dexter, 1969; Sutton, Honey, nd Gibson, 1969; Miller and Sutton, 1970). The sudden reduction in cardiac output results in the most common presentation (80 per cent of patients): sudden faintness or collapse, with frank circulatory arrest occurring in 22 per cent. The clinical manifestation of this low output state is a sinus tachycardia 90 per cent of patients) with a small sharp pulse, systemic hypotension, and signs of peripheral constriction with poor tissue perfusion (low urine flow, disturbed cerebration, etc.). The other cardinal presenting feature—sudden onset dyspnoea (74 per ent of patients)—may result from a low cardiac output ('air hunger') as well as disturbed pulmonary entilation and perfusion. It is an important clue to the diagnosis that these patients are not orthopnoeic but prefer to lie flat, as might be expected when ardiac output is critically dependent on filling pressure and in contradistinction to the orthopnoea f pulmonary *venous* hypertension (e.g., myocardial nfarction). Other presenting symptoms include central chest pain (34 per cent) and occasional pleurisy and haemoptysis, though these signs of pulmonary infarction are more commonly present as result of small premonitory emboli prior to the onset of massive embolism.

Acute right ventricular failure is detected clinically by a gallop rhythm best heard at the left sternal edge 87 per cent of patients) and elevation of the central enous pressure (79 per cent). These signs appear to be time dependent and may be absent in a patient een between 24 and 48 hours after the acute event ither as a result of some spontaneous resolution or because of some adaptation to massive embolism. The acutely failing right ventricle cannot generate a high pressure to overcome the obstruction and the physical signs of isolated acute embolism are *not* those of pulmonary hypertension.

Disturbance of pulmonary ventilation and perfusion leads to central cyanosis (detected in 62 per cent of patients). Occasionally severe arterial desaturation may be due to right-to-left interatrial shunting via the foramen ovale.

INVESTIGATION

Apart from pulmonary arteriography the electrocardiogram (E.C.G.) and chest radiograph provide the most useful information in massive pulmonary embolism. The E.C.G. abnormalities most commonly found reflect abnormalities of right ventricular conduction or repolarization; these abnormalities include the classic $S_1Q_3T_3$ pattern with or without T-wave inversion in leads V1–V3 or V4 (McGinn and White, 1935; Cutforth and Oram, 1958) and right bundle branch block. These changes may be evanescent. Occasionally left-sided E.C.G. changes occur (Medd and McBrien, 1962) and in some cases the E.C.G. may be normal despite massive pulmonary embolism.

The plain chest radiograph may appear deceptively normal but on close inspection oligaemia of the affected zones is an almost invariable finding (Westermark, 1938). Other radiographic abnormalities include an elevated dome of the diaphragm, infarct shadows, and a 'plump' hilar shadow. Radiologically detectable enlargement of the main pulmonary trunk is not a feature of acute massive pulmonary embolism without previous cardiorespiratory disease (Kerr, Simon, and Sutton, 1971).

Definitive diagnosis is provided by pulmonary arteriography. While this procedure cannot be without risk in such critically ill patients we have performed this investigation in well over 40 such patients without mortality. The volume of contrast medium must, however, be reduced to 0·75 or 0·5 ml. per kg. body-weight to avoid peripheral vasodilatation, which can lead to a profound, but transient, hypotension in patients who have a fixed and low cardiac output.

TREATMENT

Since duration and severity of embolism and the presence of coexisting cardiorespiratory disease affect the prognosis and rate of resolution of pulmonary emboli, the present series of patients in whom both the duration and the severity of embolism were known formed an ideal group in which different treatment régimes could be assessed. Three approaches to treatment have been employed: emergency pulmonary embolectomy on the one hand and medical treatment with anticoagulant (heparin) or thrombolytic (streptokinase) therapy on the other. Since none of the patients (most of whom were referred from other centres) was seen within 2 hours of embolism I have little personal experience of the initial resuscitation or of Trendelenburg or inflow occlusion embolectomy which is the only treatment available when resuscitation fails. Cross and Mowlem (1967) have reported the collective experience of 40 surgeons working in the United States. As might be expected, Trendelenburg or inflow occlusion embolectomy carried a high mortality (87 per cent) whereas by-pass embolectomy was accompanied by a 57 per cent mortality with a further 11 per cent late deaths. The patients included in the present study, having survived for 2 hours or more, were obviously a relatively good-risk group and our experience with embolectomy has been more favourable. By-pass embolectomy has been associated with an overall mortality of 23 per cent and only 1 out of 13 patients so treated has died since 1968; this patient was moribund and having cardiac massage on arrival a the operating theatre. The occurrence of cardia arrest has carried a bad prognosis; among those wit such a history the mortality has been 66 per cer whereas no patient has died following embolectom when the history did not include an episode of cardia arrest (*Fig.* 1).

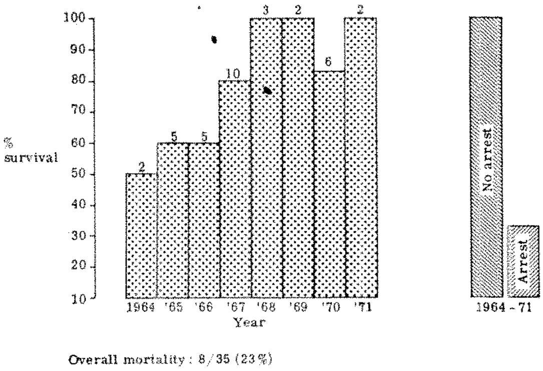

FIG. 1.—*Left-hand panel*, percentage survival following pulmonary embolectomy in patients with isolated, acute, massive pulmonary embolism. Numbers indicate the number of patients undergoing embolectomy each year. *Right-hand panel*, percentage survival for all the patients following embolectomy. For those patients in whom the history included an episode of cardiac arrest the mortality was 66 per cent; where there was no such history the survival rate is 100 per cent. (*I would like to acknowledge the help of Mr. M. Paneth, F.R.C.S., and Mr. S. C. Lennox, F.R.C.S., whose results for pulmonary embolism are presented here.*)

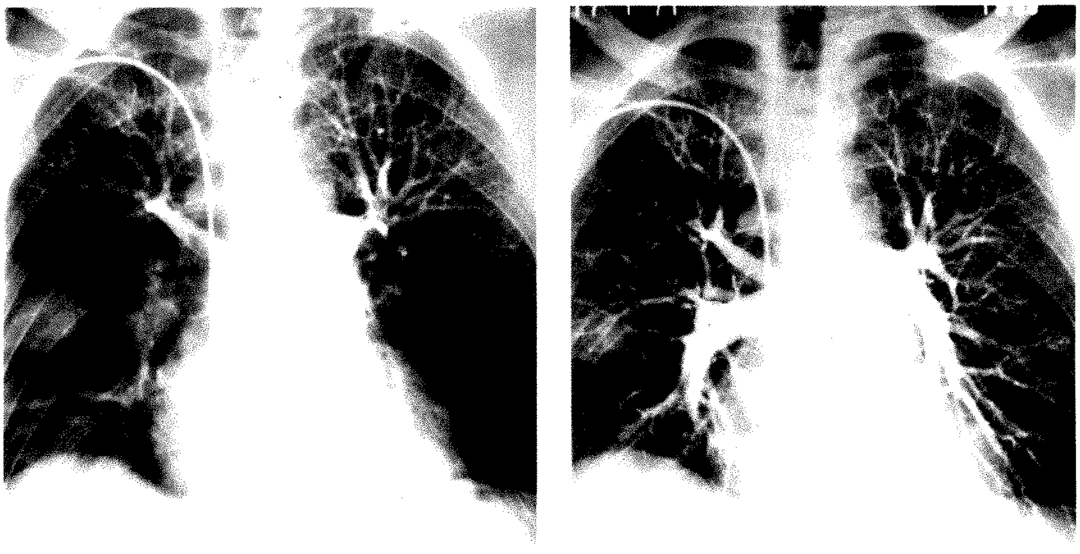

FIG. 2.—Pulmonary arteriograms of a patient with isolated, acute, massive pulmonary embolism on admission (A) and after a 72-hour infusion of streptokinase into the main pulmonary artery (B).

Recently, the effect of either heparin or streptokinas in a series of 23 patients with isolated, acute, massiv pulmonary embolism has been studied. Thes patients are not necessarily comparable with th surgically treated patients and, while no medicall treated patient has died, 2 deteriorated durin treatment (heparin) and 1 of these then had a success ful embolectomy. Equally, by-pass embolectomy i still the treatment of choice in a patient who is s critically ill that the delay in obtaining a respons which is associated with medical treatment is though to be unacceptable. Thus, the good results obtaine with medical treatment have in part depended o the potential which by-pass embolectomy has fo retrieving a deteriorating situation.

The results of the comparison between streptokinas and heparin have been reported elsewhere (Mille Sutton, Kerr, Gibson, and Honey, 1971). In sum mary, patients in the two treatment groups wer shown to be similar in terms of the haemodynami disturbance and the angiographically assessed severit of embolism before treatment was started. Patient were reassessed by repeat catheterization an pulmonary arteriography after a 72-hour treatmen period. Treatment was either with streptokinase* i a dose of 600,000 U. in the first half hour followed b 100,000 U. per hour for 72 hours, or with heparin i a dose sufficient to prolong the whole-blood-clottin time by a factor of 2–3 (40,000–60,000 U. per 24 hours). Steroid cover (hydrocortisone 100 mg. i.v. 6-hourly) was given to the streptokinase-treated patients. In both the groups treatment was by continuous drip into the catheter which was left in the main pulmonary artery and used for the subsequent post-treatment pulmonary arteriogram. Results indicate that streptokinase leads to more rapid lysis of emboli than does heparin both in terms of the haemodynamic and, particularly, of the angiographic response (*Fig.* 2), the differences between the two groups in terms of the post-treatment pulmonary arteriogram being highly significant ($P < 0{\cdot}001$). The only complication of treatment was bleeding from cut-down or operation sites with a fall in haemoglobin, which was more commonly seen in the streptokinase-treated group. In 2 patients treatment with heparin had to be abandoned because of clinical deterioration; this never happened in the streptokinase-treated group.

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* Kabikinase; Kabi Pharmaceuticals Ltd., Bilton House Uxbridge Road, London, W.5.

That streptokinase results in the accelerated lysis of emboli is a deliberately limited conclusion. Of patients dying from pulmonary embolism, perhaps two-thirds are dead within 2 hours (Gorham, 1961); clearly thrombolytic therapy is unlikely to have much to offer these patients. None the less there remains a significant number who die in the succeeding hours or days; if death in these patients is related to an unrelieved severe haemodynamic disturbance or to further embolism occurring before much of the pulmonary vascular bed has cleared then accelerated lysis of the emboli is a desirable aim. At the present time, however, there is no statistically acceptable evidence that thrombolytic therapy does reduce mortality, though such evidence may be forthcoming. Other aims of treatment include a reduction in the recurrence rate and in the incidence of late sequelae. However, in a multicentre trial of another thrombolytic agent (urokinase) and heparin reported from the United States (Urokinase Pulmonary Embolism Trial, 1970) the recurrence rate and the incidence of incomplete resolution at 1 year were the same in both treatment groups, though this large series contained very few patients with the type of life-threatening massive pulmonary embolism which has been treated in the series reported here.

At the Brompton Hospital the present policy is to use streptokinase as the treatment of choice in isolated, acute, massive pulmonary embolism and to reserve embolectomy (1) for patients with life-threatening pulmonary embolism in whom there is a contra-indication to streptokinase therapy, and (2) for patients whose condition is critical or in whom there is serious deterioration despite medical treatment. Contra-indications to streptokinase therapy are probably also contra-indications to heparin therapy and include recent surgery where bleeding would constitute a risk, known peptic ulceration, and a coagulation defect other than that due to previous anticoagulant therapy. There remains a difficult group of patients in whom embolism is not life threatening but in whom resolution is incomplete or there is a contra-indication to streptokinase therapy. In the first type of patient streptokinase might be employed; embolectomy might be advocated for the second group, although it is not known if the risks of treatment in such patients outweigh the possible gains, bearing in mind that the natural history of pulmonary embolism is probably for eventual resolution to occur in the majority of cases.

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[Although not published here, the following papers were also read:—

'Prophylaxis of Thrombo-embolism', V. V. Kakkar (London)

'Surgical Management of Thrombo-embolism', N. L. Browse (London).]

REVIEWS AND NOTICES OF BOOKS

Endocrine Therapy in Malignant Disease. Edited by BASIL A. STOLL, F.F.R., London. 9¾ × 7½ in. Pp. 442 + xvi. Illustrated. 1972. London: W. B. Saunders Co. Ltd. £7·50.

THIS work with its fifteen contributors from various parts of the world is in reality a commemorative volume honouring Charles Huggins on the occasion of his seventieth birthday. An interesting short history of the life and work of Charles Huggins is given by Paul Talalay of Johns Hopkins University, and there is a pleasing photograph of Huggins.

Every aspect of the important subject of endocrine therapy in malignant disease has been covered in an interesting and practical way. Charles Huggins himself contributes a fascinating chapter on endocrine-induced regression of cancers.

The volume is divided into five large sections. Section 1 deals with basic considerations. Section 2 is devoted to breast cancer and endocrine therapy. Section 3 is concerned with prostatic cancer. In section 4 other tumours, such as endometrial hyperplasia and carcinoma in situ, are considered. Endocrine therapy in advanced endometrial cancer also comes under review. Section 5 deals with prospective considerations, in which an evaluation of endocrine ablation therapy is discussed in some detail.

This is one of the most important medical works that have been published this year.

As a reference volume it could not be bettered.

Perspectives in Surgery. By CLARE GRAY PETERSON, M.D., Portland, Oregon. 10 × 7 in. Pp. 339 + xvi. Illustrated. 1972. London: Henry Kimpton. £9·45.

THIS is a book that all surgeons will enjoy reading. It is full of useful facts and information and considerations of important conditions with which any surgeon may be faced.

On the inside cover a copy of the Hippocratic Oath is printed in full. Many doctors have never read this oath and it is pleasing to note that the author considers it necessary to bring it into the limelight again.

The book is divided into five parts. Part 1 is concerned with the biological response to injury, which includes systemic and local responses. The electron photomicrographs of a healing wound are excellent. Part 2 deals with balance problems in surgery. The contribution on water–electrolyte balance is quite stimulating. Part 3 is devoted to thermal burns. Part 4 is given up to surgical infections, and Part 5 is concerned with the acute abdomen.

There is a very complete selected list of references and a full index.

A book which makes the reader think and ponder.

Orthopédie et Traumatologie. Conférences d'Enseignement 1970. 8¾ × 6¾ in. Pp. 311. Illustrated. 1971. Paris: Expansion Scientifique Française. No price given.

THIS book mysteriously lacks an introduction but from the title page it may confidently be concluded that it reproduces a postgraduate course given in 1970. If one opens this volume with gloomy forebodings that the contents will only be of interest and worth having t those who attended the course one will be most agreeabl surprised. There are thirteen articles with an averag length of 25 pages, which seems quite fair for the kin of information supplied. The subjects are taken fro the realm of orthopaedics and traumatology and are al of definite current interest. To mention some of them there is an opening chapter of a contemplative nature o the essence of osteo-arthritis that will be upsetting t many an established opinion; there is a section on th operative treatment of ruptures of the rotator cuff of th shoulder, meticulously describing Debeyre's origina approach and, what is more, his late results; there is good synopsis on the ever-bedevilling treatment of hallu valgus, and a fine review of patellar fractures. The boo is well produced, profusely and clearly illustrated, an the text is most lucid. Though there is a good bibliography, this is not a book of reference but one whos study should be very rewarding.

Ano-rectal Malformations in Children. By F DOUGLAS STEPHENS, D.S.O., M.S. (Melb.), F.R.A.C.S. and E. DURHAM SMITH, M.D. (Melb.), F.R.A.C.S. F.A.C.S., Melbourne. 8¾ × 5¾ in. Pp. 411 + xvi. Illustrated. 1972. London: Lloyd-Luke. £11·70.

THIS book which is dedicated to 'Children everywhere deformed anywhere' is a most comprehensive review o anorectal malformations in children.

The first chapter contains an excellent historical revie of these conditions; it is written by Dr. Reginald Webster Pathologist to the Royal Children's Hospital, Melbourne

Following this, some chapters devoted to the anatom and function of the normal rectum and anus are wel illustrated with clear line drawings. Individual deformities in the male and female are well described and illustrated.

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Throughout the book the illustrations are excellent an do enhance the written word.

The references at the end of the book are extensive an cover the international literature on this subject. A first class reference volume which should find a place in ever medical library.

Theatre Nurses Handbook. By ALICE B. CRANFIELD S.R.N., formerly Westminster Hospital, London. 8½ × 5½ in. Pp. 108 + vii, with 22 illustrations. 1972 London: The Butterworth Group. £1·40.

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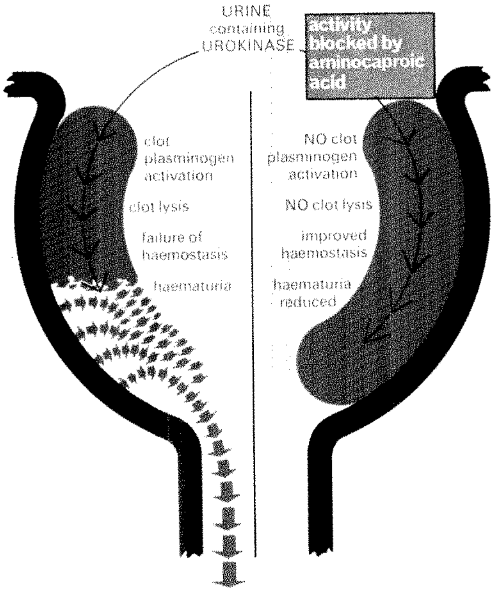
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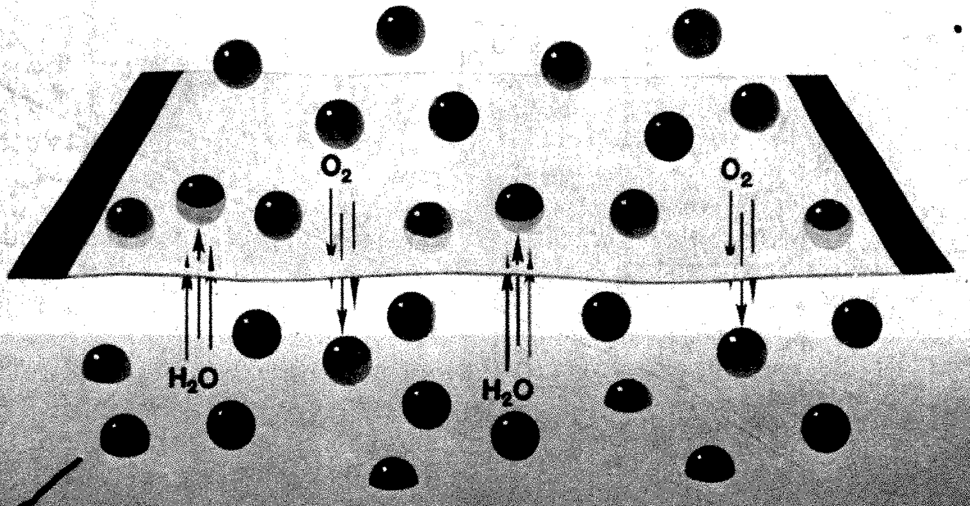

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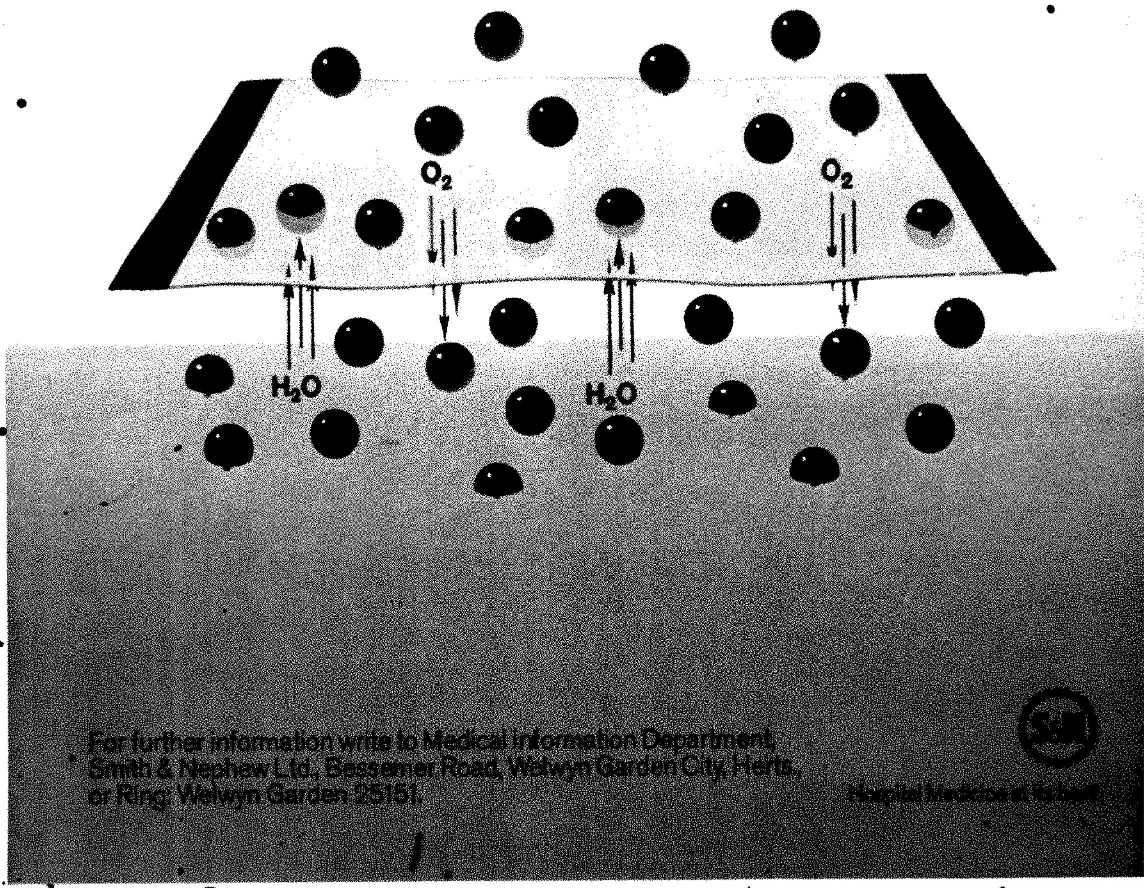

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CONTENTS

ORIGINAL PAPERS

	PAGE
Ivalon (Polyvinyl Alcohol) Sponge in the Repair of Complete Rectal Prolapse — *Sir Clifford Naunton Morgan, Nigel H. Porter, and David J. Klugman*	841
Experiences of Ivalon-sponge Implant for Complete Rectal Prolapse at St. Mark's Hospital, 1960–70 — *J. C. B. Penfold and P. R. Hawley*	846
A Prospective Study of the Immediate and Long-term Results of Polya Gastrectomy for Duodenal Ulcer — *K. C. McKeown*	849
A Technique for creating a Skin-lined Hemithorax — *Lade Worsornu*	868
An Assessment of Above- and Through-knee Amputations — *P. W. B. Green, B. S. Hawkins, W. T. Irvine, and C. W. Jamieson*	873
The Effect of Obstructive Jaundice on the Migration of Reticulo-endothelial Cells and Fibroblasts into Early Experimental Granulomata — *Emanoel Lee*	875
The Effect of Clothing on the Dissemination of Bacteria in Operating Theatres — *Caroline M. Doig*	878
Heterologous Liver Perfusion — *R. Hickman, J. R. Parker, S. J. Saunders, N. E. Goodwin, and J. Terblanche*	881
Ectopic Thymic Tissue presenting as a Lateral Cervical Swelling — *D. R. A. Finch and M. H. Gough*	885
Twenty-four-hour Preservation of Canine Kidneys exposed to 45 and 60 Minutes of Warm Ischaemia — *M. E. Snell, W. I. Hopkinson, and K. A. Porter*	886
Secondary Haemorrhage from the Arterial Anastomosis of Renal Allografts — *A. J. Robson, D. B. Evans, and R. Y. Calne*	890
Surgical Resection of Recurrent Crohn's Disease — *J. L. Grogono and A. G. Parks*	892
The Management of Congenital Hydronephrosis in the Newborn — *H. T. Williams and K. W. Wilkinson*	894
Surgical Research Society	897

SHORT NOTES OF RARE OR OBSCURE CASES

Bilateral Traumatic Renal Artery Occlusion with Survival after Late Reconstitution of Arterial Flow — *W. E. Birkenstock, R. Rabkin, and D. P. Stables*	915
Acute Myelitis presenting as Spastic Colonic Ileus — *H. T. Williams and D. T. L. Turner*	918
Ruptured Solitary Cyst of the Liver — *R. C. G. Russell*	919
Congenital Oesophago-bronchial Fistula in an Adult — *D. G. Hill and A. K. Yates*	921

REVIEWS AND NOTICES OF BOOKS

The Shoulder and Neck—*James E. Bateman.* Spezielle pathologische Anatomie, Vol. 2, Part 1: Oesophagus und Magen—*Wilhelm Doerr, Gerhard Seifert, and Erwin Uehlinger.* Acute Cholecystitis—*Clarence J. Schein.* Bacterial Infections: Changes in their Causative Agents and Possible Basis—ed. *M. Finland, W. Marget, and K. Bartmann.* Resistance to Trauma—*Zdenek Hruza.* Neonatal Emergencies and Other Problems—*John Black.* La Chimiothérapie regional des Cancers de l'Appareil Digestif—*P. Kissel, M. Bessot, A. Duprez, and G. Mauuary.* Modern Trends in Orthopaedics, 6—ed. *A. Graham Apley.* The Elephant Man—*Ashley Montagu.* Handbuch der medizinischen Radiologie—ed. *L. Diethelm.* 923

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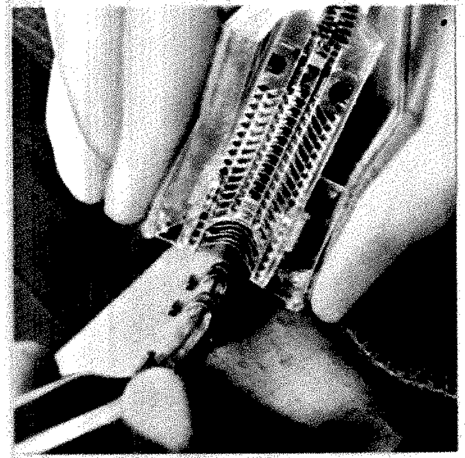

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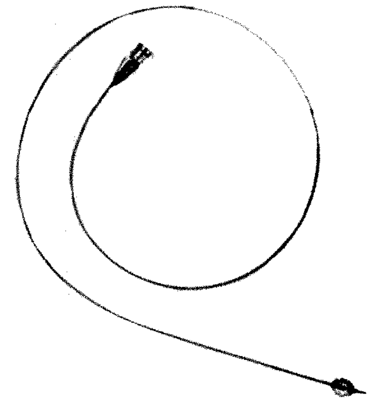

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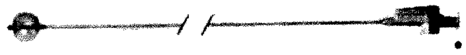

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	22	*Irrigation*
	41	*Biliary Balloon Probe (Short Tip)*
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	A	*Revision Number*
	080	*Length in Centimeters*
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32-080-8F	2.25	4.5	14
32-080-8/10F*	4.5	8	19
FOGARTY OCCLUSION CATHETER			
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12C-080-4F	0.75	1.7	
12C-080-5F	1.5	3.0	
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12C-080-7F	2.5	5.0	
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92-060-6F (Whistle Tip)	1.75	3.0	13
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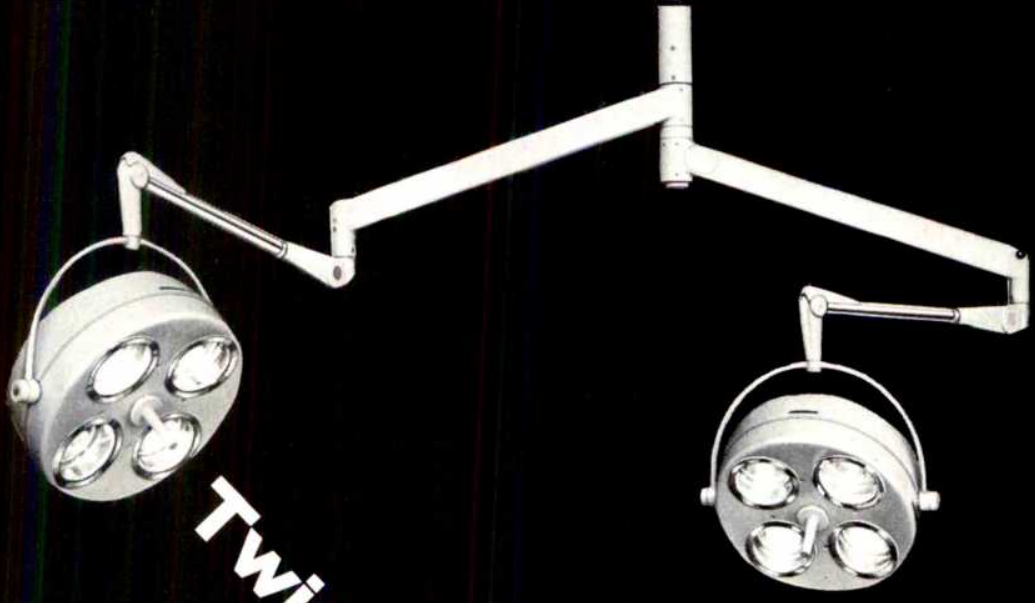

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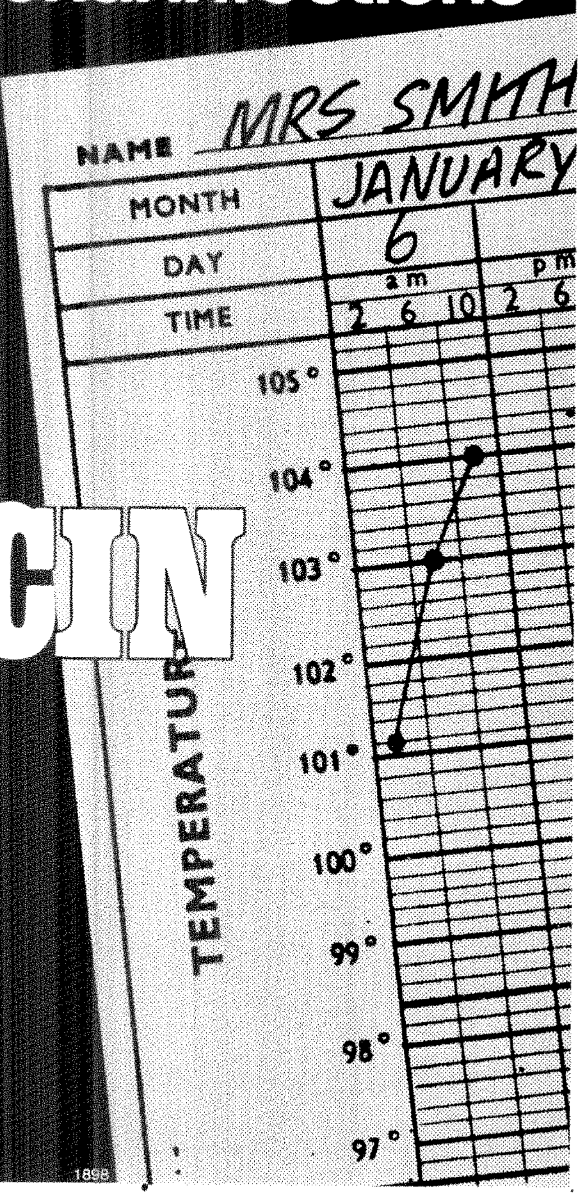

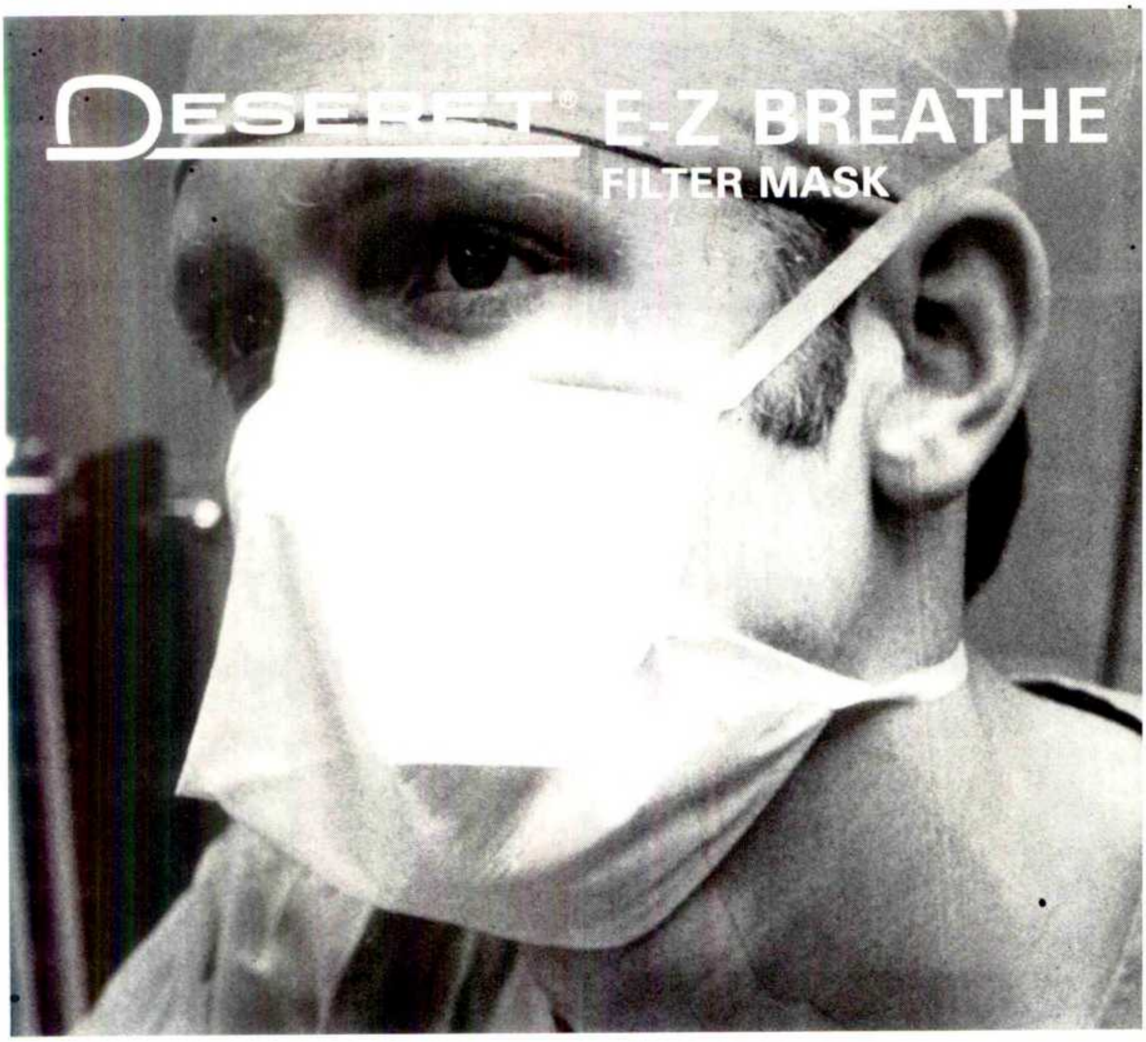

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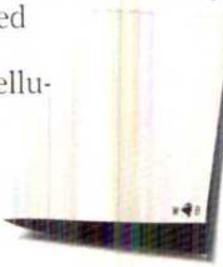

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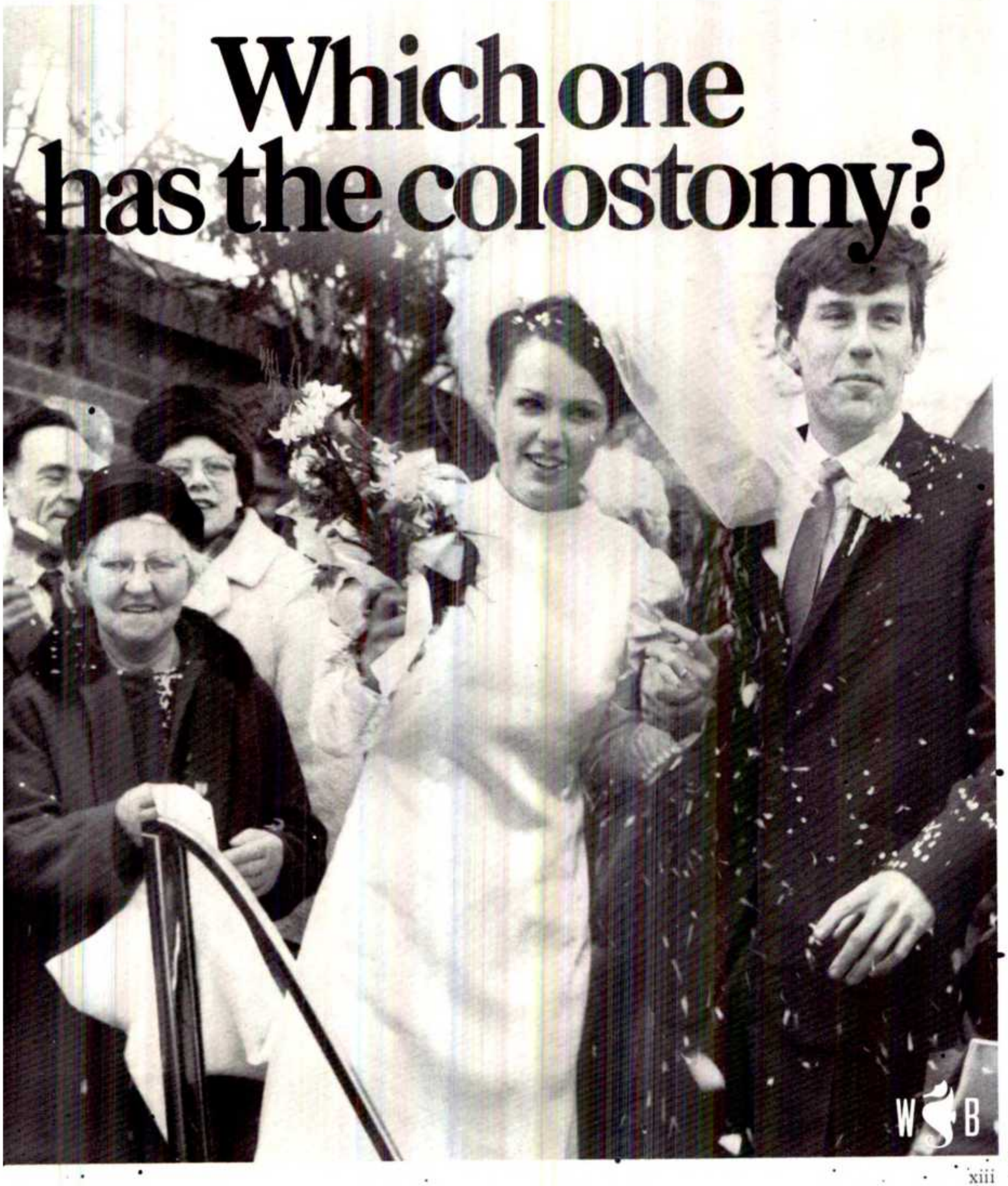
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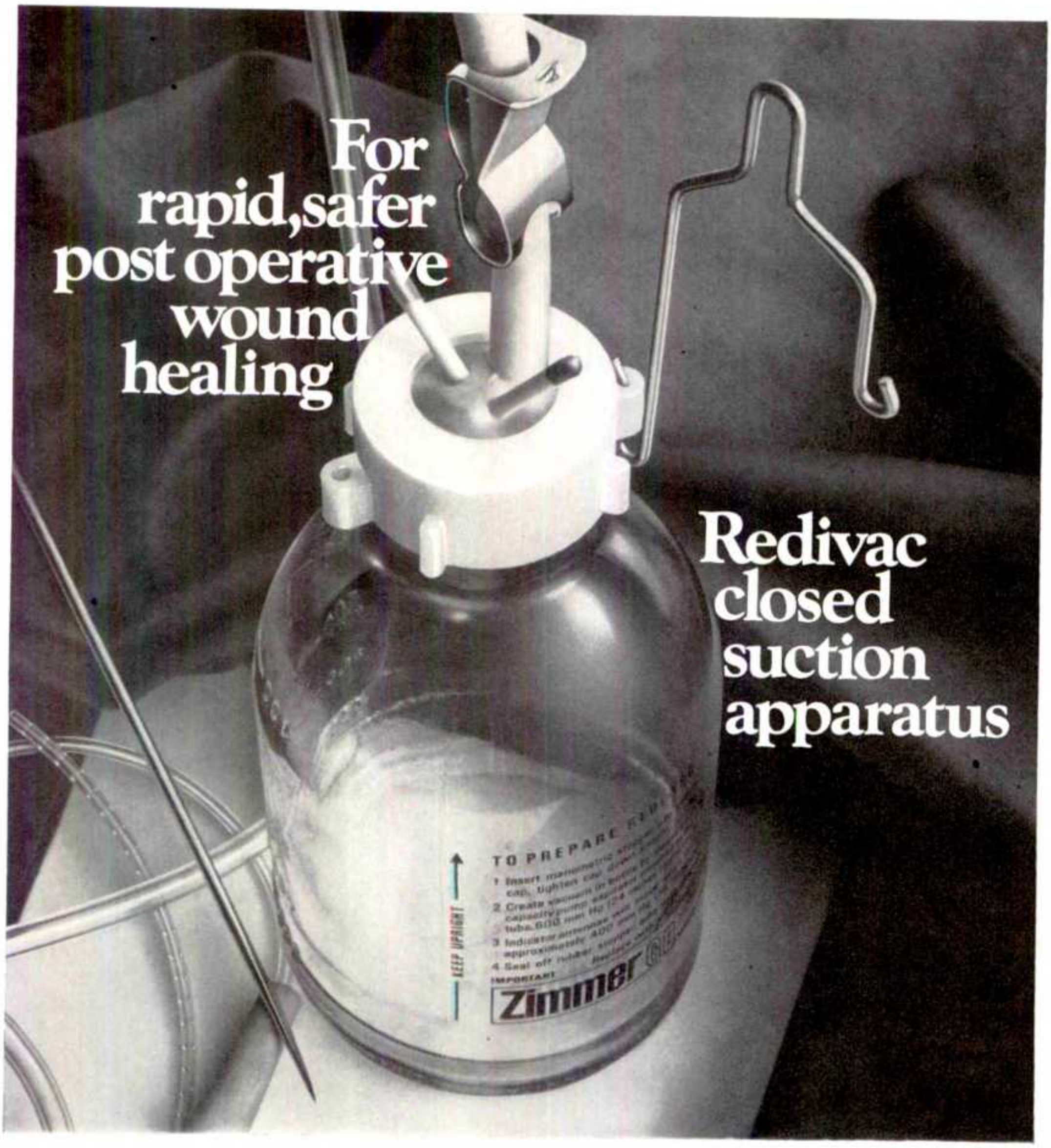
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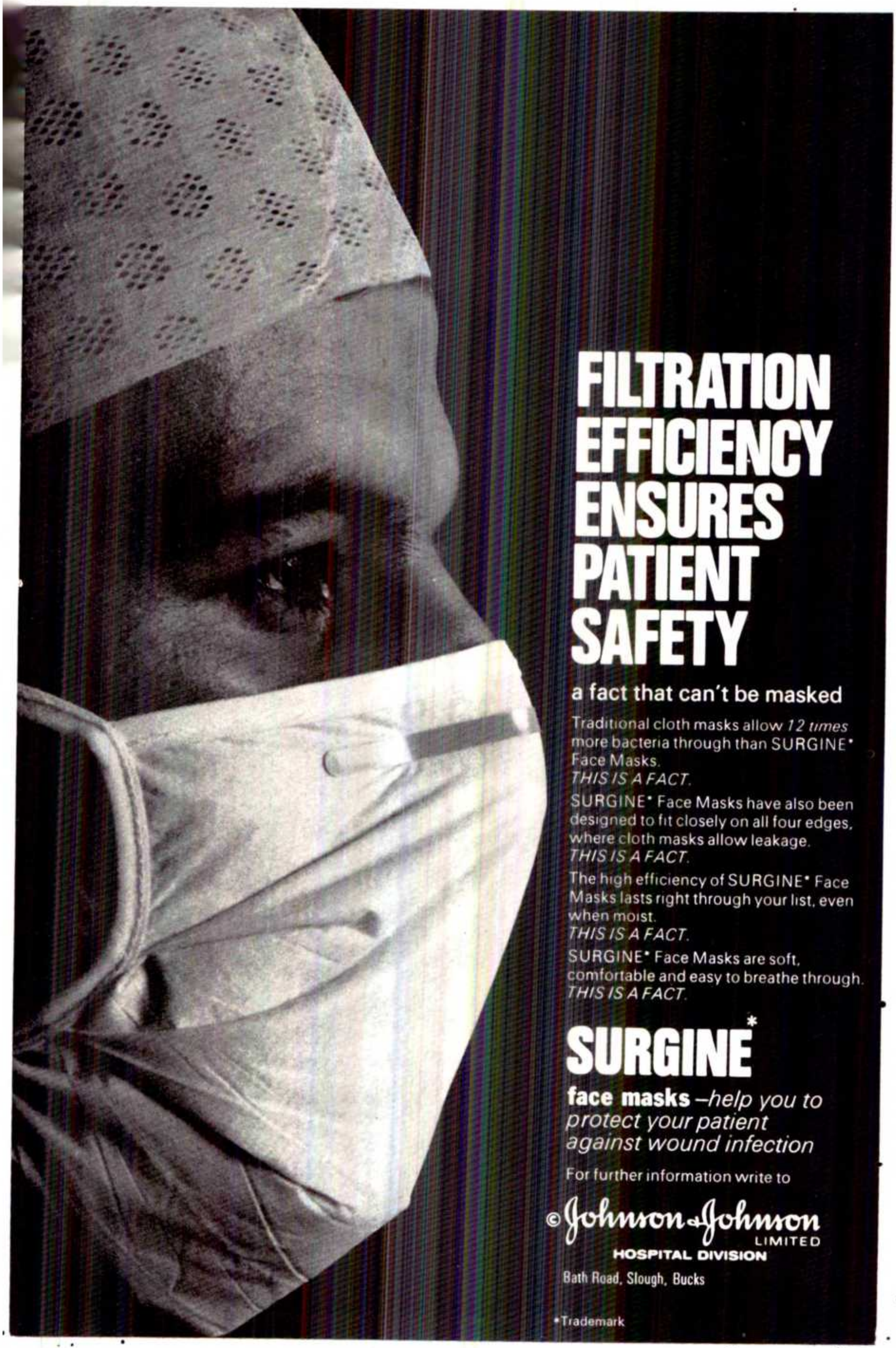

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BRITISH JOURNAL OF SURGERY

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ORIGINAL PAPERS

IVALON (POLYVINYL ALCOHOL) SPONGE IN THE REPAIR OF COMPLETE RECTAL PROLAPSE

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SUMMARY

One hundred and fifty cases of complete rectal prolapse have been operated on using an Ivalon-sponge implant, the first case being over 13 years ago. Seventy per cent of the patients were over the age of 60 years. The operation has a low mortality- and morbidity-rate. Repair using Ivalon sponge was 96 per cent successful in the cure of complete prolapse and the method appears to stand the test of time well.

In 1959 Wells first described the use of polyvinyl alcohol sponge in the repair of rectal prolapse. A follow-up study (Morgan and Wells, 1962) suggested that this technique provided a very effective method of controlling rectal prolapse and that it also went some way towards helping in the management of the notoriously difficult functional problems that beset these patients, in that 50 per cent of them became continent postoperatively and, as a result of this, were able subsequently to manage their difficult bowel habits more easily.

We have delayed publication of our figures for two reasons: first, in order to gain a significant number of patients for a worth-while statistical evaluation, and, secondly, to see how this operation stands the test of time. In the management of complete rectal prolapse these two considerations are important.

The vast amount of literature published on this subject contains a number of extravagant claims based on small series of cases which have been insufficiently followed up. We have taken considerable trouble to avoid this error in the present series.

MATERIALS

This series of 150 patients was operated on by two of us (C. N. M. and N. H. P.) between January, 1959, and May, 1972 (*Table I*). There were 127 females and 23 males. The age-range was 24–86 years with a mean of 65 years. Seventy per cent of the patients were over 60 years of age. Out of the 150 patients, 4 patients (2·6 per cent) died in the early postoperative period. There were 11 late deaths (7·3 per cent) in the series—these patients died from causes unconnected with the original operation or complaint of rectal prolapse. In none of these patients was there any history of recurrence up to the time of death. Unfortunately, 42 patients (28 per cent) have been lost to follow-up because they had originally come from distant parts of the United Kingdom or from abroad. In none of these latter patients was there any history of recurrent prolapse up to the time of their disappearance from follow-up. Thus, there is a total of 93 cases (62 per cent of the number operated on) available for study.

Table I.—THE CASE MATERIAL IN THE PRESENT SERIES

	No. of Cases	*Percentage*
Early postoperative deaths	4	2·6
Late deaths from other causes	11	7·3
Cases lost to follow-up	42	28·0
Cases studied fully	93	62·0
Total	150	

METHODS

Preoperative Investigation.—A number of patients were investigated both pre- and postoperatively by means of cine-radiography during defaecation (Fry, Griffiths, and Smart, 1966). Postoperative studies showed good fixation of the rectum in the sacral hollow and improvement in the position of the levator muscular shelf on which the distal portion of the rectum lies.

Pre- and postoperative electromyographic studies of the pelvic floor were carried out in some patients. In all the patients there was a gross disturbance of the normal postural pelvic floor reflexes preoperatively, and in only 2 of the patients who were followed up postoperatively (both were young) was there any significant recovery in the pelvic muscle function, which indicates that whatever the cause of the prolapse may be (and we think it is due to abnormal habits of defaecation to a large extent) these aetiological factors produce muscle failure in the pelvic floor before prolapse which is not cured by fixing the rectum in the sacral hollow.

These observations are in keeping with those of Parks, Porter, and Hardcastle (1966) on the 'descending perineum' syndrome and they also go some way towards explaining the fact that correction of the rectal prolapse alone does not entirely solve the functional problems of continence and abnormal bowel habit.

Operation.—The operative technique used in the present series is described by Morgan and Porter (1969) and by Morgan (1973).

RESULTS

Mortality.—There were 4 early postoperative deaths (2·6 per cent). Three of these were due to unassociated disease—2 women, aged 59 and 73 years respectively, from coronary occlusion on the fifteenth and tenth postoperative days and 1 woman of 75 years following a pulmonary embolus on the sixth postoperative day. The fourth death was attributable to the operation. This occurred in a woman of 86 years and was due to intestinal obstruction on the fifth postoperative day. At laparotomy on the sixth postoperative day she was found to have a small-bowel volvulus which was the result of an antemesenteric adhesion to the reconstituted pelvic floor. Small-bowel resection and anastomosis were performed but the patient died on the eighth postoperative day. There have been no further early postoperative deaths in this series since 1964.

Morbidity.—

Sepsis.—Four patients (2·6 per cent) have developed pelvic sepsis directly attributable to the operation. These 4 patients bear careful scrutiny as the implantation of foreign plastic materials must always constitute a hazard in this respect.

Case 1.—Female, aged 56 years. This patient developed a postoperative low-grade pyrexia and leucocytosis for which no cause could be found at first. Pelvic examination, although initially negative, revealed after 5 months a boggy swelling around the rectum, rather than the usual perirectal induration, which was palpable high in the pelvis. There was no suitable response to antibiotics and therefore the decision was taken to remove the Ivalon sponge. This was effected through an abdominal incision. Thereafter the patient made an uneventful recovery and has had no further prolapse.

Case 2.—Female, aged 83 years. This patient made uneventful progress for the first week after operation. On the eighth postoperative day she developed a vaginal discharge and pyrexia. Examination revealed a diathermy slough in the posterior vaginal fornix through which infection had entered the pelvic cavity. There was no satisfactory response to antibiotics. On the sixteenth postoperative day under general anaesthesia the orifice in the posterior vaginal fornix was enlarged and the Ivalon sponge was removed without difficulty. Thereafter the sinus in the vagina healed. The patient completely recovered and has had no further prolapse.

Case 3.—Female, aged 73 years. This patient developed persistent pyrexia from the first postoperative day. This was associated with leucocytosis and examination revealed a boggy swelling surrounding the rectum. On the eighth postoperative day she had purulent diarrhoea, and sigmoidoscopy showed a fistula into the rectum at 8 cm. through which pus was draining. Following drainage per rectum the patient's constitutional symptoms remitted, but she continued to have uncontrollable diarrhoea. For 6 weeks unsuccessful attempts were made to manage this conservatively. Seven weeks after the original operation under general anaesthesia the sinus in the posterior wall of the rectum was enlarged and the Ivalon sponge was identified, grasped with sponge-holding forceps, and removed. Postoperatively the patient made a complete recovery: the rectum healed, the pelvic infection subsided, and the patient lost her diarrhoea and gained full faecal control. She has since had no further prolapse.

Case 4.—Female, aged 76 years. This patient underwent repair of her rectal prolapse with an Ivalon-sponge implant in 1964 with an uneventful recovery and complete control of her rectal prolapse and bowel function subsequently. Eighteen months later at routine follow-up she complained of a dull aching sacral pain. Digital rectal examination revealed a boggy, tender swelling posterior to the rectum. Sigmoidoscopy confirmed the presence of a posterior bulge into the rectum above the anorectal ring. The patient had no constitutional symptoms or pyrexia. The total white-blood count was 12,000 c.mm. with a pronounced left shift and a polymorph count of 78 per cent. Antibiotics were exhibited without effect and the patient's sacral pain increased. Finally, under general anaesthesia the posterior bulge into the rectum was explored by means of sinus forceps passed via the rectal lumen. A quantity of pus was drained and digital exploration revealed a loculated cavity behind and on either side of the rectum in which fragments of Ivalon sponge could be felt; these were removed with sponge-holding forceps and the cavity was irrigated. The abscess cavity thereafter rapidly closed down and the opening into the rectum healed. The patient lost her pain and there has been no recurrence of prolapse or loss of continence.

Cure of Prolapse.—Out of 93 completely documented cases, 90 (96·8 per cent) have been cured of complete rectal prolapse (*Table II*). There have been 3 cases (3·2 per cent) of recurrent complete prolapse. All the complete recurrences occurred within 3 years of operation. The earliest of these was in a male of 60 years whose prolapse recurred at 7 months. He had a history of intractable diarrhoea following amoebic dysentery many years previously. The repair of the rectal prolapse had made no difference to his bowel habit. The other 2 complete recurrences were in women, one aged 60 years and the other aged 82 years. Both of these patients had had a previous rectosigmoidectomy. Prior to operation they had been totally incontinent and they had only been able to manage their bowel habits socially by making sure that they were grossly constipated. Both patients had had a completely patulous anus preoperatively. Pre- and postoperative electromyographic studies revealed an almost total loss of pelvic postural reflexes and continence reflexes. In addition, in each case balloon studies showed a rectal capacity of less than 50 ml. and neither patient was able to retain the balloon in the rectum. There was no postoperative improvement in continence or bowel habit.

Table II.—RESULTS OF REPAIR OF COMPLETE RECTAL PROLAPSE USING IVALON SPONGE

	No. of Cases	*Percentage*
Total No. of cases	93	
Cured of complete prolapse	90	96·8
Recurrent complete prolapse	3	3·2
Persistent mucosal prolapse	8	8·6
Further operation for mucosal prolapse	4	4·3
Further operation for incontinence	7	7·5

It is worthy of note that there have been no recurrences after the lapse of 3 years postoperatively. *Table III* provides a breakdown of the duration of follow-up in annual periods. There are 104 patients who were operated on over 3 years ago: 56 of these patients come into the total follow-up group and none of them has developed a complete recurrence, although 7 have developed mucosal recurrence. These figures indicate that complete recurrence is uncommon and, if it occurs, it does so relatively early.

Table III.—DURATION OF FOLLOW-UP OF 128 CASES WHO HAD UNDERGONE OPERATION FOR COMPLETE RECTAL PROLAPSE

YEAR	NO. OF CASES	NO RECURRENCE	MUCOSAL RECURRENCE	COMPLETE RECURRENCE	LOST TO FOLLOW-UP BUT NO RECURRENCE	DEAD FROM OTHER CAUSES (NO RECURRENCE AT THE TIME)
0–1	15	8	0	1	4	2
1–2	16	6	2	0	6	2
2–3	15	4	2	2	4	3
3–4	14	7	1	0	5	1
4–5	9	7	0	0	2	0
5–6	11	3	1	0	6	1
6–7	14	9	2	0	1	2
7–8	7	5	1	0	1	0
8–9	9	9	0	0	0	0
9–10	5	4	1	0	0	0
10–11	4	3	1	0	0	0
11–12	5	5	0	0	0	0
12–13	2	2	0	0	0	0
13–14	2	2	0	0	0	0
Total	128	74 (57·8 percent)	11 (8·6 per cent)	3 (2·3 per cent)	29 (22·6 per cent)	11 (8·6 per cent)

Eight patients (8·6 per cent) in this series prolapsed mucosa only through the anal canal at some time postoperatively. Half of these patients failed to respond to submucous injections of 5 per cent phenol in almond oil and because their symptoms troubled them they required a further operative procedure, viz., ligature and excision. This simple procedure was sufficient to relieve them of further mucosal prolapse.

Bowel Habit.—Accurate knowledge of bowel habit prior to the onset of prolapse is available for 103 cases. *Table IV* indicates that only 20 patients (19·4 per cent) had had a regular bowel habit before they developed prolapse. Eighty-three patients (80 per cent) had had an abnormal bowel habit; 67 (65 per cent) having been constipated and 16 (15·5 per cent) having had diarrhoea or loose motions more than three times a day.

Constipation has been defined for the purpose of this study as a bowel habit involving routine straining at defaecation to pass hard stools. This may also be associated with several attempts to defaecate daily in order to satisfy a feeling of incomplete defaecation whether the act is productive of a stool or not. Also included in this group are those patients who failed to open their bowels more than three times a week. These criteria are similar to those of Connell, Hilton, Irvine, Lennard-Jones, and Misiewicz (1965).

Table IV.—BOWEL HABIT IN 103 CASES OF COMPLETE RECTAL PROLAPSE

BOWEL HABIT	BEFORE ONSET OF PROLAPSE		AFTER OPERATION	
	No. of Cases	Percentage	No. of Cases	Percentage
Regular	20	19·4	60	58·2
Constipation	67	65·1	28	27·2
Diarrhoea	16	15·5	15	14·6
Total	103	100·0	103	100·0

The postoperative figures show a striking improvement in that 60 patients (58·2 per cent) have been converted to a regular bowel habit, 28 (27·2 per cent) have remained constipated, and 15 (14·6 per cent) have frequent loose stools. This latter figure is not significantly changed, nor would one expect it to be.

It must be emphasized that the conversion from constipation to a regular bowel habit is in the majority of cases achieved by the use of aperients and this is only possible because control of rectal prolapse allows a more rational use of aperients. Careful and prolonged follow-up involving, in many cases, much trial and error in the choice of the right aperient is essential if any improvement in bowel habit is to be achieved and maintained. Furthermore, patients will not tolerate the regular ingestion of aperients unless their continence has been improved. Control of prolapse and improvement in continence also allow the use of suppositories and the avoidance of straining in those patients who do not respond satisfactorily to aperients.

Continence.—For the purposes of this study we have defined incontinence as the uncontrolled leakage of solid or loose stool. The degree of incontinence within these criteria varies from gross to slight. The results are not, however, graded according to severity as attempting to do so makes statistical evaluation useless.

Prior to operation 83 patients (80·6 per cent) were incontinent (*Table V*). Postoperatively 40 patients (38·8 per cent) were incontinent.

Continence is not always established immediately after the operation. Careful supervision of the diet and an aperient régime are essential to achieve the best results and must be aided by sphincter exercises, and sometimes pelvic faradism, to re-educate the pelvic muscles. Continence improves in many patients over the first 6–12 months. During this time a number of patients transfer from the incontinent to the continent group. This is an important point in management, since this is the most distressing symptom, both pre- and postoperatively. It is worth resisting demands for further operative treatment for incontinence until a year has passed, if the patient can be persuaded to wait that long.

Table V.—CONTINENCE IN 103 CASES OF COMPLETE RECTAL PROLAPSE BEFORE AND AFTER OPERATION

	BEFORE OPERATION		AFTER OPERATION	
	No. of Cases	Percentage	No. of Cases	Percentage
Incontinent	83	80·6	40	38·8
Continent	20	19·4	63	61·2
Total	103	100·0	103	100·0

Further Operations for Incontinence.—Seven patients (7·5 per cent) of the 93 cases who were fully followed up (or 6·8 per cent of those patients who were followed up in respect of continence alone) had further operative treatment for incontinence (*Table II*). Two patients had a Thiersch wire inserted and 1 of these was subsequently continent. The other patient developed sepsis around the wire. The infecting organism was sensitive to chloramphenicol only and the patient was given this antibiotic. She then developed pancytopenia as a complication and died.

Four patients had a post-anal nylon-floss repair (Parks, 1967); 3 of these were subsequently fully continent. The fourth patient was 1 of the 2 women who had had a previous rectosigmoidectomy and who subsequently suffered a complete recurrence after the second year. As a result of the post-anal repair both her recurrent prolapse and incontinence were diminished but not cured. The seventh patient was persistently incontinent after an Ivalon-sponge repair and subsequently had a colostomy. Although thus relieved of faecal incontinence, she still suffered intermittent and uncontrolled excessive discharge of rectal mucus which was socially embarrassing. Subsequently, the rectum was excised by Hartmann's operation with relief of this distressing symptom.

In the remaining 33 patients out of the original 40 who were incontinent following the insertion of an Ivalon sponge, incontinence varied from a slight leak to gross lack of control. They were all relieved of their prolapse following operation and in this respect felt much improved. The majority managed their incontinence. This was no trouble to those with a slight occasional leak, while others opted for a pad since they wished to avoid further operation, although there is little doubt that some of them could have been improved by a further perineal procedure.

DISCUSSION

Any operation designed to cure complete rectal prolapse must be safe and effective. The majority of patients are female and elderly since the incidence of rectal prolapse rises steeply towards the seventh decade (Porter, 1962). It has been our practice to include all patients whatever their age who have a complete rectal prolapse, whether it is primary or has recurred after some other procedure, provided that the patient is fit enough for a major lower abdomi surgical procedure. In any patient with cardi respiratory disease or in whom there was any dou about fitness we have obtained the prelimina opinion of a consultant physician and anaestheti Those patients excluded on medical or anaesthe grounds have been treated by a Thiersch operati A few of those so treated in whom this operation h failed have subsequently been submitted to an Ivalo sponge operation with success. This procedure c be performed in such cases provided that on revi both the patient and the anaesthetist are prepared accept the increased risk.

In spite of these wide criteria of selection the ea postoperative death-rate was only 2·6 per cent. T deaths of the 2 patients from coronary occlusi were unavoidable. The third patient, who died o pulmonary embolus on the sixth postoperative d was operated on in 1964. She was grossly obe With modern methods of prevention, such as su cutaneous heparin (Kakkar, 1971) or galvanic ca muscle stimulation (Powley, 1969), it is possible t pulmonary embolism, a complicating factor in ma pelvic surgery, may be partly eliminated. The fou death in a woman of 86 who developed a small-g volvulus as the result of a pelvic adhesion emphasi the need to reconstitute the pelvic peritoneal fl with care and making quite sure that the Ival sponge is completely extraperitonealized. The f that there have been no further early postoperati deaths in this series since 1964 does not indicate a alteration in our criteria for case selection.

The 4 patients who developed pelvic sepsis ha been carefully studied as there is always a considera risk of infection occurring after the implantation foreign plastic materials. Three precautions are tak to prevent sepsis. First, the patient has a 5-d preoperative course of phthalylsulphathiazole, 2·5 6-hourly, and has routine preoperative bov cleansing including a careful régime of colonic was outs. Secondly, at the time of implantation of t sponge the pelvic cavity is dusted with an antibio powder. Originally this was a mixture of penicil and sulphonamide. Latterly we have used polybact or 1 g. of chloramphenicol powder (Kemicetin Thirdly, postoperatively the patient has a 7-d course of ampicillin, 500 mg. intravenously 8-hour It is also our rule that if any injury occurs to t bowel during dissection, an Ivalon-sponge impla operation should be abandoned. Fortunately this h not happened in our series.

Nevertheless, in spite of these precautions 4 cas of sepsis have occurred. In 1 of them it was clea avoidable. In this patient (*Case* 2), a female aged troublesome bleeding in the region of the posteri vaginal fornix occurred during the mobilization the rectum. The bleeding was controlled diathermy which was clearly over-enthusiastic a led to a slough in the posterior vaginal wall. We ha since exercised great restraint in using diathermy this situation and have controlled any haemorrha with hot packs, pressure, or direct ligation.

In 2 patients (*Cases* 1 and 3) in whom sep occurred within 10 days of the operation infecti must have been due to the introduction of organis at the time of operation, either by the surgeon or failure to sterilize the Ivalon sponge adequately.

the latter respect the makers give detailed advice on the method of sterilization which we have followed carefully as the standard procedure in all cases. We therefore feel that this cause is highly unlikely.

The fourth case (*Case* 4) of sepsis is inexplicable. It occurred 18 months after the operation for no obvious cause. We have no rational explanation to offer.

From our experience it is clear that should sepsis occur, an expectant policy is not justified. As soon as the diagnosis is certain removal of the sponge is a matter of urgency. If an abscess points into the vagina or rectum removal through the wall of either viscus is a simple matter, and in the 3 patients in whom this has been performed resolution has been complete and there has been no recurrence of the prolapse. In 1 other patient the diagnosis was less certain and the abdomen was re-explored from above, the Ivalon sponge was removed, and the abscess was drained. Again, full and satisfactory resolution occurred and this patient has had no further prolapse. It is probable that the advent of sepsis, though highly undesirable, produces the same effect as the Ivalon sponge in that it anchors the rectum to the pelvic parietes by fibrosis.

Polyvinyl alcohol sponge has been shown to be carcinogenic in rats (Oppenheimer, Oppenheimer, and Stout, 1948). A careful study by Walter and Chiaramonte (1965) confirmed the incidence of sarcoma in rats but only when the implant was thick and bulky (Dukes and Mitchley, 1962). Furthermore, in the rat there is a species susceptibility to the induction of neoplasms by a variety of implants, even stainless steel. There is no evidence that polyvinyl alcohol sponge is carcinogenic in man. Clinical use over the past 20 years bears out this conclusion.

We feel that a mortality of 2·6 per cent and a morbidity of 2·6 per cent constitute a reasonable safety level for major pelvic surgery in patients of an advanced age-group and also indicate that the operation is safe.

The second criterion of effectiveness is also satisfied in that in 93 cases who were studied fully there was a complete cure rate of 96·8 per cent. Furthermore, the operation stands the test of time. All the recurrent complete prolapses occurred within 3 years. Two of the patients in whom prolapse recurred had had a previous rectosigmoidectomy and such patients always present a notoriously difficult salvage problem (Porter, 1962). The third case of recurrence, in a male with post-dysenteric diarrhoea, occurred earlier and has not been significantly improved by a subsequent left hemicolectomy and anterior resection.

Mucosal prolapse appearing after operation is difficult to evaluate in that rectal fixation by Ivalon sponge does nothing for the associated inevitable mucosal redundancy. In those patients in whom it did appear (8·6 per cent) it was unnoticed subjectively in half of them, the remainder being discovered only on examination at routine follow-up. All of these patients considered it a trivial complaint compared with their previous complete prolapse. Nevertheless some anxiety is always felt by the clinician in case the advent of mucosal prolapse presages a complete recurrence, and therefore it was usually controlled by submucosal injections of 5 per cent phenol in almond oil whenever it was seen. In 4 patients in whom this simple measure was unsatisfactory, the prolapsing mucosa was excised with a satisfactory result.

In this respect we would emphasize the importance of prolonged follow-up of these patients. There is no doubt that mucosal prolapse causes leaking of faecal-stained mucus with itching and discomfort. Control of mucosal prolapse will improve the patients' incontinence and therefore their attitude towards the use of aperients or suppositories in the management of their bowel habit. In our experience this aspect of follow-up, in particular, repays a good deal of trouble and care.

The elimination of complete prolapse does in itself little for the abnormalities of bowel function which lead to constipation or diarrhoea. However, a major factor in persistent inhibition of the voluntary pelvic muscles and stretching and incompetence of the involuntary internal sphincter is removed. This allows the residual function in both these groups of muscles to work to a better advantage and thus to exercise greater control over the contents of the rectum and to restore some sensory appreciation of impending defaecation to the patient. The majority of patients can, therefore, regulate their bowels better with a more satisfactory knowledge of impending defaecation and have time to reach a lavatory. The patients who have become continent after operation have a variable degree of urgency of defaecation and some can only restrain the act with difficulty, but all of those who have been classified in our results as continent can restrain themselves for a sufficient length of time to reach a lavatory, otherwise they have not been classed as continent.

We have made no attempt to classify continence quantitatively, as we feel that such an attempt would be more confusing than useful. Nevertheless, the degree of incontinence varies greatly, from a slight leak, when the patient has liquid stools, to gross soiling with solid stools. It is worth waiting 6 months to a year, preferably the longer period, for continence to improve if it is not satisfactory immediately postoperatively.

Improvement appears to be due to three factors. First, the patients learn to adjust their aperient régime better and also find a suitable aperient. In this respect, the aperient found to be most useful is a bulk-forming one such as Normacol. The second factor is that the operation narrows the rectum by the surrounding fibrosis which is appreciable on digital examination for at least 18 months postoperatively. This often leads to the passage of frequent pellet-like stools. This type of bowel habit and rectal narrowing frequently settles down over the course of a year and allows the patients to time their bowel actions more satisfactorily. The third important factor is the absence of the continuing dilatation of the anal canal by a large complete prolapse so that there is a reduction in the diameter of the anal canal, although only rarely have we been able to detect any clear quantitative improvement in pelvic electromyograms postoperatively. There is no doubt, however, that elimination of a complete rectal prolapse allows the patient to practise sphincter exercises more effectively and the adjuvant use of faradism appears to re-educate their proprioceptive reflexes and to improve conscious knowledge of when their sphincters are contracting. Pelvic electromyograms after pelvic faradism, however, have not shown any objective improvement in performance.

Subsequent operations for incontinence are difficult to evaluate in this series because of the small numbers involved. A few patients make an early and urgent demand for operation, while others are relieved to be rid of their prolapse, are quite happy to wear a pad to control incontinence, and do not wish to have another operation. Certainly in the present series we have not pressed additional operations on these patients, mainly because we are uncertain of success. The Thiersch operation is useful but it has a number of problems associated with it, viz., faecal impaction, and as many of these patients are constipated, this can present a serious problem. When wire is used it may fracture or cause ulcers. Nylon thread has proved to be more satisfactory.

The most useful operation is the post-anal intersphincteric nylon-floss operation repair described by Parks (1967). Nevertheless, this is not an easy undertaking and there is often delay in wound healing. It is not advocated for minor degrees of incontinence or leakage.

It is also clear, from our experience of 1 case, that colostomy is not necessarily the answer to incontinence.

Lastly, there are a number of patients who might well be benefited by operations for their incontinence. The majority of these patients has declined the operation when the offer has been made, being content to be free of their prolapse. In a small number a further operation was inadvisable as their general health was poor.

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EXPERIENCES OF IVALON-SPONGE IMPLANT FOR COMPLETE RECTAL PROLAPSE AT ST. MARK'S HOSPITAL, 1960–70

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SUMMARY

Experience of using Ivalon-sponge implants in 101 patients with complete rectal prolapse at St. Mark's Hospital is reviewed. It is a straightforward operation with minimal complications producing long-term control of the prolapse in 97 per cent of cases.

Of those patients who had been incontinent, satisfactory restoration of continence was achieved in 70 per cent of cases for solid faeces and in 33 per cent for fluid faeces.

Ivalon sponge is a foreign material that only produces moderate fibrosis in the tissues. It persists for at least 6 years in humans.

Complete rectal prolapse is a very disabling but non-lethal condition. Many operations have been devised to cure it but none has been entirely satisfactory. At the present time the Ivalon-sponge implant is being increasingly used throughout Great Britain. This paper reports our experiences using this operation during the years 1960–70.

MATERIALS

One hundred and one patients underwent repair of complete rectal prolapse using an Ivalon-sponge implant (*Fig.* 1). The youngest was 21 years and the oldest 82 years. Thirty patients had had previous surgery for the prolapse, including 14 Thiersch wire or nylon operations, 6 rectosigmoidectomies, 4 Thiersch operations and rectosigmoidectomies, and 6 miscellaneous perineal repair procedures

METHODS

The technique described by Wells (1959) using a 3-mm.-thick piece of polyvinyl alcohol (Ivalon) sponge placed behind the rectum was used. The sponge was perforated and soaked in saline before insertion. It was then attached to both the rectum and the sacrum. Usually one or two non-absorbable 'hitch' sutures were inserted between the mesorectum or lateral ligaments and the lumbosacral disk. Postoperative antibiotics were not given routinely.

Surgical technique varied to a certain extent between surgeons, but we feel that there are several important steps to ensure a successful operation.

The rectum must be mobilized right down to the coccyx posteriorly. Usually only the upper one-third of the lateral ligaments is divided but this should not compromise the posterior mobilization.

Haemostasis must be perfect at this stage. On no account should the Ivalon be inserted before all pelvic bleeding has been completely controlled. The subsequent haematoma would predispose to an infected sponge should any inadvertent contamination occur.

We prefer to insert the sponge with its long axis parallel to the rectum. The caudal extremity of the sponge is tapered a little. Special care is taken to ensure that it is inserted well down behind the rectum so that its lower end extends at least to the tip of the coccyx. The sponge is then fixed firmly by several sutures to the anterior surface of the sacrum. This suture should always be non-absorbable (either nylon or linen thread).

The 'hitch' suture is then performed. Before this was done routinely 1 case developed a complete recurrence of the prolapse in the immediate postoperative period following a bout of coughing. (Fortunately it was possible to replace the rectum in the ward with a long-term satisfactory result.)

The two leaves of the sponge are then wrapped around the rectum making sure that at least 2–3 cm. of the anterior circumference of the rectum remain uncovered (to prevent causing a constriction of the lumen). The leaves of the sponge are then fixed in place with several sutures to the seromuscular layers.

The peritoneum is closed over the Ivalon sponge so that none is left exposed to the peritoneal cavity. Care must be taken here to ensure that the base of the sigmoid mesocolon is not shortened. This would predispose to postoperative sigmoid volvulus as the sigmoid is usually redundant and on a long mesentery in complete rectal prolapse.

RESULTS

Morbidity and Mortality.—Postoperative morbidity occurred in only 6 per cent of cases. One sponge became infected and had to be removed. This followed an attack of acute appendicitis in the immediate postoperative period. The patient had a persistently elevated temperature and lower abdominal pain. At operation 2 months later the Ivalon sponge was found lying in a pool of pus. Another patient developed similar symptoms but had cystitis which responded to antibiotics. Two patients developed wound abscesses that were drained. In neither case was the Ivalon-sponge implant involved.

Two patients developed large-bowel obstruction at the rectosigmoid junction. One settled conservatively, but the other required laparotomy to free a sigmoid loop which was adherent in the pelvis.

There were no operative deaths in these 101 patients.

Follow-up.—Six patients were lost to follow-up, leaving 95 available for review. The period since the operation was from 2 to 12 years, with an average of 6 years. The review was either by examination in the clinic or, if the patient was deemed too elderly for this, by a postal questionnaire. The results refer to the findings at review after July, 1971, except for 10 patients who had died before this time. For these the findings within 6 months of the time of death are used.

Recurrences.—A complete rectal prolapse recurred in 3 of the 95 patients reviewed: 1 at 6 months, 1 at 2 years, and 1 at 4 years postoperatively. Of these, 1 case had a further successful Ivalon-sponge implant as it was felt that at the first attempt the Ivalon sponge had not been placed low enough in the pelvis. Another underwent an anterior resection because he had concomitant diverticular disease and the third refused any further treatment.

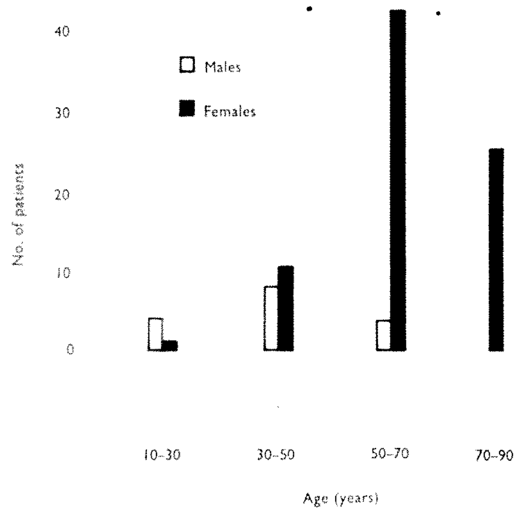

FIG. 1.—The age distribution of 101 patients undergoing an Ivalon-sponge implant for complete rectal prolapse.

Thirty-one of the 95 cases had varying degrees of mucosal prolapse on straining. Ten cases were treated by injection with 5 per cent phenol in arachis oil, 5 by a mucosal strip and ligation operation, 5 by a Thiersch-wire operation, and the rest did not receive any further treatment.

Anal Continence.—All the patients were asked specific questions about continence. Since 10 patients had died and there was insufficient information regarding their continence at the time of death and a further 6 patients had had additional major rectal surgery since the Ivalon-sponge implant, only 79 were reviewed.

Preoperatively 46 patients (58 per cent) had been continent for solid faeces, 31 (38 per cent) for fluid faeces, and 28 (35 per cent) for flatus. After the operation 70 patients (88 per cent) were continent for solid faeces, 47 (59 per cent) for liquid faeces, and 41 (51 per cent) for flatus.

Thirty-seven patients (47 per cent) found no change in bowel function following the operation, 23 (29 per cent) found defaecation more difficult, and only 19 (24 per cent) found it easier.

Postoperatively 46 (59 per cent) continued to take laxatives or suppositories to help to regulate their bowels.

Urinary-bladder Function.—Seventy-two of the 79 patients found no change in micturition following the operation. Only 3 cases found micturition more difficult, although another 4 patients developed stress incontinence.

Patient Satisfaction.—All 79 patients were specifically asked for their opinion of the results of the operation. Sixty-four patients (81 per cent) were very satisfied with the operation. (This highlights the distressing nature of prolapse as many of these patients were still incontinent.) A further 9 patients were satisfied with reservations and 6 were unsatisfied.

Of the latter 6 cases, 5 were completely incontinent and 1 has had a complete recurrence but refuses further surgery.

Failed Ivalon-sponge Operations.—Six patients underwent further abdominal operations as it was considered that the Ivalon-sponge implant had been a failure. Reoperation was for an infected Ivalon sponge in 1 case, for complete recurrence in 2, for severe incontinence in 2, and for alternating incontinence and faecal impaction in 1.

Thus, with the 6 unsatisfied patients at least 12 of the 101 operations were not successes.

EXPERIENCE OF REOPERATING ON PATIENTS WITH IVALON-SPONGE IMPLANTS

Over the past 10 years 7 patients who had had previous Ivalon-sponge implants (some implanted elsewhere) have been reoperated on at St. Mark's Hospital. Because of the natural apprehension about the insertion of a new foreign material into the body we feel that the experiences gained from these operations are of interest.

Infected Ivalon sponges were removed from 2 patients 2–3 months after they had been implanted. One had been implanted at another hospital. In both cases the Ivalon sponge was found lying in a pool of pus and was easy to remove. The cavities were drained. In 1 patient the rectum was inadvertently opened, necessitating a proximal colostomy. The abscess recurred and at re-exploration further fragments of Ivalon sponge were found and removed. Subsequent healing was uneventful. The other case healed uneventfully and the prolapse has not recurred.

Two patients had a Hartmann's operation with bowel resection for intractable incontinence 1–2 years after the Ivalon-sponge implant. In neither case was there much evidence of previous pelvic surgery or increased fibrosis behind the rectum. The mobilization was easy and only fragments of Ivalon sponge were found in the resected specimens.

Three patients had reoperations for incontinence 4–6 years after the original operation. One patient had another Ivalon-sponge implant, 1 case underwent an anterior resection, and the third had an abdominoperineal excision. In all 3 cases the mobilization was easy with little to suggest previous pelvic surgery.

FATE OF THE IVALON SPONGE IN HUMAN TISSUES

Two operative specimens were meticulously examined for evidence of the previous Ivalon-sponge implant: one was removed 2 years after insertion and the other after 5 years. Macroscopically both specimens appeared normal. There was no noticeable thickening of the mesorectum and the Ivalon-sponge implant was not obvious, although on careful dissection fragments were found to be present in both cases. Microscopically, a marked foreign-body giant-cell reaction to the Ivalon-sponge implant was noted but there was only a moderate fibrotic response. The fibrous tissue stopped abruptly at the edge of the sponge. There was no active inflammatory response to the sponge.

DISCUSSION

The Ivalon-sponge implant has given very good results for the control of complete rectal prolapse. This agrees with previous reports on smaller series (Morgan, 1962; Calne, 1966; Kupfer and Goligher, 1970). There is no evidence so far to suggest that there is an increasing recurrence rate with longer follow-up.

However, in many patients the major problem is often incontinence of faeces and flatus, and in these cases the Ivalon-sponge implant is far less successful. Incontinence has been noted previously after other operations for rectal prolapse (Kupfer and Goligher, 1970). About 40 per cent of cases still do not have satisfactory continence after the Ivalon-sponge operation. It is in these patients that further surgery aimed at improving anal function such as a post-anal repair or perhaps a Thiersch nylon operation should be considered.

Technically, repair using an Ivalon sponge is not difficult. It is tolerated well by the patients and the morbidity and mortality are low. The absence of sepsis in the present series following the insertion of a foreign material is very gratifying, especially when a previous report mentions an incidence of 16 per cent (Kupfer and Goligher, 1970).

Reoperation on patients containing previously implanted Ivalon sponge has been surprisingly straightforward. The minimal amount of fibrous tissue found between the sacrum and the rectum in these cases suggests that the success of the operation in controlling the prolapse is not due to fixation of the rectum to the sacrum but rather to a stiffening of the rectum itself, thus preventing rectal intussusception from commencing.

The Ivalon sponge, although it fragments, has been found to persist in human tissues for 5 years. It produces a foreign-body reaction with only moderate fibrosis which is limited to the sponge itself. These observations conflict with previous reports of findings in experimental animals and man (Schofield, 1955; Wells, 1959). These suggest a much greater fibrotic response than we have found. Wells (1959) referred to 'marble busts' when Ivalon sponge was implanted in the mammary region.

There is no evidence of sarcoma formation from the Ivalon-sponge implant in these patients, despite observation of up to 12 years.

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A PROSPECTIVE STUDY OF THE IMMEDIATE AND LONG-TERM RESULTS OF POLYA GASTRECTOMY FOR DUODENAL ULCER

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SUMMARY

The results of a prospective study of Polya-type gastrectomy in 800 cases of duodenal ulcer are recorded.

The series is an entirely personal one in which case selection and operative technique were standardized, though in the assessment of the results the opinions of many observers have been collated.

The results in the early years are recorded and the effects of revision surgery noted.

Special attention has been paid to the nutritional state after operation and to the long-term metabolic consequences 10–20 years after gastrectomy.

The immediate and long-term results of gastrectomy are compared and contrasted with those obtained by vagotomy and drainage.

THE surgical treatment of duodenal ulcer has occupied the attention of surgeons for over half a century. In spite of the enormous number of clinical and laboratory investigations no operation has emerged as the ideal procedure for all cases and it seems likely that none exists.

The undoubted success of simple gastro-enterostomy in the Moynihan era became clouded by the high incidence of stomal ulceration and the operation fell into disrepute. The problem of recurrent ulceration was vastly diminished by the introduction of the more formidable procedure of partial gastrectomy, and for many years this operation held pride of place in the surgical treatment of duodenal ulcer. The known post-prandial symptoms occurring in a small proportion of cases after gastrectomy were regarded as a small price to pay for the relief of pain and the removal of the hazards of haemorrhage and perforation. Disturbing reports of loss of weight, the high incidence of anaemia and of pulmonary tuberculosis, and the more remote sequelae of metabolic bone disease after gastrectomy have, however, directed attention to the more conservative measures of vagotomy and drainage.

Now that vagotomy has been in vogue for 20 years and its immediate and long-term consequences are more fully known it would seem appropriate at this time to make a further report on a prospective study of partial gastrectomy which was started in 1950 and which has continued to the present time.

The first report of this prospective study of the results obtained in 1000 cases of gastrectomy for peptic ulcer (McKeown, 1962) dealt mainly with the results obtained in the early years after operation. The present report is more comprehensive in that it not only records the immediate results but also makes a special study of the long-term metabolic consequences of gastrectomy 10–20 years after operation for duodenal ulcer.

This series is a large and entirely personal one in which all the cases have been examined, investigated, assessed, and operated on by one surgeon, and differs from that of Goligher and others (Goligher, Pulvertaft, and Watkinson, 1964; Goligher, Pulvertaft, de Dombal, and others, 1968) in which ten surgeons in different hospitals participated in the Leeds/York trial, and from that of Cox (1968) in which the recorded results were those of the Surgical Staff of the Western General Hospital, Glasgow.

THE PROSPECTIVE STUDY

This prospective study was started in 1950 in the Northallerton and Darlington area which is situated midway between the teaching centres at Leeds and Newcastle. In this area population changes in both the rural and urban districts were much less frequent than those in the big cities and in consequence follow-up was much easier.

Table I.—Indications for Surgery for Duodenal Ulcer

Absolute	*Relative*
Pyloric obstruction	A 5-year period of ulcer dyspepsia
Dangerous bleeding	Perforation
	Haematemesis or melaena

From the outset the intent was to make an objective assessment of the results of partial gastrectomy in peptic ulcer and therefore certain clinical features had to be standardized. It was essential that the criteria for selection of cases for surgery should be clearly defined and adhered to, that the operative technique be unvaried, and that the pre- and post-operative management should be the same in all cases. The follow-up was frequent and continuous, and though the series was an entirely personal one, in reviewing and grading the results the opinions of the patient, his relatives, and his general practitioner have all been collated, as well as the views of the various surgical registrars who have served in the units.

Criteria of Case Selection.—Though such factors as age, sex, social class, and individual personality should be taken into consideration in case selection for surgery, the system adopted in this trial was based purely on clinical features and the level of gastric acidity did not influence the decision to operate or modify the extent of gastric resection. Indications for operation were considered to be either absolute or relative as shown in *Table I.*

Absolute indications for gastrectomy were organic pyloric obstruction or dangerous haemorrhage. The former indication called for operation when the fluid and electrolytic balance had been restored, while dangerous bleeding was treated by emergency gastrectomy. Dangerous bleeding was considered to be present in the following circumstances:—

1. Catastrophic bleeding when it was difficult to replace blood-loss and maintain an adequate blood-pressure.

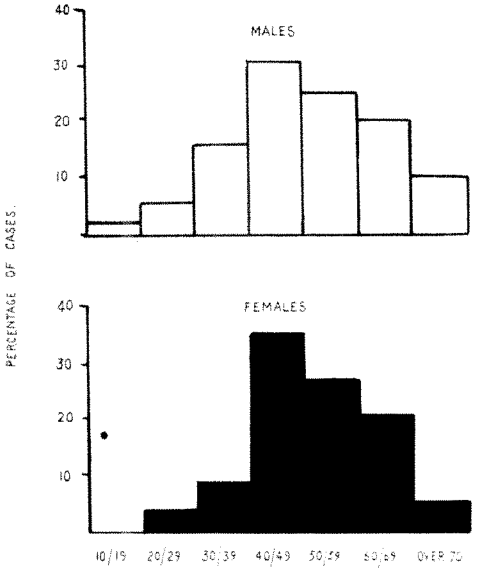

FIG. 1.—The age distribution of 648 men and 152 women in whom Polya gastrectomy for duodenal ulcer was performed.

2. Bleeding of lesser severity which continued or recurred while the patient was still in hospital.

3. Severe bleeding in patients of over 50 years who had long-standing proved duodenal ulcer.

Relative indications for surgery were based on three features: a 5-year history of dyspepsia, perforation, or bleeding. If any two or more of these clinical features were present the patient was considered suitable for operation. Also a patient who had sustained two perforations or two episodes of bleeding was considered suitable for surgery as well as those patients who had had persistent or recurrent dyspepsia for 10 years.

Because of the strict criteria of case selection most of the cases who were submitted to operation were of middle age with a peak incidence for both sexes in the decade 40–49, as shown in *Fig.* 1. In spite of the bad reputation associated with the operation in young subjects partial gastrectomy was carried out in these cases provided that the clinical criteria were present. Similarly, no cases were refused operation on the grounds of advanced age if the criteria were fulfilled, provided that the patients were fit for anaesthesia and not likely to die in the near future from concomitant disease.

Type of Operation.—At the commencement of this study it was intended to use with equal frequency either the Polya-type operation with a valved or full-length stoma or the Billroth-I operation. Experience soon showed that the high recurrence rate after the Billroth-I operation of 15·7 per cent (8 out of 5 cases) precluded its further use, while the full length stoma resulted in a higher incidence of post prandial symptoms and it too was abandoned.

The results described in this paper are thos obtained when a modified Polya operation was used This standardized operation removed the distal hal

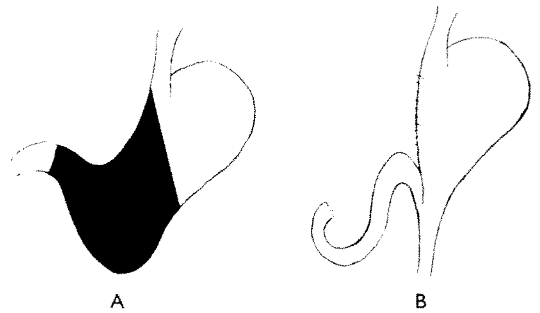

FIG. 2.—The operative procedure for duodenal ulcer. A, The complete excision of the lesser curvature, showing the amount of stomach removed at the partial gastrectomy. B, The reformation of the lesser curve and the valved gastrojejunal anastomosis.

of the stomach together with the entire lesser curvature up to the gastro-oesophageal junction. The lin of section on the greater curvature stopped at th level of the first vasa brevia so that in all abou two-thirds of the gastric tissue were removed, a shown in *Fig.* 2. The lesser curvature was suture to form a long tapering stomach remnant which wa anastomosed to the jejunum at a distance of, o average, 13 cm. from the duodenojejunal flexure. I obese patients omentum was resected to enable th afferent loop to be kept short and to prevent the pul of a heavy fat-laden omentum on the gastrojejuna anastomosis. In all the cases the pyloric end of th stomach was removed and in no case was the Bancrof or Plenk manœuvre employed. All cases had a drai inserted down to the point of duodenal closure t minimize the effects of unpredictable duodena stump leakage.

Method of Follow-up.—Each patient was issue with a *pro forma* on which all the relative clinica details were recorded with special reference to th operative findings and the postoperative progress The frequent review examinations during the firs postoperative year were regarded as a period o supervision. No attempt was made to grade th results until the end of this period as it was foun that the transient discomforts of the first few week may relegate some patients to a low grading, while i others initial success may become clouded by th onset of symptoms several months after operation After the initial grading patients were reviewe annually and were up-graded or down-graded wit the remission or development of post-gastrectom symptoms over a period of up to 20 years, so tha the elapse of time played a part in the grading o results.

Grading of Results.—Patients were placed in one of three categories:—

Grade I: Symptom Free.—In this grade the patient were able to eat, drink, and smoke without restraint and had been able to return to the heaviest duties on a farm or in a factory. This group corresponds to the 'excellent' grading of the American Society of Gastro-enterologists and to Visick's (1948a, b) grade 1.

Grade II: Satisfactory.—Patients in this category expressed complete satisfaction with the results of operation, but on inquiry would reluctantly admit to occasional mild dyspepsia. This grading corresponds to the American Society of Gastro-enterologists' grading 'good' and to Visick's grade 2.

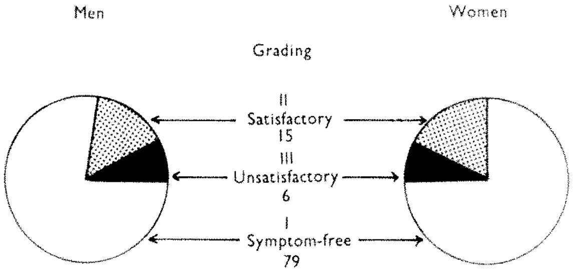

FIG. 3.—The results of gastrectomy in 800 cases of duodenal ulcer. The unsatisfactory group represents 6 per cent of the entire series. In the symptom-free grading men show marginally better results than women. (All the figures are percentages.)

Grade III: Unsatisfactory.—All the patients who could not be placed in grades I or II were included in this category, even though some patients felt that they had benefited and that the operation was well worth while (Visick's grade 3S). Also included in this category were those patients who developed recurrent ulcer, persistent post-gastrectomy symptoms, or severe nutritional disturbance (Visick's grade 3U and grade 4). Of these latter outright failures, a proportion have been improved by further operative procedures and have subsequently been upgraded.

MATERIAL AND DATA

The series consisted of 800 cases of duodenal ulcer who were operated on in the period 1950 to 1960 and who had not previously had any gastric operation other than the suture of a perforated ulcer. Sixty other cases (51 men and 9 women) who had associated gastric ulcers were excluded from this review. Of the 800 cases, 648 were men and 152 women.

RESULTS OF GASTRECTOMY FOR DUODENAL ULCER

Using the system of grading as outlined above, it was found that 79 per cent of all the patients could be included in grade I. Male patients fared better than females in that 80 per cent of the men as against 76 per cent of the women could be placed in grade I, as shown in *Fig.* 3.

Fifteen per cent of cases (14 per cent of the men and 18 per cent of the women) fell into grade II. The incidence of patients in the unsatisfactory grade III was the same in both sexes (6 per cent) but the cause of failure was different. In the male patients recurrent ulcer and a higher operative mortality accounted for over half of the subjects in this category, while in the women post-prandial symptoms were the cause of failure in the great majority of cases, as shown in *Fig.* 4.

THE SEQUELAE OF POLYA GASTRECTOMY

The sequelae of gastrectomy may arise from the technical problems and difficulties of the operative procedure, from anatomical alterations involved in gastrojejunal anastomosis, or as a result of alterations in the physiology of the digestive tract. As such, the consequences of gastrectomy may be immediate, deferred, or long term, and have been considered under the following headings:—

1. Mortality.
2. Recurrent ulcer.
3. Post-gastrectomy syndromes.
    - *a.* Dumping syndrome.
    - *b.* Bilious vomiting ('afferent-loop syndrome').
    - *c.* Mixed post-gastrectomy syndromes.
4. Oesophageal stenosis.
5. Malabsorption syndromes.
    - *a.* Weight changes.
    - *b.* Post-gastrectomy anaemia.
    - *c.* Post-gastrectomy bone disease.
    - *d.* Plasma-protein levels.
6. Pulmonary tuberculosis.

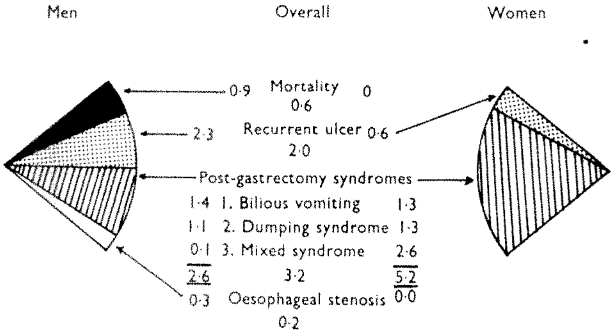

FIG. 4.—The overall failures of gastrectomy are shown together with a comparison of the causes of failure in men and women. Recurrence and post-gastrectomy syndromes are the causes of failure of gastrectomy in men, while in women post-gastrectomy syndromes account for almost all the unsatisfactory results, and recurrent ulcer is rare. (All the figures are percentages.)

The results of the analysis of the failures in the first 5 years after gastrectomy are depicted in *Fig.* 4.

1. **Mortality.**—The estimation of mortality was simple and exact. All the cases dying in hospital after operation were included, even though the cause of death was not directly associated with the ulcer or the operation performed for its cure. An analysis of the causes of death is presented in *Table II.*

Of a total of 778 cases undergoing elective gastrectomy, 6 patients died, giving a mortality figure of 0·7 per cent. In considering this figure it should be noted that there was no discrimination against the poor-risk patient. In the early part of the series a high proportion of the patients were elderly, in a very poor general condition, and suffering from long-standing penetrating ulcers. When this hard core of poor-risk patients had been dealt with the death-rate fell, and in 400 consecutive patients there was not a single operative death.

In view of many considerations, both clinical and administrative, only patients with dangerous haemorrhage were subjected to emergency gastrectomy.

Of 22 cases operated on as emergencies for dangerous bleeding, 6 patients died. This mortality figure of 22·7 per cent emphasized the increased hazards of non-elective operation, especially in the old and the unfit.

Of the fatalities, all 12 occurred in male patients who with 1 exception were in middle life or old age. Two patients died from persistent oozing from the gastric remnant and were considered to be suffering from afibrinogenaemia (*Cases* 2 and 12[*]), while a third died of a sudden massive haemorrhage from an oesophageal varix ulcerated by the indwelling nasogastric tube (*Case* 1). One obese bronchitic man of 57 (*Case* 8) died from peritonitis due to duodenal stump leakage 5 days after operation. *Case* 3 died of hepatic failure 13 days after operation, while the remaining cases died of some cardiac or pulmonary factor not directly related to the operation, as shown in *Table II*.

Table II.—THE CLINICAL DETAILS OF 12 CASES WHO DIED AFTER GASTRECTOMY

CASE	AGE AND SEX		CAUSE OF DEATH	TIME OF DEATH AFTER OPERATION (day)	COMMENTS
1. R. E. B.	50	M.	Rupture of oesophageal varix	3	Ulceration of oesophagus due to nasogastric tube
2. E. B. W.	63	M.	Persistent bleeding	22	Afibrinogenaemia
3. D. M. D.	71	M.	Liver failure	13	—
4. W. H. D.	56	M.	Coronary thrombosis	5	—
5. T. J. D.	61	M.	Pulmonary embolus	10	Emergency gastrectomy. Haemorrhage
6. J. F.	72	M.	Renal failure	9	Emergency gastrectomy. Prolonged hypotension. P vious ischaemic heart disease
7. M. McG.	72	M.	Bronchopneumonia and chronic pyelonephritis	19	Emergency gastrectomy. Long history of pyelonephri
8. W. C.	57	M.	Peritonitis due to duodenal stump leak	5	Extreme obesity and poor chest condition
9. M. L.	43	M.	Pulmonary embolus	21	Wound sepsis
10. B. C.	22	M.	Pulmonary embolus	6	Emergency gastrectomy. Bleeding
11. C. G.	50	M.	Irreversible shock	Immediately	Emergency gastrectomy. Very severe haemorrhage fr gastroduodenal artery
12. A. N. O.	80	M.	Persistent bleeding	20	Emergency gastrectomy. Transfused with 34 bottles blood over 20 days

2. Recurrent Ulcer.—An analysis of the cases of stomal ulcer is presented in *Table III*. Sixteen out of 800 cases developed stomal ulcer, giving an overall incidence of 2 per cent. Of the 648 male patients, 15 (2·3 per cent) developed stomal ulcer, but of 152 females, only 1 case (*Case* 16) had recurrent ulceration (0·6 per cent).

Thirteen of these cases presented with recurrent dyspepsia, of which 5 also suffered from haemorrhage and 1 from perforation. Of the 2 cases who denied any history whatever of postoperative dyspepsia, 1 case (*Case* 7) had recurrent haemorrhage while another case (*Case* 16) had a perforation. A feature of note was the tendency for the early onset of stomal ulcer. In 2 patients symptoms occurred within a month of operation, while in several other cas symptoms developed within 15 months. In 3 cas stomal ulcer occurred after 2 years, and in only instances (*Cases* 7 and 10) was the onset delay for 5 and 7 years respectively. No age-group w immune from recurrent ulcer, but when the numb of cases operated on in each decade is taken in consideration, as shown in *Fig.* 1, it was found th young patients were more liable to recurrent ulc In those operated on between the ages of 20 and the incidence of stomal ulceration was 4·8 per cer but in the 30–39 age-group the incidence dropp to 2·2 per cent with similar falls in succeedi decades.

Of 7 cases of stomal ulcer submitted to simp re-gastrectomy, 3 cases had further ulceration whi in 2 cases was subsequently successfully treated revision gastrectomy combined with vagotom The remaining case (*Case* 4), who had moved out the area, subsequently developed a gastrojejunocol fistula which has been successfully treated by excisi of the fistula combined with vagotomy. Because of t relative failure of re-gastrectomy all subseque cases of stomal ulcer had revision gastrectomy co bined with truncal vagotomy. Of the 8 cases treated, none had further ulceration but 2 cas (*Cases* 9 and 15) have suffered from persiste diarrhoea. In none of these cases of recurrent ulc was a Zollinger-Ellison tumour discovered thou this was specifically looked for. Of the 16 cas submitted to further surgery, 4 have been upgrad to grade I, 9 are in grade II, 2 have remained grade III, while 1 other patient was found to suffering from cirrhosis of the liver and was in co sequence not put in any grade.

Post-gastrectomy Bleeding not due to Stomal Ulc —In addition to the 16 cases of proved ston ulcer there were 7 other patients who we

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[*] Case numbers in this paper refer to cases mentioned in specific tables and are not consecutive throughout the whole series.

Table III.—THE CLINICAL DETAILS OF 16 CASES WHO DEVELOPED STOMAL ULCER AFTER POLYA GASTRECTOMY FOR DUODENAL ULCER

CASE	AGE AND SEX	OCCUPATION	TIME OF ONSET OF RECURRENCE	SYMPTOMS	TREATMENT	RESULT	COMMENT
1. G. D.	46 M.	Clerk	2 yr.	Dyspepsia and perforation	Suture	Symptom-free. Grade I	—
2. J. B.	39 M.	Railwayman	2 yr.	Dyspepsia and melaena	Re-gastrectomy	Satisfactory. Grade II	—
3. W. H.	51 M.	Builder	1 mth.	Dyspepsia and haematemesis	Re-gastrectomy	Satisfactory. Grade II	Stomal leak ?
4. A. R.	37 M.	Co-director	1 yr.	Dyspepsia	Re-gastrectomy	Unsatisfactory. Grade III	Further ulceration ?
5. H. O.	45 M.	Joiner	3 mth.	Dyspepsia	Re-gastrectomy	Symptom-free. Grade I	—
6. H. S.	61 M.	Storeman	6 mth.	Melaena	Re-gastrectomy	Vague dyspepsia	Cirrhosis of liver
7. M. J. L.	27 M.	Hotelier	5 yr.	Recurrent haematemesis	1. Re-gastrectomy 2. Re-gastrectomy and vagotomy	Stomal ulcer Satisfactory. Grade II	Hypertension
8. M. H.	50 M.	Publican	1 mth.	Dyspepsia and melaena	1. Thoraco-abdominal re-gastrectomy 2. Re-gastrectomy and vagotomy	Stomal ulcer Satisfactory. Grade II	Very obese Slight oesophageal reflux
9. A. P. W.	38 M.	Consultant	2 yr.	Pain, melaena, and haematemesis	Re-gastrectomy and vagotomy	Satisfactory. Grade II	Cholecystectomy for gall-stones and diarrhoea
10. J. O.	64 M.	Manager	7 yr.	Dyspepsia	Re-gastrectomy and vagotomy	Symptom-free. Grade I	—
11. J. McK.	29 M.	Joiner	3 yr.	Dyspepsia	Re-gastrectomy and vagotomy	Satisfactory. Grade II	Cholecystitis. Typhoid carrier
12. A. B.	32 M.	Driver	6 mth.	Dyspepsia	Re-gastrectomy and vagotomy	Symptom-free. Grade I	—
13. R. B.	48 M.	Farmer	14 mth.	Dyspepsia	Re-gastrectomy and vagotomy	Satisfactory. Grade II	—
14. L. A.	41 M.	Publican	1 yr.	Dyspepsia and melaena	Re-gastrectomy and vagotomy	Satisfactory. Grade II	—
15. G. A. E.	53 M.	Driver	9 mth.	Dyspepsia	Re-gastrectomy and vagotomy	Unsatisfactory. Grade III	Diarrhoea
16. V. W.	58 F.	Driving instructor	15 mth.	Perforation	1. Suture 2. Re-gastrectomy and vagotomy	Satisfactory. Grade II	Arteriosclerosis

Table IV.—THE CLINICAL DETAILS OF 7 CASES OF POST-GASTRECTOMY BLEEDING IN WHICH STOMAL ULCERATION COULD NOT BE CONFIRMED ON RADIOLOGICAL OR GASTROSCOPIC EXAMINATION

CASE	AGE AND SEX		OCCUPATION	SITE OF PREVIOUS ULCER	TYPE OF OPERATION	DATE	TIME OF ONSET (yr.)	PRESENTING SYMPTOMS	RADIOGRAPHY	SUSPECTED CAUSE	RESULT
1. B. B.	45	M.	Asphalter	Duodenum	Polya and valve	4 June, 1954	3	Melaena	No stomal ulcer	Aspirin	Grade II
2. H. C.	70	M.	Doctor	Duodenum	Polya and valve	23 Nov., 1953	3	Slight haematemesis	No stomal ulcer	Not known	Grade II
3. P. R. C.	53	M.	Engineer	Duodenum	Polya and valve (emergency)	20 Oct., 1957	4	Melaena	No stomal ulcer	Aspirin and whisky	Grade I
4. F. E. F.	46	M.	Haulage contractor	Duodenum	Polya and valve	18 Nov., 1956	6	Melaena	No stomal ulcer	Jejunitis	Grade II
5. G. G.	44	M.	Newspaper despatcher	Duodenum	Polya and valve	15 Dec., 1954	3	Melaena	No stomal ulcer	Aspirin	Grade I
6. G. J.	46	M.	Railway worker	Duodenum	Polya and valve	27 Aug., 1954	3	Acute abdominal pain	No stomal ulcer	Not known	Grade II
7. W. S. Mc.	52	M.	Vicar	Duodenum	Polya and valve	22 May, 1954	2	Melaena	No stomal ulcer	Haemorrhagic state	Grade II

suspected of suffering from this condition. Five o these presented with histories of melaena, 1 witl haematemesis, and 1 with bleeding and abdomina pain. In none of these cases could stomal ulceratio be demonstrated after most careful radiological an gastroscopic examinations, while the secretion test in these subjects showed low acidity not consisten with recurrent ulceration.

Details of this group of cases are shown in *Table IV* In 3 patients (*Cases* 1, 3, and 5) bleeding was attributed to the taking of aspirin in an acute febril illness. *Case* 4, a heavy drinker, suffered fron gastritis and jejunitis, but in 2 other cases the caus of bleeding was not known. One case (*Case* 7 showed a marked tendency to bleed from mino trauma, and the melaena from which he suffere was thought to be associated with a haemorrhagi state.

It might be argued that in spite of persistentl negative radiological and gastroscopic examination these 7 patients did in fact have a stomal ulce Were this contention to be accepted, there woul then be 23 cases of proved or suspected stoma ulcer out of a total of 800 cases, an incidence of 2· per cent.

Recurrent Ulcer in the Gastric Remnant.—On patient, a woman of 64 years, had a Polya gastrectom for duodenal ulcer and made a good recovery. On year later she was admitted in emergency wit severe haematemesis and diffuse peritonitis. She wa unfit for laparotomy and died a few hours afte admission to hospital. At the post-mortem examination she was found to have a large gastric ulce measuring 3·8 × 2·5 cm., which was situated in th gastric remnant well away from the stoma. Th gastrojejunal anastomosis was entirely normal bu bleeding had taken place from the gastric ulcer, whic had also perforated.

3. Post-gastrectomy Syndromes.—A sur prisingly high proportion of cases could eat an drink without restraint, even in the early weeks c convalescence. On the other hand, there were thos who experienced a wide range of post-cibal symptom of which a sensation of distension after a full mea was perhaps the most common complaint. No specia significance was attached to these discomforts in th early weeks or months after operation, but attentio was focused on those whose symptoms had persiste or had developed for the first time a year afte operation.

A general survey of the series shows that of th 800 cases, 25 patients (3·2 per cent) had persisten post-gastrectomy symptoms. The incidence i women was twice as high as that in men, and of 15 female patients, 8 (5·2 per cent) were affected, whil of 648 males, only 17 (2·6 per cent) were similarl troubled. These results are outlined in *Fig.* 4.

Persistent post-gastrectomy symptoms thoug variable and not always precise and clear cut wer considered under three headings according to th predominant feature:—

a. Dumping syndrome.
b. Bilious vomiting ('afferent-loop syndrome').
c. Mixed post-gastrectomy syndromes.

In this connexion it should be noted that thos patients who experienced persistent fullness afte a very heavy meal and who may be considered to b suffering from the 'small stomach syndrome' were included in grade II. If, however, these symptoms were severe or associated with other post-cibal syndromes, such cases were categorized as failures of gastrectomy and placed in grade III.

was greatly improved by narrowing of the gastro-jejunostomy stoma.

Four cases were managed conservatively by modification of their diet and the avoidance of drinking sweetened fluids especially at meal times. Within these limitations they were able to continue in their usual employment but were, however, considered only moderately successful and were included in grade II, partly because of the necessity of imposed dietetic restriction but also because of associated disease, as shown in *Table V*. Of these 4 cases, *Case* 1 subsequently had a cholecystectomy for gall-stones and thereafter a cystectomy for carcinoma of the bladder. *Case* 2 developed portal hypertension, while *Case* 3 suffered recurrent intestinal obstruction due to adhesions. *Case* 6 was difficult to assess as he suffered from pain due to coronary disease.

Of 4 other cases in which the Polya gastrectomy was converted to one of Billroth-I type, 2 cases (*Cases* 7 and 8) were completely cured and upgraded to grade I, while *Case* 5, though much improved, suffered from loss of weight and anaemia. The remaining patient (*Case* 9) was an interesting failure. This 49-year-old woman suffered from severe vasomotor symptoms associated with diarrhoea which were much improved by the conversion operation. Later, however, she developed ulceration at the gastroduodenal anastomosis. When submitted to re-gastrectomy and a classic Billroth-II operation was carried out the dumping syndrome recurred. Vagotomy combined with a Billroth-I operation was advised, but the patient understandably enough was

Table V.—THE CLINICAL DETAILS OF 9 CASES SUFFERING FROM THE PERSISTENT DUMPING SYNDROME

CASE	AGE AND SEX	TYPE OF OPERATION	TIME OF ONSET	MOST SEVERE SYMPTOMS	TREATMENT	RESULT	COMMENT
. A. W.	47 M.	Polya	6 wk.	Vasomotor symptoms	Conservative	Cleared up in 1 yr. Grade II	Subsequent cholecystectomy for gall-stones and total cystectomy for carcinoma of bladder
. T. W. J.	45 M.	Polya	2 mth.	Sweating, palpitations, lacrimation, and severe hunger	Conservative	Cleared up after 1 yr. Grade II	Also had portal hypertension
. O. H.	27 M.	Polya	2 mth.	Vasomotor symptoms	Conservative	Cleared up after 15 mth. Grade II	Had intestinal obstruction due to adhesion on eleventh postoperative day. Lost 1½ st. but then slow increase in weight
. T. S. A.	26 M.	Polya	3 mth.	Sickness, desire to defaecate 10 min. after food, and faintness 2 hr. after meals	Narrowing of stoma	Improved after operation Grade I	Hypoglycaemia 2 hr. after food
. A. L.	40 F.	Polya	1 mth.	Vasomotor symptoms	Conversion to Billroth-I	Much improved Grade II	Anaemia and loss of weight
. J. F.	45 M.	Polya and valve	4 wk.	Sweating, palpitations, and weakness	Conservative	Cleared up in 1 yr. Grade II	Has now developed coronary and arterial disease
. W. B.	64 M.	Polya and valve	4 wk.	Listlessness and headache	Conversion to Billroth-I	Cured Grade I	Gained 1½ st. after conversion operation
. H. A. S.	49 M.	Polya and valve	4 wk.	Sweating, palpitations, and weakness	Conversion to Billroth-I	Cured Grade I	Nervous factors
. R. S.	49 F.	Polya and valve	1–2 mth.	Fullness, sickness, and palpitations. Diarrhoea	Conversion to Billroth-I Conversion of Billroth-I to Billroth-II	After initial improvement developed stomal ulcer with stenosis Dumping became severe again after the second conversion operation	Unwilling to undergo further surgery 'Gastric cripple'

a. Dumping Syndrome.—In this group were included those patients whose post-prandial symptoms were predominantly vasomotor in type and who soon after a meal experienced a variety of symptoms such as flushing, sweating, fainting, palpitations, lethargy, giddiness, or muscular weakness. An epitome of the clinical details of such patients is shown in *Table V*.

Of the 800 cases who were submitted to a modified Polya gastrectomy, 9 developed the dumping syndrome which persisted, an overall incidence of 1·1 per cent. Two women (1·3 per cent) and 7 men (1·09 per cent) suffered from this complaint (*Fig.* 4).

Only on rare occasions did the symptoms develop while the patient was still in hospital and in the majority of cases dumping was first experienced 4–6 weeks after operation, though in 1 case (*Case* 4) the onset of symptoms was delayed for 3 months. Some of the classic vasomotor symptoms were present in all the cases, but 1 case (*Case* 2) had severe lacrimation and hunger pains immediately after food, while in *Case* 4 symptoms of 'early' dumping were also associated with sweating and faintness 2 hours after food which were attributed to hypoglycaemia. This patient, who was considered to be suffering from both 'early' and 'late' dumping, unwilling to undergo further surgery and has been considered as a total failure and regarded as a 'gastric cripple'.

b. Bilious Vomiting ('Afferent-loop Syndrome').—Nine men and 2 women complained of bilious vomiting, an incidence in both sexes of 1·4 per cent.

Table VI.—THE CLINICAL DETAILS OF 11 CASES SUFFERING FROM BILIOUS VOMITING

CASE	AGE AND SEX	TYPE OF OPERATION	TIME OF ONSET	SYMPTOMS	TREATMENT	RESULT	COMMENT
1. M. W.	36 M.	Polya	3 yr.	Vomits food and bile	Conservative	Improved Grade II	—
2. J. M.	54 M.	Polya and valve	3 mth.	Biliary regurgitation before breakfast	Conservative	Grade III	—
3. L. F.	46 M.	Polya and valve	6 wk.	Regurgitation when lying down	Conversion to Billroth-I	Grade I	Satisfactory
4. C. B.	53 F.	Polya and valve	3 wk.	Vomits bile	Conservative	Awaiting conversion operation	Hysterical attack
5. H. P.	55 M.	Polya and valve	3 wk.	Vomiting of food and bile	Laparotomy for obstruction	Cured Grade I	Had myositis oss ficans extendir into stoma
6. R. J. P.	58 M.	Polya and valve	4 wk.	Vomiting bile 1 hr. after food	Division of adhesions	Poor Grade III	Had burst abd men. Folic-ac deficiency
7. M. H.	59 M.	Polya and valve	4 wk.	Biliary regurgitation before breakfast. Pain in left hypochondrium	Suspension of afferent loop Conversion to Billroth-I	No improvement Cured Grade II	Weight-loss Marked weight-gain
8. H. B.	58 M.	Polya and valve	8 yr.	Vomits bile, occasionally bile and food	Division of adhesions of afferent and efferent loops	Improved Grade II	Conversion op ation being cc sidered
9. E. H.	38 M.	Polya and valve	15 mth.	Bilious vomiting	Conversion to Billroth-I	Cured Grade I	Increase in wei
10. D. P.	34 M.	Polya and valve	2 mth.	Vomits bile ¾ hr. after food	Conversion to Billroth-I	Cured Grade I	Increase in wei
11. E. H.	44 F.	Polya and valve	2 mth.	Vomits bile ½ hr. after food	Conversion to Billroth-I Conversion to Billroth-II	Narrowing of stoma and recurrent ulcer Poor	Loss of weight Anaemia and di rhoea; chronic psychotic (depressive); 'gast cripple'

The pattern of bilious vomiting varied from case to case, as outlined in *Table VI*. In 2 patients (*Cases* 1 and 7) vomiting of clear bile occurred on rising first thing in the morning, while in *Case* 3 biliary regurgitation took place when the patient lay down. Three patients noted the vomiting of bile and food ½–1 hour after a meal, while in the remainder of cases vomiting of bile and food occurred at irregular intervals. A characteristic feature of some cases was the ability to eat a full meal immediately after being sick and to experience no further symptoms. An epitome of the clinical details is presented in *Table VI*.

The onset of biliary vomiting occurred 4–12 weeks after operation in 8 patients, while in 3 others (*Cases* 1, 8, and 9) symptoms did not develop for from 1 to 8 years.

In 3 cases biliary vomiting was due to obstruction of the afferent loop (*Cases* 5, 6, and 8). One of these patients (*Case* 5) had a most unusual condition of calcification in the abdominal wound, which extended down to the site of the gastrectomy stoma and strikingly resembled myositis ossificans. In *Case* 6 the cause of obstruction was adhesions contribute to by the fact that this patient had a wound dehiscenc after operation.

Three of the patients were treated conservativel but of these, 1 case, a hysterical woman of 35 year who formerly refused operation, now feels that th symptoms are severe enough to warrant furth surgical treatment. Suspension of a rather depende afferent loop failed to cure *Case* 7, but with co version of the Polya operation to one of Billroth type the symptoms were cured. Of 4 other cas who had the conversion operation, 3 (*Cases* 3, 9, an 10) were so improved that they were promoted grade I, but *Case* 11 was an interesting failu This 44-year-old woman developed bilious vomiti 8 weeks after operation of such severity that a co version operation was carried out soon after t original procedure. The patient then develope stomal ulceration with narrowing of the gastr duodenal anastomosis. A further operation w carried out and a Billroth-II type of anastomos was performed. This patient then developed pe sistent diarrhoea and became anaemic. She was known depressive psychotic who had failed respond to drug or electroconvulsive therapy. It w considered in retrospect that insufficient attenti had been given to the psychiatric state befo operation and she is now regarded as a 'gast cripple'.

Review of the treatment given to these patients, as outlined in *Table VI*, shows that half of the group has been upgraded as the result of revision surgery.

c. Mixed Post-gastrectomy Syndromes.—Five patients suffered from post-prandial discomforts in which the symptoms formed a complex of dumping, bilious vomiting, and the 'small-stomach syndrome', each feature contributing equally to the patient's discomfort. The clinical details of these 5 cases, which represent 0·6 per cent of the total series, are outlined in *Table VII*. Four of these patients suffering from mixed post-gastrectomy syndromes were middle-aged women, but 1 case was a young man of 29 years.

Table VII.—THE CLINICAL DETAILS OF 5 CASES WHO DEVELOPED MIXED POST-GASTRECTOMY SYNDROMES

CASE	AGE AND SEX	TYPE OF OPERATION	PRESENTING SYMPTOMS	TIME OF ONSET	WEIGHT CHANGES	TREATMENT	RESULT	COMMENT
1. L. H.	44 F.	Polya	Fullness and flushing after food Eructations of bile	2 wk. 2 mth.	Gain of 7 lb.	Conversion to Billroth-I	Marked improvement Grade III	Post-gastrectomy anaemia
2. E. M.	49 F.	Polya with valve	Pain and fullness after food; bilious vomiting	2 mth.	Gain of 1 st. 7 lb.	Conversion to Billroth-I	Some improvement Grade II	Emotional factors
3. R. D.	57 F.	Polya with valve	Weakness and giddiness Bilious vomiting twice a week	2 mth. 6 mth.	Loss of 3 st.	Conservative (did not want further operation as she was pain-free)	Grade III	—
4. C. D. H.	29 M.	Polya	Faintness and weariness Bilious vomiting	2 mth. 9 mth.	Loss of 2 st.	Narrowing of stoma Conversion to Billroth-I	Bile vomiting continued Much improved Grade II	Gained 2 st.
5. R. G.	43 F.	Polya with valve	Faintness after food Dyspepsia and bilious vomiting	3 mth. 4 yr.	Gain	Division of adhesions Conversion to Billroth-I	No improvement Improved	Mucosal prolapse at stoma

In 4 cases the Polya gastrectomy was converted to a Billroth-I type, with considerable improvement of the symptoms in all the cases. One of the patients (*Case* 1) developed post-gastrectomy anaemia and therefore has subsequently been downgraded to grade III. Of these 4 cases, 2 had had earlier operations; 1 for narrowing of the gastrojejunostomy stoma (*Case* 4) and 1 for the division of adhesions (*Case* 5), but with no amelioration in symptoms in either case. Both were much improved by the conversion operation. *Case* 5 was of special interest in that mucosal prolapse at the gastrojejunal stoma was thought to be a factor in producing her post-gastrectomy symptoms.

As can be seen from *Table VII*, revision surgery only allowed 2 of the 5 patients to be upgraded from grade III to grade II.

It is interesting to note that 2 female patients who had the Polya operation converted to one of Billroth-I type developed ulceration at the site of the gastro-duodenal anastomosis, thus further emphasizing the unsuitability of Billroth-I operation for duodenal ulcer.

4. **Oesophageal Stenosis.**—Two cases developed dysphagia 3 weeks after operation which was found to be due to an inflammatory condition of the lower end of the oesophagus. A full description of these cases has already been recorded (McKeown, 1958). In each case there was a previous history of oesophageal reflux, and though in both patients operation had produced complete achlorhydria it was felt that they were suffering from reflux oesophagitis. The *p*H of the gastric contents ranged from 6·8 to 7·0, at which hydrogen-ion concentration peptic digestion is minimal and therefore unlikely to cause inflammatory changes in the lower oesophagus. On the other hand, after Polya gastrectomy alkaline duodenal and jejunal contents with high tryptic activity may enter the stomach remnant, and if oesophageal reflux occurred may cause 'tryptic oesophagitis' with resulting stenosis. On these premisses both patients had the Polya operation converted to one of Billroth-I type and in each case a cure was obtained. Since an indwelling nasogastric tube was employed after the second operation as well as after the first it was thought that the presence of the tube did not play any major part in the production of the oesophageal stenosis, as has been suggested by Bingham (1958).

Results of Revision Surgery.—Of a total of 43 patients placed in the unsatisfactory grade III because of recurrent ulcer, post-gastrectomy syndromes, or oesophageal stenosis, 35 patients had a further operation and 8 cases were treated conservatively either because of concomitant disease or because the patient felt that the symptoms were not severe enough to warrant further surgery. Of the 16 cases who suffered from recurrent ulcer, revision gastrectomy with or without vagotomy eradicated this complication in 14 cases but only 3 of them could be upgraded to grade I. Eleven patients were improved sufficiently to place them in grade II, while the remaining 2 cases stayed in grade III, one because of persistent dyspepsia due to suspected stomal ulceration and the other because of post-vagotomy diarrhoea (*Table III*).

Seventeen of the 25 patients with persistent post-gastrectomy syndromes were submitted to further surgical procedures as outlined in *Tables V*, *VI*, and *VII*. Of 11 male patients submitted to reoperation, 7 were upgraded to grade I, 3 grade II, while 1 case remained in grade III. Revision surgery in 6 female patients enabled 3 to be recategorized as grade I, 1 placed in grade II, while the remaining 2 subjects were dismal failures and were designated as 'gastric cripples'.

Both cases of oesophageal stenosis were cured by conversion of the Polya gastrectomy to one of Billroth-I type and were appropriately upgraded.

As the result of revision surgery in 35 of the 43 cases in the unsatisfactory grade III, the percentage of men in this category was reduced from 6 to 1·9 per cent and that of women from 6 to 3·9 per cent. The results of revision surgery are illustrated in *Fig.* 5.

5. **Malabsorption Syndromes.**—Though the primary objective of gastrectomy in the surgical treatment of duodenal ulcer is to diminish the secretion of acid-pepsin, the Polya operation has certain other inevitable consequences. The gastric reservoir is diminished, the regulating mechanism of the pyloric sphincter is abolished, and food is directed from the duodenal circuit and from the first 10–15 cm. of the jejunum. As the result of these factors the digestion of protein, fat, and carbohydrate may be significantly impaired with changes in the nutritional state, as reflected in possible weight-loss. In addition, alteration in the *p*H of the upper intestinal contents, as well as the consequent changes in the bacterial flora, may affect the absorption of iron, vitamin B_{12}, and calcium so that anaemia and metabolic bone disease may occur.

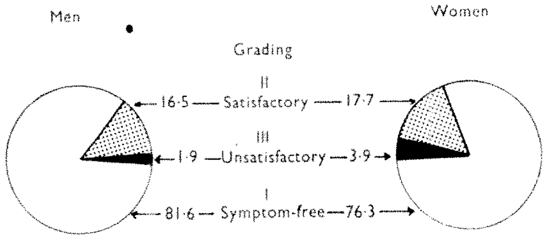

FIG. 5.—The grading of the results of revision surgery after Polya gastrectomy for duodenal ulcer.

a. Weight Changes.—Estimation of weight changes after gastrectomy are hampered by the fact that many patients are overweight at the time of operation as the result of prolonged medical treatment with a milk diet and a high-carbohydrate intake. On the other hand, those suffering from pyloric stenosis may be grossly underweight because of poor food intake and as the result of vomiting and dehydration before operation.

In spite of these known disadvantages, pre- and postoperative weight measurements have been taken and annual records have been made of the weight changes for 5 years after operation. Of 294 patients, 248 (78 per cent) had gained weight 1 year after operation and 44 (12 per cent) had lost weight, while in the remaining 10 per cent the weight remained unchanged. These findings are illustrated in *Fig.* 6.

On further analysis it was shown that the average preoperative weight of those who gained weight was 136 lb. One year after operation the average weight increase in these patients was 15 lb., followed by a further increase of 7 lb. in the second postoperative year. Of the 12 per cent who lost weight, the average preoperative weight was heavier at 151 lb., and the major loss was in the first postoperative year when on average the patients lost 17 lb. There was, however, a tendency for these latter patients t recover weight over the next 4 years. The results o these weight studies are shown in *Fig.* 7.

b. Post-gastrectomy Anaemia.—In the long-ter follow-up all the patients who had had a gastrectom 15–20 years previously had routine estimations of th haemoglobin level, as well as of the serum iron serum vitamin B_{12}, and serum folic acid. In all 116 cases were examined, of which 96 were men an 20 were women.

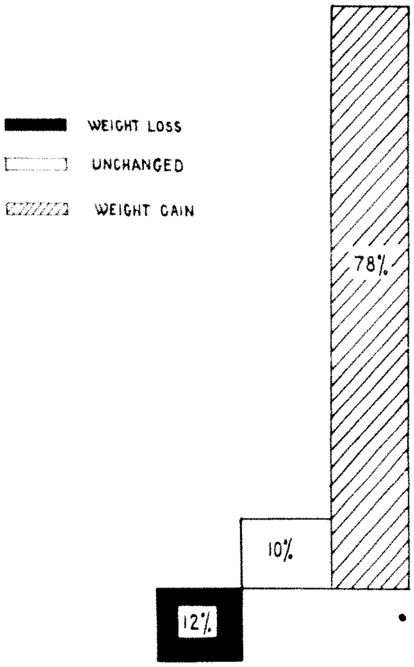

FIG. 6.—The percentage weight-gain or weight-loss in 294 patients after Polya gastrectomy for duodenal ulcer.

i. *Haemoglobin*: The range of haemoglobin level is illustrated in *Fig.* 8. Taking as normal a rang of 13·5–18 g. per 100 ml. in men and 11·6–16·5 g per 100 ml. in women, it is seen that though th haemoglobin levels in the majority of the patient fall within normal limits in both men and wome there is a substantial number of subjects in who the haemoglobin was much below the lower limit of normal.

ii. *Serum iron*: Routine screening of the levels o serum iron was carried out in all the cases even in th presence of a normal haemoglobin. The result o this investigation showed that the levels in th majority were equally distributed throughout th normal range of 60–160 μg. per ml. as illustrate in *Fig.* 9. A considerable number of patients, how ever, were below the lower limits of normal an were regarded as iron-deficient, while in som subjects the serum iron was above the norma range.

iii. *Serum vitamin B_{12}*: The levels of seru vitamin B_{12} are illustrated in *Fig.* 10. There was marked tendency for the levels to be in the lowe half of normal range with only a few of the reading being in the upper limits of normal. An appreciable number of men had readings below the lower limits of normal but no women had serum levels below 200 pg. per ml.

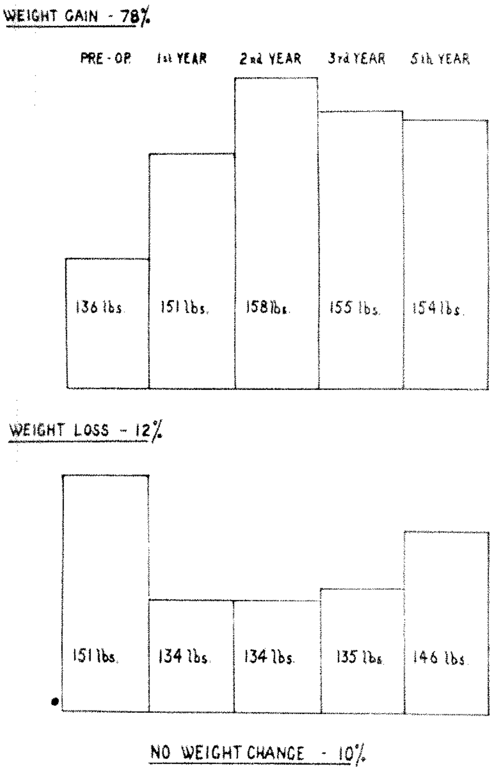

FIG. 7.—The weight changes in 294 patients during the 5-year period after Polya gastrectomy for duodenal ulcer.

iv. *Serum folic acid*: The distribution of the serum folic acid levels bore a very close resemblance to that found for vitamin B_{12}, in that the majority of patients were found to have readings at the lower limits of the normal range of 3–18 ng. per ml., as illustrated in *Fig.* 11. As in the case of vitamin B_{12} a few men but no women had levels below 3 ng. per ml.

Review of Cases found to be Anaemic.—Of the 116 cases under review, 31 cases were found to have haemoglobin levels below normal or to have reduced serum levels of iron, vitamin B_{12}, and folic acid. Investigations of these 31 patients showed that 9 had

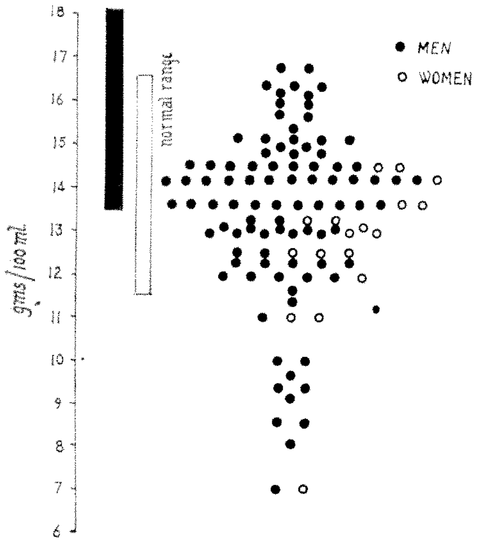

FIG. 8.—The levels of haemoglobin in 116 patients 15–20 years after Polya gastrectomy.

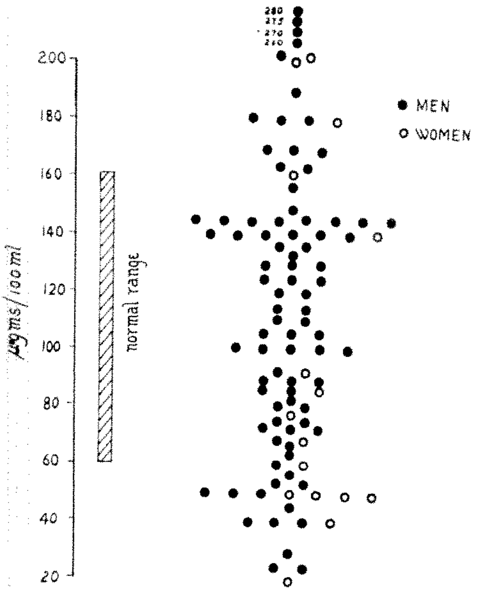

FIG. 9.—The levels of serum iron in 116 patients 15–20 years after Polya gastrectomy.

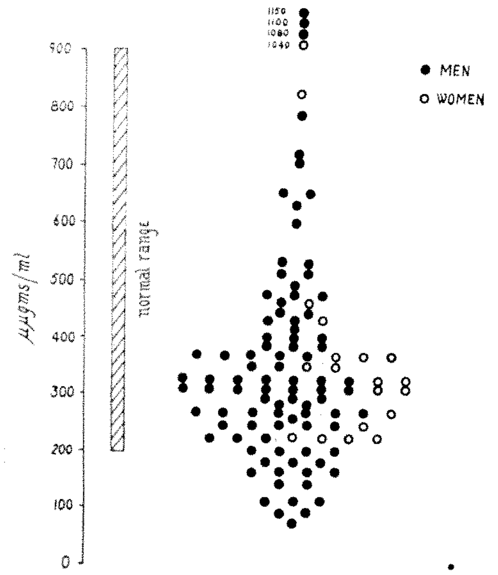

FIG. 10.—Showing the tendency for the serum vitamin B_{12} to be in the lower limits of normal, with a substantial number of subjects showing vitamin-B_{12} deficiency.

developed anaemia for some reason not in any way related to the gastrectomy. The causes of the anaemia in these 9 subjects are shown in *Table VIII*. Repeated haemorrhoidal bleeding accounted for 3 cases, while carcinoma of the colon, cirrhosis of the liver, and bronchogenic carcinoma each accounted for 1 case. One unusual discovery was the occurrence of amoebiasis of the caecum in a 50-year-old man who had had a gastrectomy 17 years previously. One woman of 55 had donated blood regularly twice a year since the time of her operation 15 years previously. The fact that there were no cases of anaemia as a result of uterine bleeding was due to the fact that in this long-term follow-up all the women patients were post-menopausal with ages ranging from 60 to 75 years.

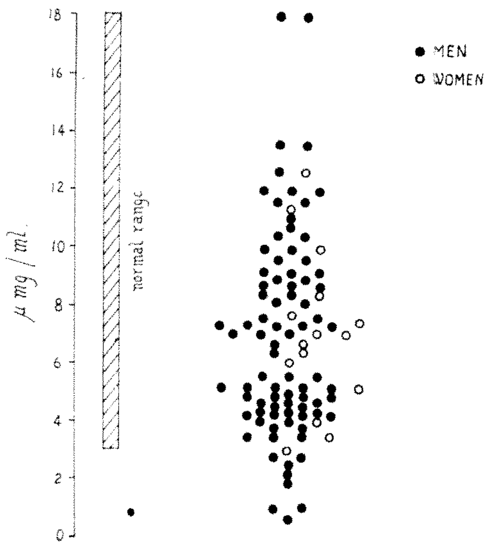

FIG. 11.—Showing that the levels of serum folic acid bear a very close resemblance to those of vitamin B_{12} 15–20 years after Polya gastrectomy.

Table VIII.—ANALYSIS OF CASES OF ANAEMIA WHICH WERE NOT RELATED TO GASTRECTOMY

Cause	*No. of Cases*
Haemorrhoids	3
Carcinoma of colon	1
Cirrhosis of liver	1
Amoeboma of caecum	1
Jejunitis	1
Bronchogenic carcinoma	1
Blood donor	1
Total	9

Of the remaining 107 cases, 22 were considered to be suffering from post-gastrectomy anaemia. Eighteen of these were men and 4 were women. These cases included anaemia due to deficiency of iron, vitamin B_{12}, and folic acid, as well as those suffering from more than one deficiency. Also included are 3 patients in whom though the haemoglobin was normal the serum iron (2 cases) and the serum vitamin B_{12} (1 case) were below the normal level. These subjects were in consequence regarded as cases of incipient iron deficiency or of macrocytic anaemia.

An analysis of the cases of post-gastrectomy anaemia is presented in *Table IX*. The overall incidence of all types of anaemia was 20·6 per cent. Men were less frequently affected (19·9 per cent) than women, of whom 23·5 per cent suffered from anaemia. Iron-deficiency anaemia was more common in women (23·5 per cent) than in men (10·0 per cent), but vitamin B_{12} deficiency (4·4 per cent) and folic acid deficiency (2·2 per cent) were found in male patients only.

The overall picture showed that iron-deficiency anaemia (12·1 per cent) was much commoner than vitamin-B_{12} and folic acid deficiency, in which the incidence of anaemia was 3·74 and 1·89 per cent respectively. Combined deficiencies of iron and vitamin B_{12} (1·87 per cent) and of folic acid and vitamin B_{12} (0·9 per cent) were also encountered in this analysis.

Response of Post-gastrectomy Anaemia to Replacement Therapy.—The response to oral iron in doses of 200 mg. of ferrous sulphate three times a day was rapid and satisfactory in those cases of iron-deficiency anaemia in which the serum vitamin B_{12} was within normal limits. Two middle-aged patients presented as cases of incipient iron deficiency with near-normal haemoglobin but with serum-iron levels of around 50 mg. per cent. The clinical improvement and sense of well-being following iron therapy were more than commensurate with the increase in the haemoglobin level. In 2 cases, however, the response to iron was disappointing. In one of these patients there was an associated low level of serum vitamin B_{12}, and though the response to oral iron and to parenteral

Table IX.—ANALYSIS OF CASES OF ANAEMIA 15–20 YEARS AFTER POLYA GASTRECTOMY FOR DUODENAL ULCER

TYPE OF DEFICIENCY	MALES		FEMALES		TOTAL	
	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage
Iron	Actual, 7 Incipient, 2	10·0	4	23·5	13	12·10
Vitamin B_{12}	Actual, 3 Incipient, 1	4·4	—	—	4	3·74
Iron and vitamin B_{12}	2	2·2	—	—	2	1·87
Folic acid	2	2·2	—	—	2	1·87
Folic acid and vitamin B_{12}	1	1·1	—	—	1	0·90
Total	18	19·9	4	23·5	22	20·60

vitamin B_{12} was poor when given separately, when given in combination a satisfactory response was attained. In the other case who suffered from persistent post-gastrectomy symptoms and who was regarded as a 'gastric cripple' the response to Cytamen and iron was disappointing.

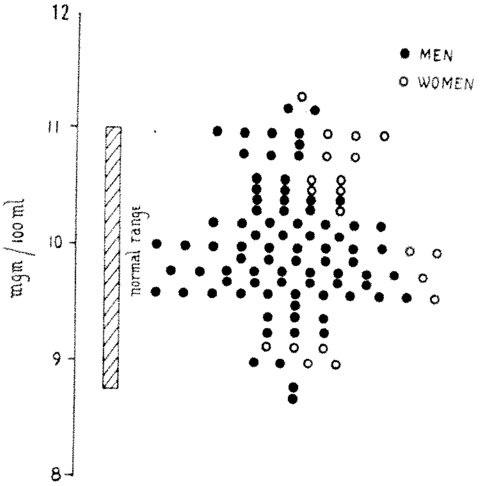

FIG. 12.—The levels of serum calcium in 102 cases 15–20 years after Polya gastrectomy.

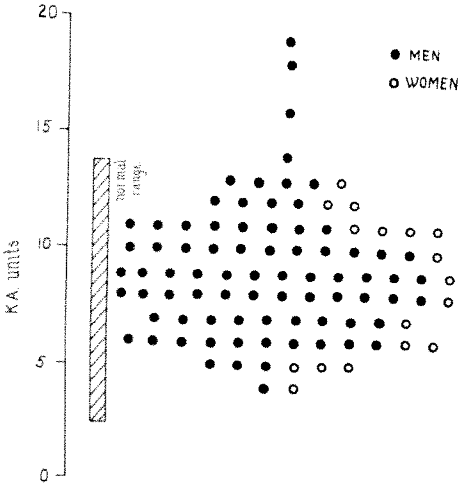

FIG. 13.—The levels of serum alkaline phosphatase 15–20 years after Polya gastrectomy. Three cases showed levels above the upper limits of normal and were subsequently investigated.

Vitamin-B_{12} deficiency was treated by the injection of 1000 μg. of Cytamen at fortnightly intervals for 2 months followed by monthly injections. In folic acid deficiency 2 mg. of folic acid were given three times a day followed by monthly injections of 1000 μg. of Cytamen. The response to therapy was satisfactory in all except 1 subject.

c. Post-gastrectomy Bone Disease.—The maintenance of normal bone structure depends on the provision of an organic osteoid matrix and adequate mineralization by the constant ionic interchange across the surface of the crystalline bone. Inadequate intake of calcium, vitamin-D deficiency, increased bowel loss of calcium as a result of steatorrhoea, post-cibal acidosis, and poor intake of protein may all affect bone structure. Since these conditions of impaired absorption are likely to be present after gastrectomy, such subjects may be more susceptible to alterations of bone structure and prone to develop either osteomalacia or osteoporosis, or a combination of both conditions. Review of the literature suggests that metabolic bone disease may occur after gastrectomy more frequently than is realized.

Because of these considerations all the long-term post-gastrectomy patients were screened specifically to discover evidence of metabolic bone disease. It was realized from a review of the literature that the parameters indicating incipient or established post-gastrectomy bone disease are ill defined, and diagnosis rests on the assessment of a combination of a number of factors—biochemical, radiological, histological, and clinical.

Biochemical examination consisted of routine estimations of the serum calcium, the serum phosphatase, and the calcium/phosphate product. The serum alkaline phosphatase was estimated in all the cases and levels above 13 K.A. units were regarded as abnormal. In certain cases the 24-hour urinary calcium excretion was estimated, though the limitations in the value of this estimate were appreciated.

Radiological screening consisted of estimation of the 'metacarpal', 'femoral', and 'vertebral biconcavity' indices as described by Nordin (1970), together with the observation of osteoporotic changes in the spine, fracture of the ribs, or the presence of Loosers zones in the long bones.

Histological tests consisted of open-bone biopsy of the iliac crest, but this procedure was confined to those cases with a strong suspicion of bone disease.

Clinical inquiry recorded the grading of the results of gastrectomy as already outlined, noting the occurrence of weight changes and examination of the haematological state. Inquiry was made regarding muscle weakness or bone pain, but the results of this inquiry in elderly arthritic patients were confusing and unhelpful. The presence or absence of steatorrhoea was especially noted.

In this review 102 cases who had had gastrectomy 15–20 years previously were screened routinely by the tests outlined above.

Serum calcium: The serum-calcium levels in 102 cases are depicted in *Fig.* 12. As will be seen the vast majority of readings fall well within the normal limits in both men and women, except for 2 patients marginally below and 3 patients marginally above the limits of normal.

Serum alkaline phosphatase: The results of the routine screening of the serum-alkaline-phosphatase levels are shown in *Fig.* 13. All the subjects were well within the normal range, except for 3 who were significantly above the upper limits of normal and who were subsequently more fully investigated.

Bone radiography: Any patient showing an abnormality in the routine radiological examinations as outlined was subjected to further biochemical and clinical study.

Of the 102 cases screened in this long-term follow-up, 13 cases were suspected of suffering from bone disease either because of biochemical or radiological abnormality. The details of these cases are presented in *Table X*. All were male patients in middle life or old age, the youngest being 36 and the eldest 77, with an average age of 64. Operation had been performed 13–19 years previously.

Cases 1, 2, 3, and 9 were selected for scrutiny because the alkaline phosphatase was well above the normal level of 13 K.A. units. *Case* 1, an elderly hypertensive man of 71, had frequent epistaxis and suffered from hypochromic anaemia and coronary disease. All other investigations including bone biopsy failed to confirm the presence of metabolic bone disease. *Case* 2, a cripple from dysentery and gassing in the First World War, had developed pulmonary tuberculosis in 1958. After a full investigation of the metabolic state post-gastrectomy bone disease could not be confirmed and he was considered to be suffering from senile osteoporosis and arteriosclerosis. *Case* 3 was found to have secondary deposits in his bones from a bronchogenic carcinoma and from which he has since died. *Case* 9 was found to be suffering from Paget's disease and suspected carcinoma of the prostate.

Table X.—THE INVESTIGATIVE DETAILS OF 13 CASES O

CASE	AGE AND SEX	GRADE	TIME INTERVAL (years)	WEIGHT	TOTAL PLASMA PROTEIN	BLOOD STATE	SERUM			DAILY URINARY Ca (mg.)
							Ca	P	Ca × P	
1. N. L.	71 M.	I	14	Gain	8·0	Hypochromic anaemia	10·6	2·7	28·6	102
2. J. W. S.	71 M.	II	17	Loss	7·6	Hypochromic anaemia	10·2	3·6	36·7	168
3 C. W. W.	69 M.	I	15	Loss	7·6	Normal	—	—	—	—
4. M. H.	54 M.	I	18	No change	7·4	Normal	10·0	4·5	45·0	48·0*
5. P. K. G.	77 M.	I	19	Gain	7·5	Normal	9·8	—	—	—
6. R. T. P.	72 M.	III	17	Loss	7·6	Normal	10·1	4·1	41·4	121
7. T. M.	75 M.	I	17	Gain	7·6	Normal	10·4	3·3	34·3	190
8. J. M.	65 M.	I	17	Gain	6·6	Hypochromic anaemia	11·2	3·0	33·6	134
9. F. S.	68 M.	I	16	Gain	8·0	Normal	10·8	2·6	28·8	217
10. W. A.	56 M.	I	13	Gain	7·4	Normal	10·8	3·2	34·6	—
11. A. C.	36 M.	I	14	Gain	7·6	Normal	11·2	—	—	225
12. E. F.	53 M.	I	19	No change	7·2	Normal	11·4*	—	—	119
13. H. C. R.	73 M.	II	13	No change	6·8	Normal	10·1	3·8	38·4	14* Unsatisfactory

Ca, calcium; P, phosphorus.

* The special features which were discovered on routine screening and which evoked further investigation.

Case 8, an alcoholic aged 65 who suffered from hypochromic anaemia, was selected for scrutiny because of spinal osteoporosis. He was found to be suffering from Paget's disease of the pelvis and osteoporosis was confirmed on bone biopsy. *Case* 4, a man of 54, was also selected for investigation because of the presence of spinal deformity and a low urinary-calcium excretion. Further inquiry elucidated the history of spinal injury, and all other tests showed no evidence of post-gastrectomy bone disease.

Cases 5, 6, 7, 11, and 13 were all selected for scrutiny because of the radiographic appearances of the spine. Of these, *Cases* 5, 7, and 13 were considered to have osteoporotic changes consistent with their average age of 74. *Case* 6, a man of 72 who showed signs of avitaminosis and weight-loss, was considered to be a failed gastrectomy and was placed in grade III mainly because of bilious vomiting.

TOMY SUSPECTED OF SUFFERING FROM BONE DISEASE

	Bone Radiographs			Bone Biopsy	Bone Pain	Muscle Weakness	Steatorrhoea	Comment
e	Ribs	Long Bones	Metacarpal Index					
ty 0·9	Normal	0·64 Normal	0·44 Normal	Normal	Normal	None	None	Repeated epistaxis. Coronary thrombosis. No evidence of bone disease
osis	Normal	Normal	—	—	None	None	Present	Chronic dysentery since war; gas casualty in 1917. Pulmonary tuberculosis in 1958
y	—	—	—	—	—	—	—	Found to have bronchial carcinoma
y of ty normal	Normal	0·57 Normal	0·47 Normal	—	None	None	None	Old spine injury; no evidence of bone disease
osis*	Normal	0·91 Normal	0·57 Normal	—	None	None	None	Radiographs of spine considered normal for age
osis*	Normal	—	—	Normal	None	None	None	Afferent-loop syndrome. Avitaminosis
osis*	Normal	0·56 Normal	0·5 Normal	—	None	None	Occasional	—
osis*	Normal	0·51 Normal	0·39 Low	Moderate degeneration of osteoporosis	None	None	None	Heavy drinker. Paget's disease of pelvis
ry ?	Normal	—	—	—	Present	None	None	Carcinoma of prostate? Paget's disease? Renal function normal
	Normal	—	Periarticular osteoporosis in left hand	—	—	None	None	Early rheumatoid arthritis?
* ty 0·33	—	0·55 Normal	0·55 Normal	—	None	None	None	Old Scheuermann's disease
	Normal	0·56 Normal	0·38 Low	—	None	None	None	High blood-pressure. Amoebiasis
osis ?*	Normal	0·48 Normal	0·4 Normal	—	None	None	None	Pulmonary fibrosis involving all the aorta

The serum calcium and phosphorus were normal and the daily urinary output of calcium was within normal limits. Bone biopsy was also normal. This patient has now agreed to have the Polya operation converted to one of the Billroth-I type. *Case* 11, one of the younger patients in the series, was also selected for investigation because of spinal curvature and suspected bone change. Investigations suggested that he had developed kyphosis in adolescence owing to Scheuermann's disease.

Case 12 was rather unusual in that this hypertensive 53-year-old man showed a low 'metacarpal' index of 0·38 on radiographs of the hand and he also had a high serum calcium. On admission he was found to be suffering from amoebiasis affecting the caecum and terminal ileum. *Case* 10 also showed an unusual appearance on radiographs of the metacarpal bone and was thought to be an early case of rheumatoid disease. The final case, *Case* 13, showed slight osteoporotic changes of the spine but the spinal 'biconcavity' index was normal, as were the 'femoral' and 'metacarpal' indices.

In this group of 13 cases, 9 were assessed as symptom-free in grade I, 3 as satisfactory in grade II, and 1 case suffering from bilious vomiting, loss of weight, and avitaminosis as a failure in grade III. This group of cases of suspected metabolic bone disease therefore showed the same percentage of patients in each category and mirrored the grading results of the series as a whole.

After the most careful consideration of the biochemical, clinical, or radiological state none of these cases could be considered to be suffering from post-gastrectomy bone disease, and bone biopsy was normal in those considered to be most likely examples of bone dystrophy.

d. Plasma Proteins.—Though it was realized that the plasma-protein levels do not reflect the extent of nitrogen loss unless this is severe, it was considered that long-continued protein depletion might over a period of 15–20 years affect the levels of the plasma proteins. In view of this, routine estimation of the plasma-protein levels was carried out in all cases of long-term review.

The levels for total plasma protein are shown in *Fig.* 14. The levels in all patients fall well within the normal range for total plasma proteins. Estimation of the serum-globulin levels, however, produced different and surprising results, as shown in *Fig.* 15. The levels of globulin showed marked reductions in both men and women, with appropriate alterations in the albumin : globulin ratio.

Pulmonary Tuberculosis.—In 8 cases in the series there was an association between tuberculosis and partial gastrectomy. In 3 patients who had had pulmonary tuberculosis associated with a long-standing duodenal ulcer the treatment of the pulmonary lesion was inhibited by the presence of severe dyspepsia. All 3 responded satisfactorily to gastrectomy with marked improvement in their general health. Another patient who had formerly had pulmonary tuberculosis had a gastrectomy for duodenal ulcer and subsequently developed stomal ulceration. Revision gastrectomy and vagotomy were performed and at no time was there any evidence of recrudescence of the pulmonary lesion.

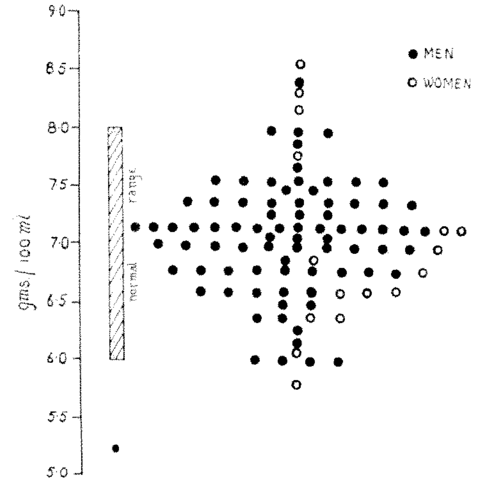

FIG. 14.—Showing that the total blood-protein levels were within normal limits in 102 cases 15–20 years after Polya gastrectomy.

Three other cases were known to have had active tuberculosis before operation and in none of these cases was the result entirely satisfactory. One of the patients had had a nephrectomy for a tuberculous kidney in 1948 and had doubtfully controlled pulmonary tuberculosis at the time of gastrectomy. Four years after gastrectomy he developed tuberculous epididymitis and recently has had a spontaneous pneumothorax. Another patient with pulmonary cavitation has made only moderate progress after gastrectomy, but this may be partly accounted for by advancing age and chronic urinary infection. The remaining case of known pulmonary tuberculosis before operation was a casualty of dysentery and gassing in the First World War. Progress after gastrectomy was only moderate and he has recently been investigated as a possible example of post-gastrectomy bone disease.

In only 1 patient has pulmonary tuberculosis developed after operation. This woman, who had a Polya gastrectomy in 1952, lost weight consistently after her operation and was found to have a pulmonary focus 9 months later. She died of a fulminant pulmonary tuberculosis in 1954, 2 years after operation.

DISCUSSION

It is not proposed in this commentary to discuss at length the details recorded in this 20-year prospective survey but merely to emphasize certain features of this series in the light of recent publications on the immediate and long-term results of various surgical procedures in the treatment of duodenal ulcer.

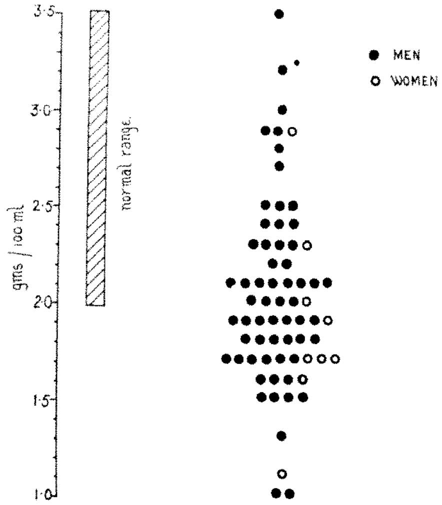

FIG. 15.—Showing that the levels of serum globulin tended to be in the lower limits of normal or to be reduced in both male and female patients 15–20 years after Polya gastrectomy.

This paper records the results of a carefully planned prospective and entirely personal study which was started in 1950 when gastrectomy was considered the treatment of choice in duodenal ulcer. In spite of the fact that the tide of surgical opinion began to ebb away from gastrectomy on account of its mortality and its long-term consequences, this prospective study has continued up to the present time when the tide of opinion has changed and has once again begun to flow in favour of gastrectomy.

The Overall Results.—Of the 800 cases of duodenal ulcer, 80 per cent were entirely symptom-free after operation. In these patients there was a degree of excellence in the results which was particularly noticeable when the ulcer was extensive and penetrating deeply into the pancreas or liver. The effect of the removal of such an ulcer was quite dramatic in producing an almost immediate improvement in the general condition and appearance of the patient. It is perhaps permissible to note that many of the registrars who took part in the follow-up examinations commented on an indefinable well-being in post-gastrectomy patients which was not present in the post-vagotomy cases which they were accustomed to see in other follow-up clinics.

The results were marginally better in men than in women in grade I, which reflects the usual experience. The failure rate of 6 per cent was, however, the same in both sexes though the cause of failure was different. A higher mortality-rate and the greater tendency to stomal ulceration were the main causes of the unsatisfactory results in men, while in women the occurrence of post-prandial symptoms accounted for 5·2 per cent of the failures.

Mortality-rate.—The risk of death from elective operation was 0·7 per cent even though there was no exclusion of elderly and poor-risk patients suffering from extensive penetrating ulcers. Most of the deaths occurred in the earliest years of the study when a hard core of very difficult cases had to be dealt with, but in the later years the mortality fell to a much lower level. The mortality-rate is comparable to those recorded by Pannett (1938; 0·86 per cent) and Hosford (1949; 0·5 per cent) in retrospective studies and to that recorded by Goligher and others (1968), who in the Leeds/York trial did not have a single death after gastrectomy in 109 cases. The 'escape clause' though not often evoked for the very difficult case must, however, be considered in assessing these excellent results.

The dangers of emergency gastrectomy are shown by the much higher mortality-rate of 22·7 per cent. The high death-rate was contributed to by a variety of factors. Many of these deaths occurred in the early part of the trial when patients with giant penetrating ulcers suffered from massive haemorrhage from erosion of the gastroduodenal or right gastric artery. Most of these patients were old and decrepit or those who had adamantly refused operation and only came for surgical help *in extremis*. Administrative and nursing attitudes required change so that adequate staff and facilities could be available during the night to cope with these desperate cases. As the result of a more enlightened outlook and the earlier reference of cases by most co-operative and helpful physician colleagues the mortality of the emergency procedure has fallen rapidly in recent years, but it would be preferable for all cases of gastroduodenal bleeding to be admitted directly to the surgical division.

The mortality-rate was entirely confined to male patients, and in the 152 women submitted to operation there were no deaths.

Stomal Ulcer.—In this series of 800 cases of Polya gastrectomy there were 16 cases of stomal ulcer, an incidence of 2·0 per cent. This recurrence rate is almost identical with that recorded in the Birmingham series by Brookes, Waterhouse, and Thorn (1960), where out of 826 cases there were 15 instances of stomal ulceration. The incidence in men in the present series (2·3 per cent) was higher than that in women (0·6 per cent), which reflects the usual experience. As shown in *Table III*, this complication occurs in the early months or years after gastrectomy. Half of the cases had symptoms within a year of operation. In this respect gastrectomy differs from gastro-enterostomy in which this complication can occur many years after operation (Davey, 1960).

The tendency to stomal ulcer was more marked in the younger age-groups, and though no age-group was immune from this complication the tendency to recurrence became less with advancing years.

Simple re-gastrectomy cured only 5 out of the 7 cases in which this operation was performed, but the addition of vagotomy to revision gastrectomy obviated further ulceration and was regarded as essential in the management of stomal ulcer. In no case of recurrent ulcer was there any evidence of hyperparathyroidism or of Zollinger-Ellison tumour, though these conditions were specifically looked for.

Of the 9 cases of post-gastrectomy bleeding not due to stomal ulcer, 3 developed symptoms after taking aspirin for a febrile illness. This appears to emphasize the general consensus of opinion that certain patients appear to be sensitive to aspirin and are prone to gastrojejunal bleeding with this drug.

Post-gastrectomy Syndrome.—Post-cibal symptoms of various kinds have come to be regarded as the *bête noire* of partial gastrectomy and it was partly because of these symptoms that the operation fell into disfavour. The results of the Leeds/York controlled trial of elective surgery in duodenal ulcer (Goligher and others, 1964, 1968) suggest that such post-prandial syndromes are not confined to partial gastrectomy but occur as frequently or even more frequently after vagotomy and gastro-enterostomy. In the present series women were affected twice as frequently (5·2 per cent) as men (2·6 per cent), as shown in *Fig.* 4. The incidence of post-gastrectomy syndromes in women presents a major hazard and is so well recognized that experienced surgeons approach the operative treatment of ulcer dyspepsia in female subjects with extreme caution.

In this study 17 out of the 25 cases of persistent post-gastrectomy syndrome were treated operatively. Two cases were improved by narrowing the gastrojejunal stoma, but the main success came from converting the Polya operation to one of Billroth type. In 2 cases, however, recurrent ulcer occurred after conversion, and it would seem that vagotomy should be added to the conversion procedure.

In the failed case after gastrectomy, revision procedures reduce the ultimate failure rate in men to 1·9 per cent, while in women 3·9 per cent of the patients remained in grade III (*Fig.* 5).

Weight Changes after Gastrectomy.—The difficulties of assessing weight changes after operation have already been mentioned. In this careful prospective study of 294 patients weight-loss was observed in 12 per cent of the subjects. This figure accords with that obtained by Kemp (1967), who found weight-loss in 18 per cent of 317 cases. Review of the literature shows that the recorded incidence of weight-loss varies widely from 9 to 75 per cent (Wallensten, 1954). The cause of this variation may be due to a variety of factors, of which the extent of gastric resection and diminished food intake are probably the most important.

The concept that partial gastrectomy aims primarily at excision of a proportion of the parietal cell mass has encouraged more radical gastrectomy in an effort to produce achlorhydria and freedom from recurrent ulceration (Bruce, Card, Marks, and Sircus, 1959). The misfortunes of this concept have been anticipated by the 'measured gastrectomy' of Visick (1945), who excised nine-tenths of the stomach, heedless of the elastic recoil of the measured greater curvature. The long-term review of these cases by Pulvertaft (1964) makes dismal reading.

The concept of removing the alkaline gastrin-secreting area (Kahlson, 1948), and especially the lesser curvature (Dean and Mason, 1964) and the pyloric mucosa (Ogilvie, 1938), encourages a less radical excision, as depicted in *Fig.* 2, as a means of reducing acid secretion. The technique of measuring the extent of the gastrectomy from the pylorus towards the fundus rather than from the oesophagus towards the pylorus leads to vastly improved nutritional results and with no material increase in the incidence of stomal ulceration.

In this series patients were encouraged to eat and drink as much as they liked and neither alcohol nor smoking was forbidden. Operation was to be regarded as a substitute for dietetic restriction. It may well be that the attitude of mind thereby engendered encouraged patients to eat more, and it was quite surprising how many patients had to institute slimming measures to restrict the progressive increase in weight, as shown in *Fig.* 6. Even those patients who showed an initial loss of weight in the first year tended to regain lost ground in subsequent years.

It seems likely that weight-loss is due to poor food intake as pointed out by Johnston, Welbourn, and Acheson (1958). A too radical excision of the stomach or a badly constructed anastomosis will cause postprandial discomfort and discourage the patient from eating, and nutritional changes will be inevitable. This confirms the dictum of Kinsella (1956) that the results of bad gastrectomies are bad.

Post-gastrectomy Anaemia.—The blood status has already been so fully considered that little further comment is necessary. The overall incidence of anaemia of all types was 20·6 per cent, a figure which is much lower than that recorded by Wastell (1968), who found that 5–6 years after Polya gastrectomy 33 per cent of patients suffered from anaemia, but corresponds more closely to the figure of 23 per cent quoted by Cox, Williams, and Tasman Jones (1963). The incidence was only slightly greater in women (23·5 per cent) than in men (19·9 per cent), but as already mentioned all the women in this series were post-menopausal.

The overall occurrence of iron-deficiency anaemia was much more common (12·1 per cent) than that due to vitamin-B_{12} deficiency (3·74 per cent). Women seemed to be much more prone to microcytic anaemia (23·5 per cent) than men (10·0 per cent). Anaemia due to vitamin-B_{12} and folic acid deficiency, however, was the prerogative of men with incidences of 4·4 and 2·2 per cent respectively. No woman in this series suffered from macrocytic anaemia. The overall incidence of macrocytic anaemia was somewhat higher than the 2 per cent recorded by Cox and others (1963), but the follow-up in the present series covered the period of 15–20 years after gastrectomy.

The response to appropriate iron or vitamin-B_{12} therapy or to a combination of both when multiple deficiencies were present was highly satisfactory. This emphasizes the fact that these supplements should be given prophylactically unless a constant review of every case is carried out.

Post-gastrectomy Bone Disease.—The screening of all long-term cases with a view to uncovering any case of post-gastrectomy bone disease has already been fully described. In none of the 13 suspects (*Table X*) admitted for extensive scrutiny could the diagnosis be established. It is of importance to note that 6 of the patients were over 70 and all except 1 were above the age of 53, so that the radiological bone changes might well be those associated with advancing years (Newton-John and Morgan, 1968). It may well be that a similar review of patients in the same age and sex grouping would reveal a similar state of the bone metabolism, and that the incidence of post-gastrectomy bone disease has been overstressed (Slaney, 1971).

Plasma Proteins.—Though it was not expected that the total plasma-protein levels would be materially altered in the absence of gross malnutrition the marked reduction in the globulin levels was an accidental finding for which at present no explanation can be offered.

COMPARISON OF PARTIAL GASTRECTOMY WITH VAGOTOMY AND DRAINAGE FOR DUODENAL ULCER

In drawing comparisons between the results of these two procedures difficulties are encountered for a variety of reasons. Prospective studies are rare and the criteria of case selection so frequently ill defined that comparisons may be attempted between groups of patients in whom the natural history of their ulcers may be quite different. The type and extent of the duodenal ulcer are virtually unimportant in gastrectomy where the ulcer is removed, except in that it presents a technical operative problem. In vagotomy and drainage, however, the extent and type of the ulcer are of considerable importance, not only in determining the type of drainage procedure but also for other reasons. The results obtained from vagotomy in a case of a large duodenal ulcer penetrating deeply into the pancreas or liver may be very different from those obtained in a case where the duodenum is scarred and only somewhat deformed, and yet the condition of the duodenum remains undescribed in the recorded series of the results of vagotomy and drainage.

The variants of vagotomy produce further difficulties in making comparisons, in that the effects of truncal as opposed to selective vagotomy are not yet accurately assessed and the incidence of incomplete vagotomy is not always recorded. The different drainage procedures, such as gastro-enterostomy, the various types of pyloroplasty, and even anterior pylorectomy (Holt and Lythgoe, 1965) add still further to the confusion and uncertainty.

The present popularity of vagotomy and drainage is due to the low mortality, the ease of performance, the supposed freedom from side-effects, the preservation of the gastric reservoir, and the better nutritional state of the patient. Though the first of these claims is generally accepted, the latter features are somewhat in doubt.

Mortality.—It must be admitted that the generally accepted mortality figure for partial gastrectomy for duodenal ulcer is 2–3 per cent though much higher rates are recorded in special gastro-intestinal units (Small, Cay, Dugard, Fircus, Falconer, Smith, McManus, and Bruce, 1969; 4·4 per cent). The death-rate in the present series of 0·7 per cent for gastrectomy corresponds to that recorded for vagotomy by Hoerr (1953; 0·5 per cent) and Crile (1952; 0·4 per cent). The very lowest mortality figures after vagotomy have, however, been recorded by Feggetter and Pringle (1963), where out of 1600 cases there were only 6 deaths, a mortality-rate of 0·37 per cent.

The surgical opinion of recent years has been so much in favour of vagotomy and drainage that a new generation of surgeons has grown up with limited experience in gastrectomy for peptic ulcer. A major return to gastrectomy as the operation of choice would undoubtedly lead to a temporary increase in the mortality-rate.

Recurrent Ulcer.—The apparent ease of vagotomy is illusory in that the Hollander (1948) insulin test shows that in 10–40 per cent of cases nerve section is incomplete and, as might be expected, success is related to the experience of the surgeon (Ross and Kay, 1964). Recurrence of ulceration after incomplete vagotomy is prohibitively high, but even in experienced hands the generally accepted figure of 5 per cent compares unfavourably with the 2 per cent recurrence rate recorded in this and many other series after gastrectomy. Late recurrence after gastrectomy is exceptional but may still take place 10 years after vagotomy, as noted by Feggetter and Pringle (1963).

Post-gastrectomy Syndromes.—The preservation of the gastric reservoir may lead to the impression that post-cibal symptoms are much less likely to occur after vagotomy than after gastrectomy. This reputation has, however, become somewhat tarnished recently. The findings of Cox (1968) and the results of the comparative series in the Leeds/York trial (Goligher and others, 1964, 1968) indicate that side-effects are marginally more common after vagotomy and gastro-enterostomy than after partial gastrectomy.

Oesophageal Lesions.—The rare occurrence of oesophageal stenosis after Polya gastrectomy for duodenal ulcer, as described here and elsewhere (McKeown, 1958), has its counterpart in the occasional dysphagia and oesophageal reflux which occurs after vagotomy, as recorded by Williams and Woodward (1967) and Tanner (1951), who recorded an incidence of 'cardiospasm' or 'achalasia' in 3 per cent of cases.

Diarrhoea.—Just as the dumping syndrome has been regarded as the *bête noire* of partial gastrectomy, diarrhoea is now regarded as the curse of vagotomy. Though much controversy rages over the incidence of this complication, in a series of 209 cases followed up for 10–14 years by Feggetter and Pringle (1963) 29 per cent of the patients had diarrhoea, which proved troublesome in 9 per cent of cases. In certain cases more easy bowel action was regarded as beneficial (Feggetter, 1970).

The Nutritional State.—It is in regard to the nutritional state both immediately after operation and in the long term that advantages are so specially claimed for vagotomy and drainage. Preservation of the gastric reservoir does not prevent weight-loss, as emphasized by Wheldon, Venables, and Johnston (1970), while the figure of weight-loss in 11 per cent of vagotomy cases recorded by Burge and Pick (1958) corresponds closely to the 12 per cent of patients who lost weight in this series.

Anaemia.—The onset of anaemia bears a definite relationship to the time interval after operation, with a tendency for microcytic anaemia to appear 3–5 years after operation and macrocytic anaemia to occur at a much later date. By good fortune a recent review of the long-term results of vagotomy in the Feggetter (1970) series by Wheldon and others (1970) provides an excellent opportunity for comparison of the incidence and types of anaemia occurring 15–20 years after operation. In the present series the incidence of all types of anaemia was 20·6 per cent, compared with 43·5 per cent in patients 15 years after vagotomy and gastro-enterostomy. The fact that Wastell (1968) noted a lower incidence after pyloroplasty suggests that the type of drainage procedure might be significant. After vagotomy and gastro-enterostomy anaemia was of the iron-deficiency type and in only a few was the anaemia of the vitamin-B_{12}-deficiency type. In post-gastrectomy patients, as has already been outlined, about one-quarter of the cases of anaemia were due to vitamin-B_{12} (and folic acid) deficiency.

Bone Disease.—Neither in the present series nor in the very comparable post-vagotomy series (Wheldon and others, 1970) of long-term follow-up has there been a single case of bone dystrophy.

From these considerations it would appear that the pendulum of surgical opinion which had swung away from partial gastrectomy to vagotomy with drainage is more equally poised at the present time. Now that it is more fully realized that the preservation of the gastric reservoir in vagotomy does not lead to less post-prandial symptoms, adjudication between the two procedures must rest on other considerations.

The low mortality and higher recurrence rate after vagotomy must be set against the higher mortality but lower recurrence rate after partial gastrectomy. In this assessment the mortality-rate is of paramount importance. If the facilities and skills of the unit are able to reduce the mortality of partial gastrectomy to under 1 per cent, then gastrectomy is preferable, in that the recurrence rate is lower, diarrhoea is not a complication, and the post-prandial discomforts are no worse than those after vagotomy and drainage. In addition, the effect of removing a deep penetrating ulcer is quite dramatic in improving the appearance and well-being of the patient to a degree not obtainable by vagotomy and drainage. The nutritional state of a successful gastrectomy is similar to that after vagotomy, and in the long term the incidence of anaemia appears to be somewhat less.

Vagotomy and drainage, however, provides a most effective surgical treatment and in average hands carries a low mortality. The higher recurrence rate can be dealt with by further surgery, and recurrent ulcer is by no means the worst complication of the surgery of peptic ulcer.

The choice of operation will therefore depend more on the local facilities available and on the experience of the individual surgeon rather than on the intrinsic merits of either procedure.

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A TECHNIQUE FOR CREATING A SKIN-LINED HEMITHORAX

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SUMMARY

Prosthetic lungs could permanently occupy the pleural space which must first be lined with silicone 'skin', i.e., Dacron-backed silicone membrane (Peirce, 1966). Initial experiments in dogs showed that the pleural membrane would not readily accept silicone 'skin'; rather, the solution lay in the use of autogenous skin-grafts. A readily reproducible technique has been developed for transforming the left hemithorax of SPF rats into stable skin-lined cavities which can be opened to atmospheric pressure without embarrassing breathing in the contralateral lung.

Autogenous skin was formed into 35 × 20-mm. sacs and grafted into the left pleural spaces of 150 male SPF rats of mean weight 240 ± 30 g. One hundred and thirty-two (88 per cent) survived 4 weeks or more. In these the skin-lined cavity grew to occup the hemithorax, displacing the left lung. In 75 rat the cavity was opened to the exterior and sutured t the skin, thereby creating a permanent 5–8-mm opening directly through the chest wall. Fifty-nine c the 75 rats so exposed survived.

The mean pressure in the cavity was $+2{\cdot}9 \pm 0{\cdot}6$ cm H_2O before it was opened to the exterior; after th creation of the stoma the mean pressure in the cavit became $-2{\cdot}5 \pm 0{\cdot}6$ cm. H_2O ($P < 0{\cdot}001$), and the nev pressure was in phase with and was similar in mag nitude to the oesophageal pressure. The skin-line hemithorax is presented as the model of a cavity whic could be employed to house prosthetic organs de signed for permanent implantation inside the ches cavity.

IT has been shown in short-lived experiments that i is feasible to implant prosthetic lungs (Bodell, Head

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Head, and Formolo, 1965). Taking the concept further, Peirce (1966) described a prosthetic lung which permanently occupied the pleural space which must first be lined with silicone ‘skin’ (i.e., Dacron-backed silicone rubber membrane); if this was achieved the pleural cavity would have been exteriorized effectively. Peirce assumed that the pleural membrane would readily accept silicone ‘skin’, an assumption which others have questioned (Melrose, 970).

Initial experiments showed that in dogs silicone skin’ provoked much pleural effusion which needed protracted chest drainage; 1 dog developed empyema (Wosornu, 1971). A different lining for the pleural pace was sought in the use of autogenous skin-grafts, and experiments in 9 other dogs showed that free skin-grafts would ‘take’ on the normal pleural surfaces (Wosornu, 1972).

The aims of the observations recorded here were twofold. First, to attempt to transform the hemithorax into a skin-lined cavity. Secondly, to investigate the possibility that the skin-lined hemithorax could be opened to the exterior without embarrassing breathing in the contralateral lung (*Fig.* 1). The work was undertaken because the skin-lined hemithorax could be employed to house prosthetic organs designed for permanent implantation inside the chest cavity.

The first consideration, however, was the choice of a suitable experimental animal in which the two objecives could be pursued and Specific Pathogen Free SPF) rats were chosen. The experimental model was obtained in two stages: in stage 1 autogenous skin was grafted into the normal pleural space and in tage 2 the skin-lined hemithorax was opened to the exterior.

MATERIALS AND METHODS

Male albino Wistar rats of mean initial weight 240 ± 30 g. (purchased from Carworth, Huntingdon, England) were used. They were kept under standard laboratory conditions and all the operations were performed under general anaesthesia. A glass jar containing methoxyflurane (Penthrane) was connected to an open Perspex box which measured 20 cm.^{3} When oxygen was bubbled at the rate of 1–2 litres a minute hrough the methoxyflurane and the box was closed the concentration of methoxyflurane was sufficient to anaesthetize a 240-g. rat in 5–8 minutes.

An elliptical piece of full-thickness skin was excised as a free graft from the shaved back of the rat and the defect was closed without tension. The skin was pinned down and defatted in the usual way with a scalpel. It was then folded on itself and a 35 × 20-mm. rectangular piece was cut out. The free edges were sutured together with 00 silk, after which the specimen was turned inside out so that the hair-bearing surfaces faced inside and were thus isolated. A piece of soft silicone capillary tube (70 mm. long and 0·6 mm. external diameter) was inserted into the capsule to splint it and to give it a roughly rectangular shape (*Fig.* 2).

The rat, anaesthetized but not intubated, was placed on its right side. Through an incision 15–20 mm. long in the seventh or eighth intercostal space the capsule of skin was implanted inside the normal pleural space. The first pericostal suture was placed in the middle of the incision and tied to control the open pneumothorax. (It usually took under 90 seconds to open the parietal pleura, implant the skin capsule, and tie the first pericostal suture.) The chest was then closed in layers without drainage (*Fig.* 3).

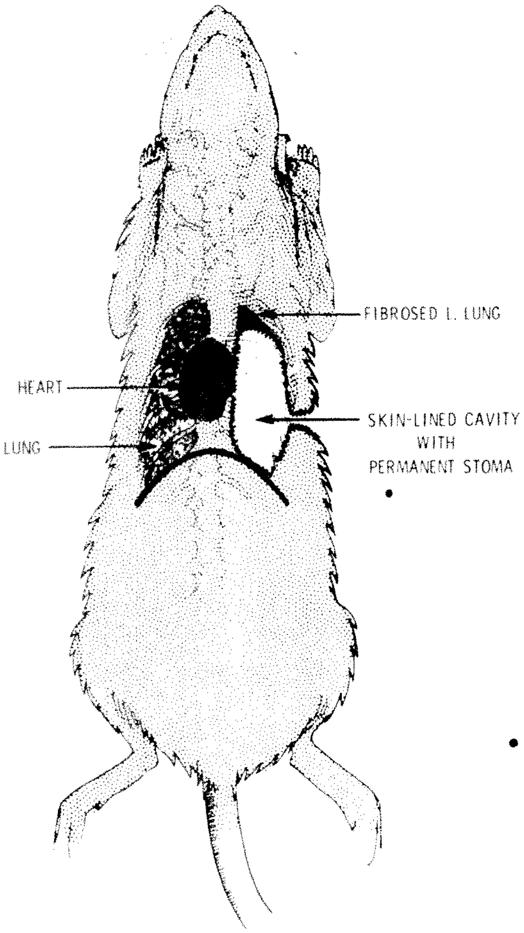

FIG. 1.—Experimental model of a cavity which could house prosthetic organs designed for permanent implantation in the chest.

Observations on the Closed Skin-lined Hemithorax.—The 150 rats which had the operation of intrapleural skin-grafting were divided into three overlapping groups and studied as follows. In group 1 (30 rats) serial chest radiographs were taken once a week for 4 weeks. The rats were anaesthetized and 1 ml. of 45 per cent Hypaque was injected into the skin-lined pleural cavity under radiographic control. The transverse diameter of the cavity was measured from the radiographs, corrected for magnification, and plotted against time. The 30 rats (and 10 unoperated rats) were weighed once a week for 4 weeks; the test rats were then killed and sectioned transversely.

At the end of the fourth week the pressure inside the skin-lined hemithorax was measured in 15 other rats (group 2). A strain-gauge manometer and recorder (Emma: S. E. Laboratories, Type SE 4912 and

Type SE 3006) were employed. A rigid nylon catheter, 40 cm. long and 1 mm. internal diameter, was connected to the transducer head. The free end of the catheter was connected to a hypodermic needle (18 gauge) and both were filled with water. The needle was then introduced into the skin-lined cavity in the region of the inferior angle of the scapula with the anaesthetized rats prone. Oesophageal and normal pleural pressures were also measured. To measure oesophageal pressure the open end of the water-filled nylon catheter without the needle was used. The 15 rats and 7 others were kept for up to 8 months to ascertain their natural fate.

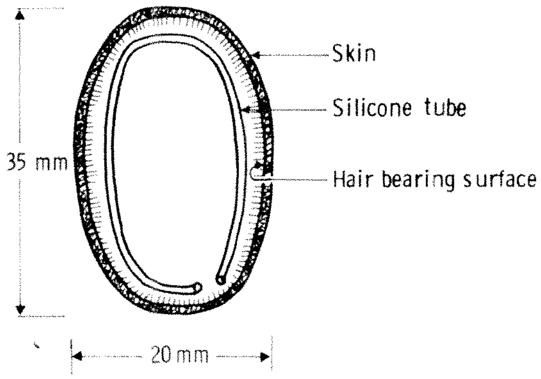

FIG. 2.—Diagram of the skin capsule for grafting into the pleural cavity of rats.

In group 3 the skin-lined hemithorax was opened to the exterior and sutured to skin, thereby creating a permanent stoma directly through the chest wall.

Table I.—COMPARISON BETWEEN WEIGHT GAINED WEEKLY BY UNOPERATED RATS WITH THAT OF THE TEST RATS

WEEK No.	WEEKLY WEIGHT-GAIN (g.)		STATISTICAL ANALYSES (d.f. = 38)	
	Test Rats ($n = 30$)	Unoperated Rats ($n = 10$)	t	P
1	1·7 ± 3·8	22·5 ± 2·4	3·08	0·004*
2	19·2 ± 2·5	31·0 ± 2·2	2·62	0·012*
3	18·5 ± 2·9	19·5 ± 2·2	0·194	0·847†
4	9·8 ± 5·1	14·5 ± 1·2	0·528	0·601†

* Significant. † Not significant.

Values in the table are given as the mean ± S.E.

Each rat was anaesthetized as before but supplementary anaesthetic was provided by keeping the face of the rats at the mouth of a beaker containing absorbent cotton-wool soaked in methoxyflurane. With the rat supine a disk of skin (about 10 mm. in diameter) was excised from a point centred 20 mm. above and lateral to the xiphoid process. The skin-reinforced parietal pleura was exposed, a disk of about 5 mm. in diameter was excised, and fluid under pressure was allowed to escape. The edges of the skin lining the hemithorax were sutured to the skin covering the chest wall to establish a skin-to-skin stoma. The operation was performed on 75 rats and consisted of 65 rats 4 weeks after the creation of a skin-lined hemithorax and 10 (out of the 15 from group 2) at week 16. (It was necessary to interrupt the operation from time to time and to change the position of the rats because they could not tolerate the supine position throughout the procedure.)

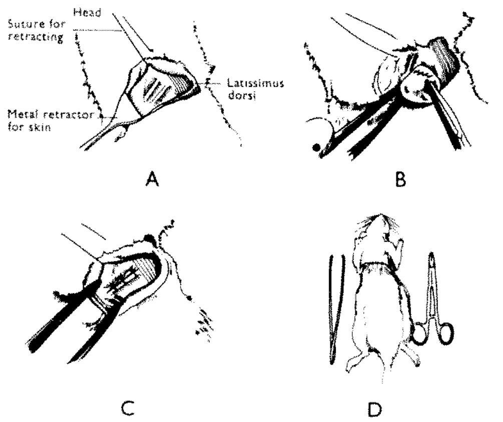

FIG. 3.—The thoracotomy and intrapleural skin-grafting in rats. A, The intercostal space is exposed. B, Implanting the skin capsule into the pleural space. C, Closure; the pericostal sutures in place. D, Closure; the final appearance with no chest drain.

Table II.—COMPARISON OF NORMAL PLEURAL PRESSURE WITH THE PRESSURE IN THE SKIN-LINED HEMITHORAX AFTER CREATION OF THE THORACOSTOMY IN RATS

	PRESSURE (cm. H_2O)		
	End of Expiration	End of Inspiration	Mean Pressure
Normal pleura ($n = 10$)	−3·4 ± 0·2	−8·7 ± 0·5	−3·7 ± 0·2
Skin-lined hemithorax ($n = 15$)	1·7 ± 0·6	−7·7 ± 1·1	−2·5 ± 0·6
Statistical analyses (d.f. = 23)			
t	7·22	0·704	1·59
P	0·001*	0·489†	0·126†

* Significant. † Not significant.

Values in the table are given as the mean ± S.E.

Observations on the Open Skin-lined Hemithorax.—After the creation of the stoma the rats were screened radiologically and chest radiographs were taken. The pressure in the open cavity was measured. A piece of nylon tube (3 cm. long, internal diameter 3·5 mm.) was wedged firmly into the stoma and connected to the strain-gauge manometer; oesophageal pressure was measured simultaneously. The arterial pH, Po_2, and Pco_2, the volume of the skin-lined hemithorax, and its minute ventilation were measured (Wosornu and Melrose, 1971).

RESULTS

1. **General Progress.**—Out of 168 rats, 150 had successful intrapleural skin-grafting and 132 of these survived the next 4 weeks or longer. The grafted skin-capsule enlarged to occupy the left hemithorax as fluid accumulated in it (*Fig.* 4). Beyond the fourth week the preparation became stable.

At the end of the first 2 weeks the unoperated rats gained significantly more weight than the test rats. However, by the end of the third week the difference was lost as the test rats also thrived (*Table I*). A radiographic demonstration of the cavity before and after creation of the stoma is shown in *Fig*. 5.

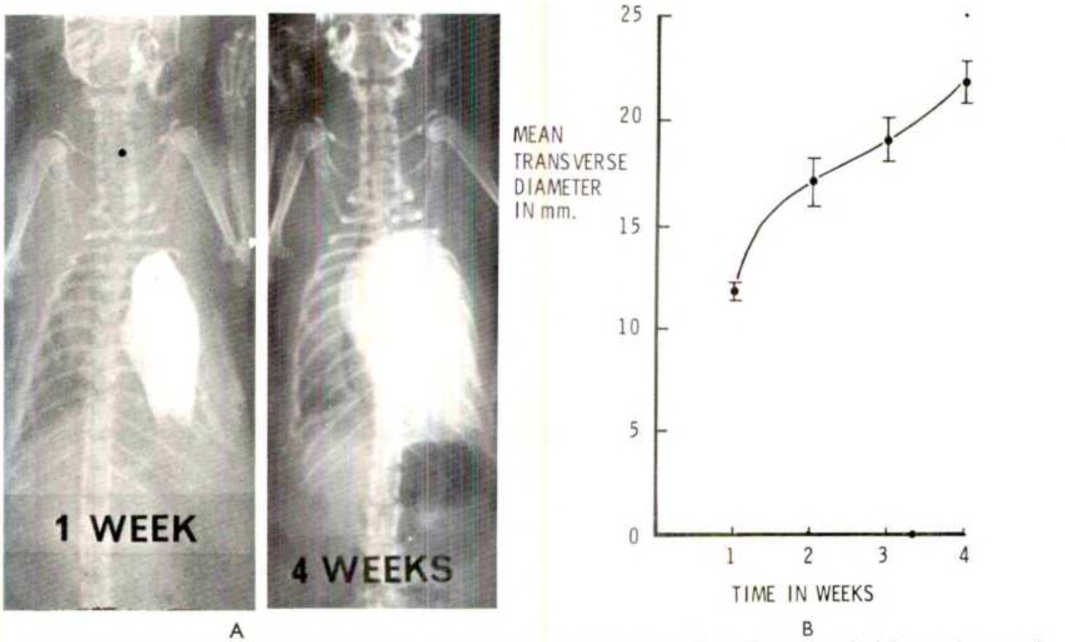

FIG. 4.—A, Radiographs of a rat with the left hemithorax outlined with 1 ml. of Hypaque. The radiograph on the left was taken 1 week after intrapleural skin-grafting; the one on the right was taken 3 weeks later. B, The transverse diameter of the cavity was measured from a series of radiographs, corrected for magnification, and plotted against time.

2. Pleural Pressure before and after Creation of the Stoma.—The mean pressure was $+2.9 \pm 0.6$ cm. H_2O in the closed skin-lined hemithorax (*Fig*. 6 A). However, after the creation of the stoma the mean pressure became -2.5 ± 0.6 cm. H_2O ($P < 0.001$). During respiration the pressure in the open skin-lined hemithorax was in phase with the oesophageal (pleural) pressure and similar to it in magnitude (*Fig*. 6 B; *Table II*).

DISCUSSION

SPF rats were chosen for the present study for three reasons. First, rats have much loose skin relative to their body weight so that if needed sufficient free skin-graft would be available. Secondly, rats need little supervision and a large series could be built up rapidly. Thirdly, SPF rats had to be used because it is generally known that non-SPF rats suffer from endemic chronic lung disease which renders them unsuitable for experiments on the respiratory system (King and Bell, 1966; Binns, Clark, and Healey, 1971).

Reports are conflicting on a simple and safe method of anaesthesia for rats intended to recover after chest surgery (Griffith and Farris, 1942; Kluge and Tveten, 1968). In the present study each rat was anaesthetized but not intubated, the chest was opened, the skin capsule was implanted into the pleural space, and the chest was closed again. It was thought that if the chest was opened for only a short time and the investigator was quick in operation the rats would survive the thoracotomy. With this approach 150 out of 168 rats (89·3 per cent) survived.

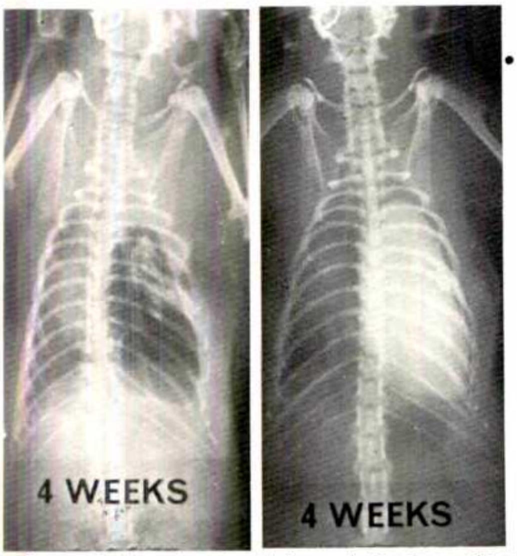

FIG. 5.—Radiographs of a rat before and after the creation of the chest stoma. The radiograph on the right shows the closed skin-lined hemithorax outlined with 1 ml. of Hypaque; the one on the left is the same cavity opened to the exterior—an artificially produced gas cavity.

The rationale behind the technique employed to create the skin-lined hemithorax was as follows. Closed capsules of autogenous skin were grafted into the normal left pleural space of 150 SPF rats of which

132 (88 per cent) survived the next 4 weeks or longer. The grafts 'took' on the surrounding structures and the skin capsules expanded as fluid accumulated in them until by the end of the second week the grafts occupied the left hemithorax, displacing the ipsilateral lung (*Fig.* 4). The cavity kept pace with the rat's growth.

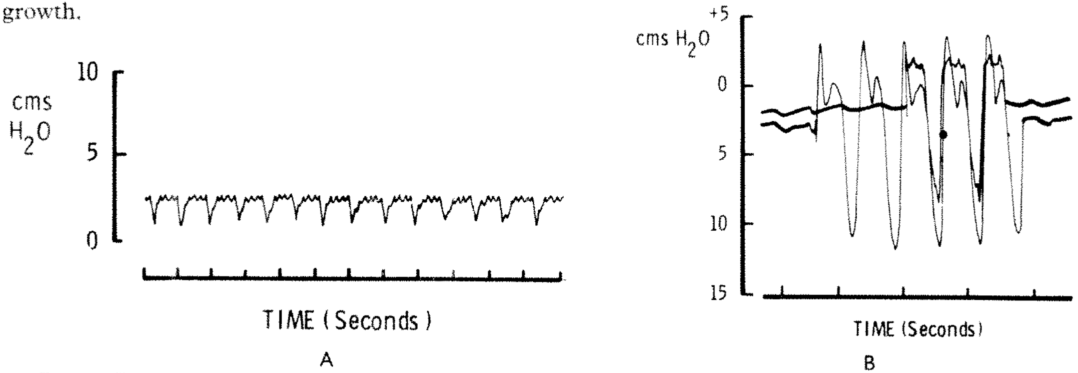

FIG. 6.—Tracings of the pressure from the skin-lined hemithorax before and after the creation of the chest stoma in rats. A, With the cavity closed the pressure was above atmospheric; the characteristic pause at the end of expiration in the rat is shown and during these pauses cardiogenic oscillations were recorded. B, After the creation of the stoma the pressure (top trace) in the cavity was subatmospheric. When oesophageal pressure (bottom trace) was recorded simultaneously the two pressures were in phase and similar in magnitude.

The mean pressure in the closed skin-lined hemithorax was $+2{\cdot}9 \pm 0{\cdot}6$ cm. H_2O, which was significantly higher than the normal mean rat pleural pressure of $-3{\cdot}4 \pm 0{\cdot}4$ cm. H_2O ($P < 0{\cdot}001$). In 59 of 75 rats (78·7 per cent) the skin-lined hemithorax was opened successfully to the exterior and a permanent skin-to-skin thoracostomy was established. Since over 78 per cent of the rats so exposed survived it was concluded that the procedure was compatible with life in most SPF rats. After creation of the stoma the mean pressure in the skin-lined hemithorax was $-2{\cdot}5 \pm 0{\cdot}6$ cm. H_2O, and during respiration the pressure was in phase with the oesophageal (pleural) pressure and similar to it in magnitude (*Fig.* 6; *Table II*).

The experimental preparation (*Fig.* 1) differs in two ways from the one suggested by Peirce (1966). First, the pleural space was lined with autogenous skin and not with silicone 'skin'. Secondly, the skin-lined and exteriorized pleural cavity could receive air from a separate opening directly through the chest wall and not from the trachea.

CONCLUSION

Three conclusions are drawn. First, a readily reproducible technique has been developed for transforming the left hemithorax of SPF rats into stable skin-lined cavities. Secondly, the cavities could be opened to the exterior without embarrassing respiration in the contralateral lung. Thirdly, the skin-lined hemithorax appeared to function as an open ventilated gas cavity. The experimental preparation was put forward as a model of a cavity which could be employed to house prosthetic organs designed for permanent implantation inside the chest. A series of experiments are in progress to see whether these conclusions are valid for larger animals also.

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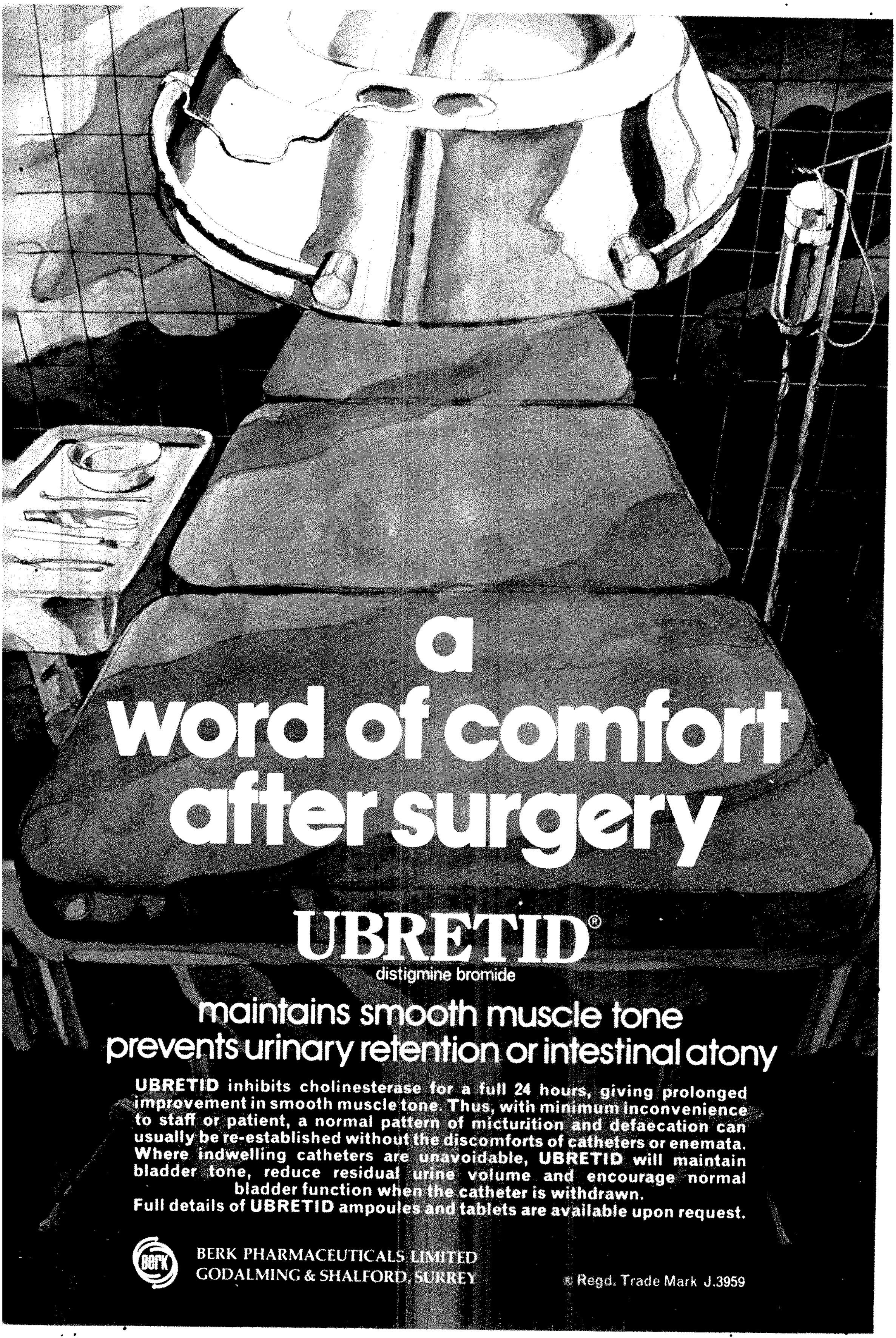

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AN ASSESSMENT OF ABOVE- AND THROUGH-KNEE AMPUTATIONS

By P. W. B. GREEN, B. S. HAWKINS, W. T. IRVINE, AND C. W. JAMIESON
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SUMMARY

Above- and through-knee amputations have been performed in 126 patients at St. Mary's Hospital between 1961 and 1970.

Whilst there was a higher operative mortality amongst the above-knee amputees, the local complication rate was much higher in the through-knee group. The mortality rate in the two groups following discharge from hospital was high. The through-knee amputation provides a better functional result than the above-knee type but mobility in both groups might be improved by 'refresher courses' in walking training.

OVER the 10-year period from January, 1961, to December, 1970, both above- and through-knee amputations were performed by the Surgical Unit at St. Mary's Hospital. These operations were performed in consultation with the Limb Fitting Centre at Roehampton which had requested that through-knee amputations be performed on suitable patients, as it had been claimed that the procedure offered advantages over the above-knee amputation in morbidity and ease of rehabilitation. At the same time it was decided that a myoplastic technique should be used in above-knee amputations.

Table I.—NUMBER OF AMPUTATIONS PERFORMED AND THE SEX DISTRIBUTION

	TYPE OF AMPUTATION	
	Above-knee	Through-knee
No. of patients		
Unilateral	67	40
Bilateral	17	2
Total	84	42
Sex		
Male	87	38
Female	14	6
Total	101	44

All the patients in this series suffered from peripheral ischaemia. Eighty-four patients had above-knee amputations and 42 had through-knee amputations. The distribution of these patients as regards sex and whether amputation was unilateral or bilateral is shown in *Table I*. The age incidence (*Fig.* 1) of the amputees was very much the same in the two groups, except that there was a small group of young above-knee amputees who were victims of vascular trauma.

The patients with peripheral vascular disease, which was chiefly atheromatous, presented with either rest pain or gangrene. A few presented acutely with embolic phenomena. A significant number of the above-knee amputees had failed through- or below-knee amputations. The distribution of the presenting symptoms and signs is shown in *Table II*. On examination 82 per cent of the through-knee amputees had a palpable femoral pulse as opposed to 69 per cent of above-knee amputees.

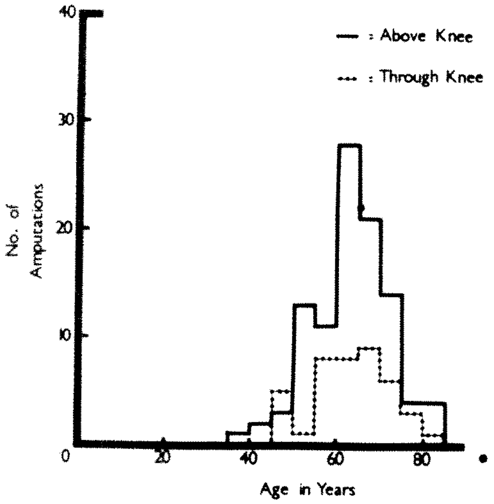

FIG. 1.—The age distribution of the amputees.

Table II.—PERCENTAGE DISTRIBUTION OF THE PRESENTING SYMPTOMS AND SIGNS

REASON FOR PRESENTATION	TYPE OF AMPUTATION	
	Above-knee	Through-knee
Peripheral vascular disease		
Rest pain	54	77
Gangrene	33	14
Embolus	3	9
Failed amputation		
Through-knee	7	—
Below-knee	3	—

Coexistent diseases have been divided into manifestations of generalized atheroma and other systemic diseases. The overall incidence of other vascular disease and the three most common individual manifestations of vascular disease are indicated together with the frequency of systemic diseases in *Table III*. The incidence of smoking in the amputees has also been included because it has an important relationship to atheromatous vascular disease, as shown by Larson, Haag, and Silvette (1961). About three-quarters of the patients in both groups were smokers, either at the time of the amputation or within the previous 10 years. Approximately half of the patients in both groups of amputees had been subjected to reconstructive surgery relating to the amputated limb before amputation was carried out, and this was evenly divided between disobliteration and by-pass in the two groups.

OPERATIVE TECHNIQUE

In the through-knee amputation the patella was preserved, the patella tendon being sutured to the cruciate ligaments, as proposed by Batch, Spittler, and McFaddin (1954). A slightly longer anterior than posterior flap was cut so that the resultant scar lay posteriorly. The wound was drained and firmly bandaged at the end of the operation. In the above-knee amputation the technique described by Dederich (1963) was used, flaps of equal length being made. The quadriceps femoris and the hamstring muscles were sutured over the end of the femur; again the wound was drained and firmly bandaged.

Table III.—PERCENTAGE INCIDENCE OF RELATED VASCULAR DISEASE AND OTHER SIGNIFICANT FACTORS

DISEASE	TYPE OF AMPUTATION	
	Above-knee	Through-knee
Vascular	43	55
Myocardial infarct	9	27
Angina	8	2
Cerebral ischaemia	8	7
Systemic		
Hypertension	28	27
Diabetes	10	12
Smoking	84	73

Table IV.—PERCENTAGE INCIDENCE OF POSTOPERATIVE MORTALITY AND MORBIDITY

	TYPE OF AMPUTATION	
	Above-knee	Through-knee
Mortality		
Unilateral amputation	13	5
Bilateral amputation	41	—
Delayed healing		
Sepsis and ischaemia	22	55
Flap necrosis	4	43
Reamputation	3	18

RESULTS

Mortality was twice as great in the above-knee as in the through-knee group amongst unilateral amputees. The death-rate was very much higher in bilateral above-knee amputees. This is shown in *Table IV* together with the incidence of local complications in the two groups.

The most prominent local complication following amputation was delayed healing which was due to either sepsis or ischaemia or a combination of the two. Many more of the through-knee amputees suffered flap necrosis than did their above-knee counterparts. The converse was true as regards infection. The predominant organisms causing infection in both groups were *Staphylococcus aureus* coagulase positive, *Staphylococcus albus*, and *Bacillus proteus*. However, in only 1 patient in whom *Staph. aureus* was isolated from the wound was *Staph. aureus* also found on the nasal swab. It will be seen from *Table IV* that the rate of delayed healing was over twice as high in the through-knee group of amputees as in the above-knee group. It is not surprising to find, therefore, that the rate of conversion of a through-knee amputation to the above-knee type was higher than the rate of reamputation in the above-knee group.

The average time from operation to discharge from hospital was approximately the same in both groups of unilateral amputees, namely 50 days in the case of above-knee amputees and 48 days in the case of through-knee amputees. In the bilateral group, however, the above-knee amputees spent twice as long in hospital as did their through-knee counterparts, above-knee amputees remaining in hospital for 141 days as opposed to 64 days in the case of the bilateral through-knee amputees. The average time taken to complete walking training on both temporary and permanent prostheses was very similar in both unilateral above- and through-knee amputees. In the case of the temporary prosthesis the through-knee amputees took 16 days as opposed to 19 days in the above-knee group. Similarly, on the permanent prosthesis the through-knee amputees took 9 days as opposed to 12 days for the above-knee amputees.

Eleven through-knee amputees were lost to follow-up. Of the remainder, 55 per cent of the patients had died in a mean follow-up period of 4·2 years. Of the above-knee amputees who were discharged from hospital, 17 were lost to follow-up. Thirty-four per cent of the remainder had died in a mean follow-up period of 5·9 years. The high late mortality of both groups is an indication of the severity of their associated vascular disease and may partly explain the high operative mortality.

Objective assessment of the walking ability both on the flat and on obstacles such as stairs of a group of above- and through-knee amputees who had completed their walking training on the permanent prostheses showed a much greater degree of freedom of movement in the through-knee group of unilateral amputees. The through-knee amputees were able to walk without aids such as sticks except on rough ground, whereas most of the above-knee amputees needed at least one stick at all times. Hitching of the prosthesis was much more evident in the above-knee group of amputees. All the through-knee amputees interviewed had had phantom limb pain, but some of the above-knee amputees were free of this complaint. It was intermittent in all cases and was rarely troublesome. All the patients in both the above- and through-knee groups showed deterioration in their walking ability since completing their walking training owing to the development of some bad habits as far as their walking technique was concerned.

DISCUSSION

In view of the high mortality of amputation great care should be exercised in the preparation of the patient. The postoperative mortality-rate of the through-knee amputation was lower than that of the above-knee amputation. Although these patients were not randomly sampled and therefore are not strictly comparable, the higher late mortality in the through-knee group than in the above-knee group and the similar age distribution and incidence of other diseases suggest that the amputees in the through-knee group were no fitter than those in the above-knee group. It is therefore suggested that the through-knee amputation is the safer operation. In common with other published series of amputations (Taylor, 1967) it has been found that the local complication rate is much higher in the through-knee group of patients. In our experience it is only necessary to make flaps of equal length in designing a through-knee amputation. The fashioning of a long anterior flap which has been recommended by Batch and others (1954) jeopardizes the blood-supply of the distal end of the flap and therefore enhances the likelihood of delayed healing of the wound. When equal flaps are cut the resultant scar still tends to lie posteriorly owing to the different elasticity of the patella and popliteal skin. It is therefore felt that the use of flaps of equal length may help to reduce the local complication rate in the through-knee amputation. The better walking ability of through-knee amputees suggests that when it is possible a through-knee amputation should be performed in preference to an above-knee amputation. In view of the deterioration in walking ability in both groups of amputees some form of 'refresher course' in walking technique might help to maintain mobility.

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THE EFFECT OF OBSTRUCTIVE JAUNDICE ON THE MIGRATION OF RETICULO-ENDOTHELIAL CELLS AND FIBROBLASTS INTO EARLY EXPERIMENTAL GRANULOMATA

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SUMMARY

Clinical and experimental evidence indicates that obstructive jaundice inhibits the healing of wounds. Experiments in the rat designed to investigate the migration of reticulo-endothelial and fibroblasts into experimental granulomata are described. Standard preparations of obstructive jaundice and controls were devised using Wistar rats. The effects of bile-duct obstruction and sham ligation are described. In another group of animals which was similarly prepared granuloma-pouch experiments were carried out by burying sterile cotton-wool pledgets of a known weight. These pledgets were removed from the jaundiced and control animals on the third, fifth, seventh, and ninth days after implantation, dried to remove the fluid component of the inflammatory process, and weighed on a microbalance. The weights were compared and it was found that a significant inhibition of weight increase occurred in the jaundiced animals during the first week, suggesting a delay in the migratory activity of reticulo-endothelial cells and fibroblasts.

A HIGH incidence of wound dehiscence and ventral herniation has been observed in patients in whom operations had been carried out to relieve obstructive jaundice (Lee, 1972). Experimental studies have shown that skin wounds in rats with obstructive jaundice were not able to resist a separating stress as well as wounds in control animals and it was deduced that this resulted from an abnormality of the process of collagen deposition. However, the exact mechanism by which jaundice interferes with this process is not known, nor whether other parts of the healing mechanism are affected. In particular, before collagen fibres are deposited in the ground substance the early stage of healing in man and animals is characterized by a massive infiltration and proliferation of reticulo-endothelial cells and fibroblasts into the wound (Schilling, 1968; Alexander, Bossert, McClellan, and Altemeier, 1971). The experiments described in the present paper were carried out to see whether obstructive jaundice interferes with the migratory activity of these cells and prevents their appearance in foreign-body granulomata.

STANDARD RAT OBSTRUCTIVE JAUNDICE PREPARATION AND CONTROLS

It was felt that the anaesthetic and operative trauma used to produce the obstruction might be additional factors other than the jaundice itself which would make normal animals unsuitable as controls. A standard technique of 'sham ligation' of the bile-duct was therefore used to produce a control group of animals.

Materials and Methods.—Three-month-old albino male Wistar rats (no strain number), weighing 250–300 g., were fed on a high-protein diet supplemented with ascorbic acid and vitamin K_1. The surgery was carried out under sterile conditions using anaesthetic ether administerd by the open method.

The chest and abdomen were shaved and each animal was fixed in a supine position on the operating table. The abdomen was cleaned with 1 per cent hibitane in alcohol and, when dry, the operating field was covered with a sterile Steridrape sheet. The abdomen was opened through a midline supra-umbilical incision. The rat has a mobile duodenum which can be brought out of the wound with little difficulty. Gentle traction of the duodenum to the right stretches the free border of the lesser omentum, and in it the two lowest hepatic ducts can be seen uniting to form a long, thin, common bile-duct which lies closely applied to the pancreas for most of its length (*Fig.* 1). The rat has no gall-bladder. The bile-duct was ligated just distal to the junction of the hepatic ducts and divided between ligatures. The abdominal wall was closed with interrupted silk sutures and the edges of the skin were approximated with a subcuticular silk stitch. Two animals died whilst under anaesthesia, but all the others recovered consciousness within 10 minutes after the ether had been discontinued.

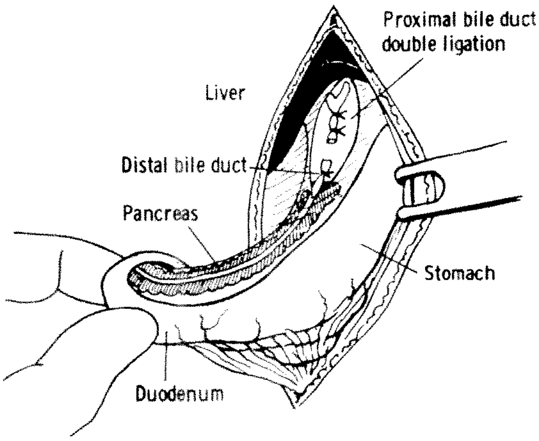

FIG. 1.—Point of ligation of the common bile-duct just distal to the junction of the common hepatic duct.

The control group of animals was prepared by a technique exactly similar to that outlined above except that the bile-ducts were not ligated or divided after being mobilized. Silk ligatures were passed around the duct and then removed. Particular care was taken to standardize the duration of anaesthesia (12 minutes) and the degree of operative trauma.

Wright and Braithwaite (1964) have doubted whether permanent obstruction of the bile-duct can be produced in the rat by ligation of the bile-duct because of 'new channels encircling the obstructed duct'. Restoration of bile secretion into the gut is said to occur within 12 days. The technique described above produced permanent obstructive jaundice in all except 1 animal in whom the ligatures were found to have slipped. Gross dilatation of the duct system proximal to the ligatures was invariably found when the obstruction was permanent. None of the animals became infected.

The Results of Bile-duct Ligation.—The results of obstructing the bile-duct were observed in a series of experiments and compared with the sham-ligated controls. Most animals in both the groups survived the first 6 weeks after surgery without becoming seriously ill. The skin of the obstructed animals became noticeably yellow within 2 weeks and the animals passed dark urine after the first few days. During the first 5 weeks there was no significant deviation of the graphs plotting the weight increases of the two groups of animals. Thereafter the weight of the rats in the control group increased above that of the jaundiced animals.

The serum albumin was measured in 5 normal and in 15 jaundiced rats, killed in groups of 3 at weekly intervals. In both groups the albumin remained within normal limits (*Table I*). Blood was also taken for haemoglobin and prothrombin estimations during the first 4 weeks after operation. One 4-week-jaundiced rat was found to have a low haemoglobin. After 5 weeks of jaundice the haemoglobin showed a tendency to fall below 13 g. per cent (*Table II*). In all the jaundiced animals the prothrombin time was adequately controlled by vitamin-K_1 administration.

Table I.—SERUM ALBUMIN IN NORMAL RATS AND IN JAUNDICED ANIMALS AFTER BILE-DUCT LIGATION

TIME AFTER BILE-DUCT LIGATION	SERUM ALBUMIN (g. per 100 ml.)		NO. OF MEASUREMENTS
	Average	Range	
Normal rats	2·4	1·8–3·2	5
1 week	2·2	1·8–2·4	3
2 weeks	2·6	1·9–3·1	3
3 weeks	2·4	1·9–2·9	3
4 weeks	2·4	2·0–2·6	3
5 weeks	2·6	2·0–3·0	3

Table II.—HAEMOGLOBIN LEVELS IN NORMAL RATS AND IN JAUNDICED ANIMALS AFTER BILE-DUCT LIGATION

TIME AFTER BILE-DUCT LIGATION	HAEMOGLOBIN (g. per cent)	NO. OF MEASUREMENTS
Normal rats	13·4	4
1 week	13·5	3
2 weeks	13·2	3
3 weeks	13·3	3
4 weeks	13·2	3
5 weeks	12·9	3

Thus, a group of jaundiced animals was produced whose health remained relatively normal for at least 1 month after duct ligation and in whom vitamin-C deficiency, anaemia, hypoproteinaemia, and clotting defects had not developed. Subsequent experiments were carried out 4 weeks after duct division or sham ligation—a time when the jaundice was maximal but the general health of the animal was well maintained.

EXPERIMENTS TO ASSESS MIGRATION OF RETICULO-ENDOTHELIAL CELLS OR FIBROBLASTS

Materials.—Dental cotton-wool pledgets manufactured by Johnson & Johnson of Slough were obtained from Messrs Claudius Ash & Sons, 26 Broadwick Street, London, W.1. As supplied the pledgets are non-sterile and 'dry' but it was found that a pledget could contain as much as 3 mg. of water after removal from the packing. Therefore the pledgets were placed in a drying oven at 60° C. for 24 hours to remove the water and the dried pledgets were weighed individually in an Oertling microbalance to the nearest 0·1 mg. Pledgets of identical weight were placed in a glass container for sterilization in a steam autoclave (Baird & Tatlock) at 120° C. and at 1060 g. per sq. cm. pressure for 1 hour. Sterile pledgets in their containers were then placed in a drying oven for 24 hours at 60° C. After drying, the caps of the containers were screwed tight and sealed until the pledgets were required for implantation in the animals.

Technique.—Fifty rats (25 jaundiced and 25 controls) were prepared by the technique outlined above. Twenty-eight days after the initial operation the rats were again anaesthetized and placed in a prone postion and the granuloma-pouch experiments were carried out under sterile conditions.

A 1·3-cm. incision was made across the midline in the skin above the tail. The skin edges were grasped with dissecting forceps and pouches were burrowed subcutaneously on both sides with a curved artery forceps. A sterile pledget of cotton-wool which had been prepared in the manner described above was pushed into each pouch. The incision was closed with a size-20 stainless-steel-wire suture which anchored the skin to the deep fascia. Groups of animals were anaesthetized on the third, fifth, seventh, and ninth days after the creation of the granuloma pouch and the incisions were reopened and the wool granulomata removed. The animals were then killed.

Table III.—Increase in Weight of the Granuloma Pouch in Jaundiced Rats after Bile-duct Ligation and in Control Animals

Time after the Creation of Granuloma Pouch	Jaundiced Rats		Control Rats		Statistical Analysis	
	Weight of Pledget (mg.)	No. of Experiments	Weight of Pledget (mg.)	No. of Experiments	*t*-Test	Level of Significance (per cent)
3 days	7·3 ± 0·6	12	7·8 ± 0·4	10	2·247	95
5 days	7·7 ± 0·9	10	10·0 ± 0·6	14	7·531	99
7 days	6·9 ± 0·8	10	9·4 ± 0·6	10	7·906	99
9 days	10·6 ± 0·9	14	10·3 ± 1·2	9	0·685	None

Each pellet was immediately placed in a siliconized tray and dried at 60° C. for 48 hours, after which time it was weighed to the nearest 0·1 mg. on a microbalance. The change in weight of each pledget was calculated by subtracting the weight before implantation from the final weight. The standard error of the mean of the weights of the pledgets from jaundiced and control animals was calculated. Forty-six satisfactory granulomata developed in the jaundiced animals and 43 in the controls. If pus was found the granuloma was discarded. The increase in weight of the pledgets was compared in the two groups of animals on the third, fifth, seventh, and ninth days after implantation.

Results of Granulomata Weighing Experiments (*Table III*).—The weight increase in the 3-day granuloma of the control animals was found to be higher than the increase in the jaundiced animals and the difference was significant at the 95 per cent range of confidence. A marked difference in weight between the two groups was noted on the fifth and seventh days, but by the ninth day both jaundiced and control animals had weight increases which were not significantly different.

DISCUSSION

The term 'reticulo-endothelial system' was coined by Aschoff and Kiyono (1913) to describe cells which stored vital dyes and took part in the inflammatory process. Fibroblasts have been excluded from the system although they play a very important role during healing (Downey and Weidenreich, 1912). Both reticulo-endothelial cells and fibroblasts migrate into foreign-body granulomata, particularly during the first week of their development, and it is possible that macrophages may be the precursor cells for fibroblasts under some conditions (Barnes and Kruschov, 1968). Selye (1953) devised a 'granuloma-pouch' technique to assay compounds which produce an inflammatory reaction. Croton oil was injected into a pneumatic pouch by the injection of air between the skin and the body wall. Meier, Schuler, and Desaulles (1950) implanted small cotton-wool pellets and then weighed the granulomata which developed. Quantock (1967) studied the microscopic changes during the development of such a granuloma within the cotton-wool and showed that the increase in the weight of the pledget resulted initially from the absorption of tissue fluid and thereafter mainly from the invasion of migrating cells.

In the present experiments a significant inhibition of the expected increase in weight of experimental granulomata was noted in rats with obstructive jaundice when compared with the control animals. The difference in weight of the two groups increased during the first week but by the ninth day no significant difference was found.

CONCLUSION

The results of granuloma-weight experiments suggest that there exists a delay of migration of reticulo-endothelial cells and fibroblasts during the first week of the development of a cotton-wool granuloma in the presence of obstructive jaundice. The abnormality may reflect a defect of cell migration or a decreased availability of such cells during the early part of the inflammatory process in the jaundiced animals. The deficiency in cellular components could account for at least some of the impaired healing which is observed in jaundiced patients.

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THE EFFECT OF CLOTHING ON THE DISSEMINATION OF BACTERIA IN OPERATING THEATRES*

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SUMMARY

The effect of different types of clothing in modifying the dissemination of bacteria was studied in an experimental chamber, using a slit-air sampler to quantify the aerial contamination. Observations were made on volunteers wearing conventional operating-theatre clothing, outdoor clothing, and specially designed theatre wear, both with and without a gown, mask, cap, and boots in all three groups.

The results showed that aerial contamination was least when outdoor clothing was worn. The addition of a sterile theatre gown, mask, cap, and boots reduced this dissemination by half in all the groups. Leaving aside considerations of comfort and hygiene of the staff, it is concluded that outdoor clothing need not be removed before entering an operating theatre (or clean area) provided that a gown, mask, etc., are worn.

THE presence of persons in an operating theatre causes dissemination of bacteria into the environment and this is increased by traffic in the theatre (Blowers, Mason, Wallace, and Walton, 1955). An attempt to reduce this dissemination by modifying operating-theatre wear led to the present study.

The ritual of changing into clean clothes before operating is undertaken for two reasons—the comfort of the wearer and the reduction of bacterial contamination. Duguid and Wallace (1948) found that standard theatre wear did not prevent dissemination of bacteria, but when all the theatre staff wear trousers dissemination is decreased (Bernard, Speers, O'Grady, and Shooter, 1965). Although a correlation between airborne bacteria and wound sepsis has not been proved (Martin, 1967) it is generally assumed that the limitation of bacterial dissemination in the theatre would be worth while. The role of clothing in relation to the dissemination of bacteria into the air has been studied.

MATERIALS AND METHODS

The investigation consisted of determining the bacterial dissemination with various types of clothing under experimental conditions. An experimental polythene tent (560 c.ft.) gave an enclosed but not airtight environment in which to determine the dissemination of bacteria by volunteers (*Fig.* 1). A Casella slit-air sampler (Bourdillon, Lidwell, and Thomas, 1941) was used to determine the aerial contamination quantitatively. Air (at the rate of 1 litre per minute) was drawn through the funnel of the sampler by a soundproof electrical pump on to a revolving blood-agar plate 1 mm. below the slit. The blood-agar plates were incubated at 37° C. overnight and all colonies grown were counted.

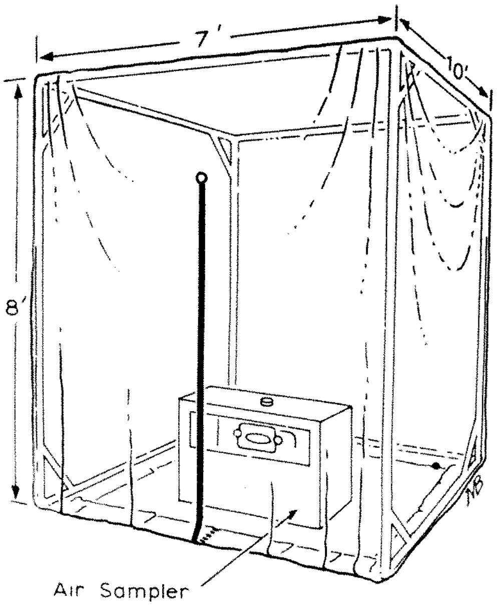

FIG. 1.—The experimental tent with the sampler in situ. Entrance is gained through a long zip in one side of the tent.

Three types of clothing were investigated to determine the amount of bacterial dissemination allowed into the environment:—

1. Outdoor clothing, i.e., ordinary everyday clothing (excluding overcoats).
2. Standard theatre wear consisting of an Aertex shirt and cotton trousers or a short-sleeved cotton shift dress.
3. Specially designed theatre wear. This consisted of thick-weave cotton vests with elastic armbands and cotton trousers with elastic at the waist and anklebands; or a thick-weave cotton frock with draw-string waist and armbands worn over cotton bloomers with elastic at the waist and drawstrings at the thighs (*Fig.* 2). Experiments were carried out with and without the addition of a sterile surgical gown, mask, cap, gloves, and boots.

Control sampling was carried out for 10 minutes when the tent was empty. A volunteer wearing one of the types of clothing then performed a standard exercise in the experimental tent for a further 10-minute sample period. After an hour, during which it was found that the aerial bacterial count fell to almost the control reading, another 10-minute standard exercise period in the tent was sampled while the volunteer wore another type of clothing. This was followed by an hour's rest period, a 10-minute control sample period, and a final 10-minute exercise sample period with the volunteer wearing the third type of clothing. The order of wearing the three types of clothing was random. A further, smaller series of observations was made with volunteers wearing either outdoor clothing or swimsuits.

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* Based on a communication to the Association of Surgeons of Great Britain and Ireland in April, 1968. Part of a thesis which was awarded the degree of Ch.M. by the University of Dundee, 1970.

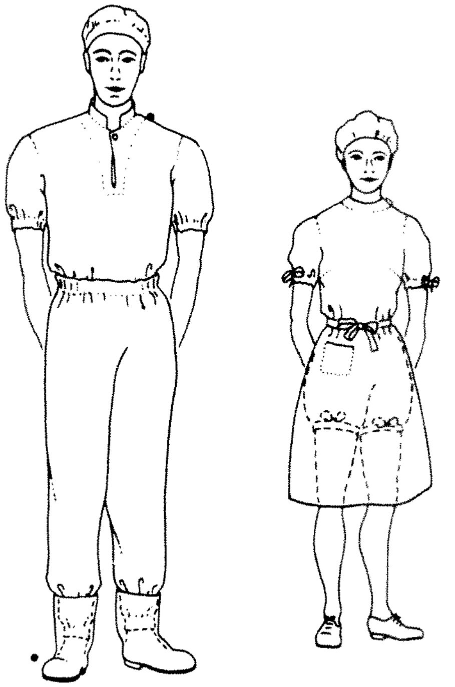

FIG. 2.—The specially designed theatre clothing for both sexes.

RESULTS

Air Sampling in the Experimental Tent.—In the first series of 20 experiments standard exercises were carried out in the tent by a volunteer wearing the three types of clothing in turn; the background colony counts were low, so that a low constant control environment was maintained (*Fig.* 3). Although there was a wide range of results from individual to individual, a difference between the three types of clothing was observed. With outdoor clothing a mean value of 29 colonies per plate per 10 minutes (range, 8–166) was obtained, compared with 72 colonies when our special theatre clothing was worn (range, 8–240), and 73 colonies with standard theatre wear (range, 10–320). Thus, no significant difference in the dissemination of bacteria into the air by either type of theatre wear when worn without gowns was noted ($P > 25$), but there was significantly less dispersal of bacteria with everyday clothing ($P < 0{\cdot}01$).

If in addition to the freshly laundered theatre clothing a sterile gown, mask, cap, gloves, and boots were worn over the clothing, there were variations in the results. During the control periods the counts were again low in these 16 experiments (*Fig.* 4); the lowest mean value for bacterial colony counts under these conditions was obtained when standard theatre clothing was worn, i.e., 16 colonies (range, 4–35). Bacterial dissemination with everyday clothing gave a mean value of 20 colonies per plate (range 6–40), while special theatre clothing allowed a high number of colonies to be dispersed—a mean value of 41 colonies (range 16–99). A significantly higher dissemination of bacteria occurred when special theatre clothing was worn under gowns as opposed to outdoor clothing or standard theatre wear as undergarments ($P < 0{\cdot}01$). If comparisons are made between each type of clothing, with and without gowns, there was a significant decrease in the dissemination of bacteria if gowns were worn over either type of theatre wear ($P < 0{\cdot}01$) (*Fig.* 5). The addition of gowns to outdoor clothing reduced dissemination to a lesser degree ($P < 1$). The reduction in dissemination varied from 32 per cent when outdoor clothing

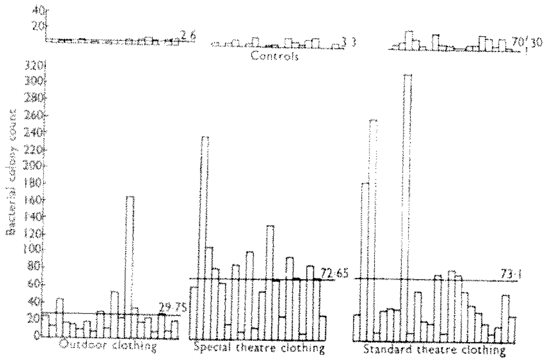

FIG. 3.—The effect of various types of theatre clothing without gowns on aerial contamination. Each block consists of one experiment. Figures indicate mean value. The controls at the top of the figure refer to the control sampling prior to the test period indicated directly below it.

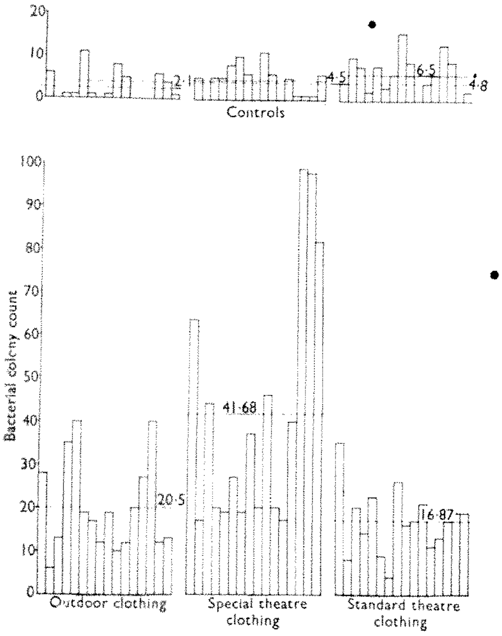

FIG. 4.—The effect of various types of theatre clothing with the addition of sterile gowns, caps, and masks on aerial contamination.

was the undergarment to 42 per cent when special theatre clothing was under the sterile gown, and 77 per cent when standard theatre clothing was the undergarment. It must be remembered that there was no significant difference in the dispersal of organisms when either outdoor clothing or standard theatre clothing was worn with sterile gowns and masks.

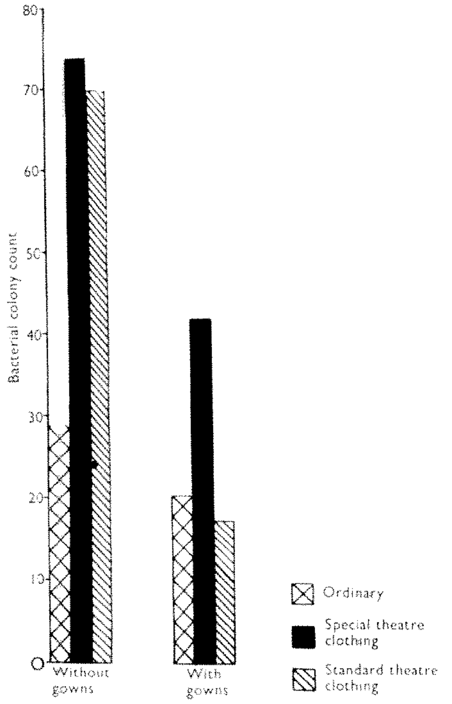

FIG. 5.—Comparison of mean values of aerial contamination for volunteers with and without sterile gowns and masks.

To determine the actual dissemination of bacteria on skin scales when little or no friction is involved a further series of 20 experiments was carried out in the tent. Sampling was performed while volunteers wore either swimsuits or everyday clothing (*Fig.* 6). Background colony counts were again low. Studying the results from the whole group, there was a significantly increased bacterial dispersal when outdoor clothing was worn ($P < 0.02$). However, if males are excluded from the study there was no difference in bacterial dispersal (i.e., swimsuits, 10 colonies per plate; outdoor clothing, 12 colonies per plate). The dispersal of bacteria when wearing swimsuits was similar in both males and females, whereas women in outdoor clothing dispersed fewer bacteria than males similarly clad. However, the numbers in the series were small and further work is necessary to elucidate the results.

DISCUSSION

Activity accentuates the dissemination of bacteria on skin scales (Davies and Noble, 1962). This dispersal of bacteria is not prevented by standard theatre wear and only reduced by 50 per cent by the wearing of sterile theatre gowns (Duguid and Wallace, 1948). The findings in the present study reassert these conclusions, except with regard to theatre gowns worn over standard theatre clothing when the reduction was of the order of 70 per cent. With outdoor clothing under gowns the reduction in dispersal was only 30 per cent. Various attempts have been made to reduce this bacterial dissemination into the environment by operators; the more successful results have been with the use of trousers in the theatre (Bernard, Cole, and Gravens, 1967) and the wearing of a boilersuit type of theatre wear (Blowers and McClusky, 1965).

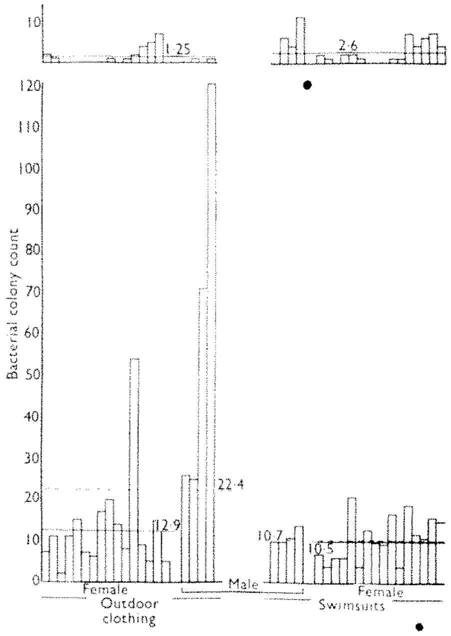

FIG. 6.—Comparison of mean values of aerial contamination for male and female volunteers wearing either swimsuits or outdoor clothing.

Our own design of theatre wear with the addition of bloomers rather than trousers proved less effective in reducing bacterial contamination of the atmosphere. It is likely that the friction of the freshly laundered theatre clothing allowed dissemination of the bacteria-laden skin scales in a similar manner to the counterpane effect demonstrated by Rubbo, Stratford, and Dixson (1962), a view supported by the swimsuit study since, despite extensive skin exposure, there was less contamination. The more numerous layers of outdoor clothing of differing weave material might act to prevent dispersal of scales and so account for the low colony counts for aerial contamination. The abnormal high dispersal with male volunteers in outdoor clothes could be due to the fact that males change their clothing less frequently than females, and so tend to have more scales accumulated in their clothing which if disturbed by friction would increase bacterial liberation. When swimsuits were worn the results for the male were the same as those for the female, indicating again the relationship of friction, scale detachment, and bacterial contamination.

As yet there is no ideal theatre wear that is comfortable, easy to wear, and efficient in preventing the dispersal of bacteria (Medical Research Council, 1968). There would appear to be little value in outine changing into theatre wear apart, perhaps, rom the wearing of sterile surgical gowns, caps, masks, and footwear; although this would seem ufficient for visitors and in special units, it is advisble from the personal hygiene viewpoint for the urgeon to change into fresh clothing.

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HETEROLOGOUS LIVER PERFUSION

A COMPARISON OF THE USE OF LIVERS FROM FOUR DIFFERENT SPECIES

BY R. HICKMAN, J. R. PARKER, S. J. SAUNDERS, N. E. GOODWIN, AND J. TERBLANCHE

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SUMMARY

Isolated perfusion of livers from calves, pigs, and ambs with human blood resulted in thrombocytopenia within 30 minutes of the establishment of the circuit. No rebound of platelet levels was noted during a urther 3½ hours of perfusion. The levels of total complement and the heterophile antibody titres dropped during the same time in all the experiments. Levels of lymphocytotoxic and leuco-agglutinating antibodies decreased in blood perfusing lamb and pig livers but these were not measured in the calf-liver perfusions.

In contrast, isolated perfusion of livers from baboons with human blood did not provoke significant thrombocytopenia and the results of perfusion were similar to those noted in homologous perfusions of the pig liver with pig blood. There were no differences in platelet levels using livers from baboons with blood groups either compatible or incompatible with the human blood. Complement levels and heterophile antibody titres did not drop and no lymphocytotoxic or leuco-agglutinating antibodies were detectable in human blood against baboon cells.

Measurement of electrolytes, glucose, aspartate transaminase, plasma haemoglobin, and lactate and ammonia clearance showed no significant difference in perfusions of the baboon liver when compared with perfusions of the pig liver with pig blood.

Based on these results, clinical hepatic assist procedures in this hospital will in future only be performed with livers from baboons. These animals will be kept in isolation for a period of virological study in order to minimize the hazard of virus transmission to the patient or personnel.

LIVERS from various animals have been used for hepatic assist procedures in patients with acute liver failure. These include the pig (Abouna, Ashcroft, Muckle, Skillen, Hull, Kirkley, and Hudson, 1970), the calf (Vang and Drapanas, 1966), the baboon (Abouna, Boehmig, Serrou, Amemiya, and Martineau, 1970; Abouna, Fisher, Still, and Hume, 1972), and the human (Sen, Bhalerao, Parulkar, Samsi, Shah, and Kinare, 1966). Recent investigations in this laboratory (Hickman, Saunders, Goodwin, and Terblanche, 1971; Hickman, Parker, Saunders, and Terblanche, 1972) showed that marked thrombocytopenia occurred within 30 minutes of commencement of perfusion of the isolated pig liver with human blood. No subsequent increase in platelets was noted. In addition, complement levels and heterophile antibody titres decreased and lymphocytotoxic and leuco-agglutinating antibodies disappeared during this period. Similar observations had been made in perfusions of the kidney with xenogeneic blood (Pineo, Regoeczi, and Dempster, 1970), but not with the liver.

The thrombocytopenia which had caused clinical assist procedures to be abandoned in this unit (Hickman, Saunders, Harrison, King, and Terblanche, 1971) was thought initially to be due to the inclusion of a bubble oxygenator in the circuit (Hickman, Saunders, and Terblanche, 1969). After investigation in homologous perfusions (Hickman, 1972) further studies were performed with human blood and pig livers and the marked decline in platelets was noted. Since the calf and the lamb had also been used by others for experimental perfusion studies, livers from these animals were perfused with human blood to detect any altered response. In addition, the livers of baboons were investigated. The latter animals may be blood grouped according to the human ABO system using saliva specimens (Wiener and Moor Jankowski, 1963) and the effect of perfusion of the liver with human blood of compatible or incompatible groups was investigated.

MATERIALS AND METHODS

Livers from young calves, lambs, and baboons were removed in a similar manner to that described for the pig liver (Hickman and others, 1969). The organs were flushed with 2 litres of Krebs Ringer bicarbonate solution modified according to Dawkins, Judah, and Rees (1959). The volume distribution through the portal vein was 1·75 litres and through the hepatic artery 0·25 litre. The temperature of this solution was 38° C. (rather than 4° C. as has previously been reported), which appeared to cause a more diffuse wash-out of the liver.

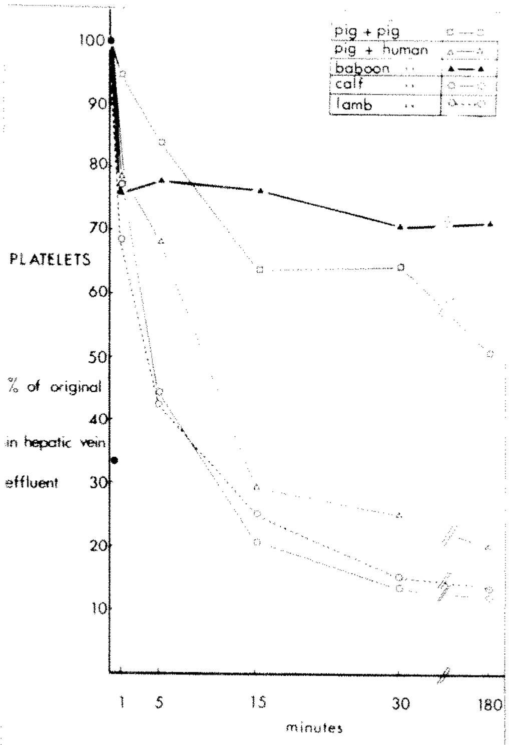

FIG. 1.—The levels of platelets (calculated as a percentage of the initial perfusate level and corrected for small variations in haematocrit) during the perfusion of various animal livers with heterologous and homologous blood.

The organs were inserted into a circuit which was pre-primed with 0·25 litre of McCoy's medium 5A (Hyland Laboratories) and 1·1 litres of fresh heparinized human blood. The mean temperature of the livers upon insertion into the circuit was 26° C. After initial sampling, perfusion was commenced and the livers were warmed rapidly, reaching 38° C. within 15 minutes. During the 4-hour perfusion a continuous infusion was maintained of 150 ml. of 5 per cent dextrose water to which was added 100 U. of soluble insulin, 21 U. of secretin (Boots), and 200 mg. of deoxycholate (Decholin, British Drug Houses) to promote choleresis. Alpha-oxo-glutarate (15 mM.) was added to the flushing solution, the perfusion prime, and the infusion according to the work of Dawkins and others (1959).

Biochemical investigations included the measurement of electrolytes, glucose, aspartate transaminase, ammonia, urea, and lactate/pyruvate ratios, and acid-base analyses, as has previously been described (Hickman, Saunders, Simpson, and Terblanche 1971). Platelets and leucocytes were counted visually by standard techniques, and total complement lymphocytotoxic (Kissmeyer-Nielsen and Kjerbye 1967), leuco-agglutinating antibodies (Boyum, 1968) and heterophile antibodies (Rapaport, Kano, and Milgrom, 1966) against the rat, guinea-pig, and pig were measured. Samples were taken at 1, 5, 15, and 30 minutes, and 1, 2, 3, and 4 hours after perfusion had commenced. After 3 hours a dose of sodium lactate (3·5 g.) and ammonium citrate (2·0 g.) was given and additional samples were taken to determine the rates of clearance.

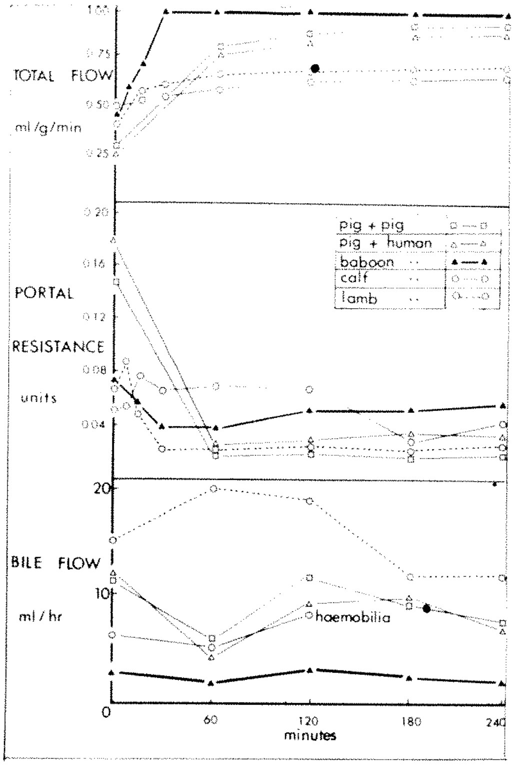

FIG. 2.—The total flow rates, portal resistance, and bile-flow rates during the perfusion of various animal livers with heterologous and homologous blood.

During perfusions the liver was moved rhythmically up and down by mechanical oscillation of the diaphragm.

Three calf and 3 lamb livers were perfused with human blood of group A; 4 baboon livers were perfused with human blood of a compatible group and 5 were perfused with blood of an incompatible group. The latter combinations were livers from groups A, B, and AB animals with human blood of group O, and livers of group B or AB with blood of group A. Human blood of group B is scarce and was not used.

RESULTS

No differences were observed when incompatible human blood was used in baboon-liver perfusions nd hence all the results with baboon livers are combined in the graphs. The following graphs represent the comparative results of the 4-hour perfusions of various animal livers with human blood. The previous results obtained in homologous perfusions of the pig liver with pig blood are presented for comparison.

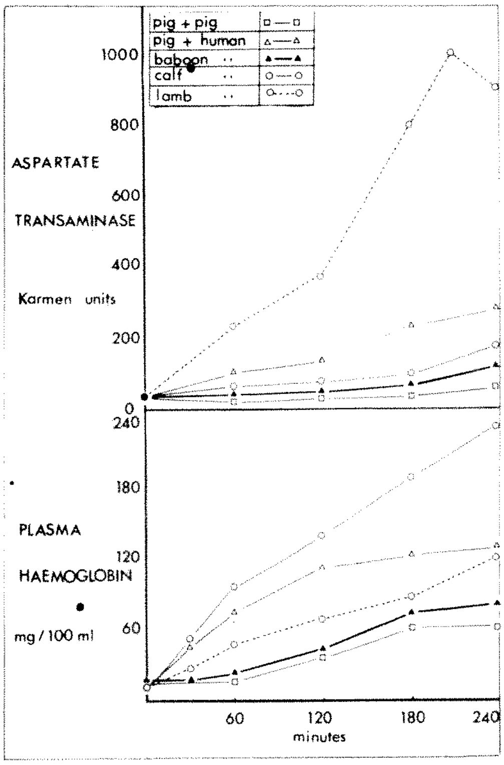

FIG. 3.—The levels of aspartate transaminase and plasma haemoglobin during the perfusion of various animal livers with heterologous and homologous blood.

Table I.—THE PERCENTAGE DECREASE IN COMPLEMENT AND THE PRESENCE AND ABSENCE OF ANTIBODIES DURING THE PERFUSION OF LIVERS FROM DIFFERENT SPECIES

SPECIES OF LIVER	COMPLEMENT (percentage decrease)	ANTIBODIES			
		Heterophile		*Lymphocytotoxic and Leuco-agglutinating*	
		Before Perfusion	After 30 Minutes' Perfusion	Before Perfusion	After 30 Minutes' Perfusion
Pig	28	+	±	4 +	1 +
Calf	47	+	±	N.M.	N.M.
Lamb	40	+	±	4 +	1 +
Baboon	12	+	+	0	0

N.M., Not measured.

The levels of platelets in the hepatic vein samples, calculated as a percentage of the initial perfusate value and corrected for small variations in haematocrit, are shown in *Fig.* 1. A significantly lesser thrombocytopenia accompanied perfusion of the baboon liver with both compatible and incompatible blood ($P < 0{\cdot}001$). The slight decrease seen was similar to that observed in perfusions of the pig liver with pig blood.

In *Table I* it can be seen that the percentage decrease in the complement levels was significantly less when baboon livers were perfused with human blood, and that lymphocytotoxic and leuco-agglutinating antibodies were not detected in human blood against baboon cells. Similarly, heterophile antibodies were not reduced during perfusion. In perfusions of the pig, lamb, and calf livers a marked reduction occurred in the complement and antibody levels. It was found impossible to measure lymphocytotoxic and leuco-agglutinating antibodies in human blood against calf cells owing to an inability to separate lymphocytes and leucocytes from calf blood by standard techniques.

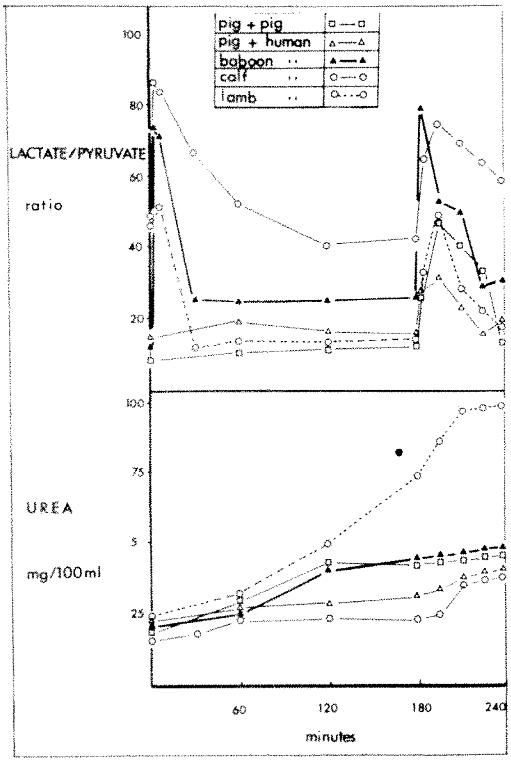

FIG. 4.—The changes in the lactate/pyruvate ratio and the levels of urea during the perfusion of various animal livers with heterologous and homologous blood.

In *Fig.* 2 total flow rates, the portal resistance, and bile-flow rates are shown. It is notable that only in the perfusions of the baboon liver with human blood was the arbitrary optimal rate of flow of 1·0 ml. per g. per minute achieved. This occurred within 30 minutes. The portal resistance in all the experiments was within the suggested 'normal' limits (Eiseman, Knipe, Koh, Normell, and Spencer, 1963) after 1 hour of perfusion. The bile-flow rate from the baboon livers was considerably slower than that in the other liver perfusions, but this might be related to the very small size of the animals (7–10 kg.) since a similar rate was noted intraoperatively.

The rapid rate of bile secretion in the perfusions of the lamb liver and the development of gross haemobilia in the perfusions of the calf liver are notable observations.

The levels of aspartate transaminase and plasma haemoglobin are shown in *Fig.* 3. In all the perfusions except those of the lamb liver the levels of aspartate transaminase did not rise above 300 Karmen units. In the perfusions of the lamb liver a mean final level of 1000 Karmen units was reached. In the perfusions of the calf liver a rapid rise in plasma haemoglobin to 230 mg. per 100 ml. occurred, but in other experiments the highest mean level was 120 mg. per 100 ml.

Fig. 4 illustrates the change in the lactate/pyruvate ratios and the levels of urea. In all the perfusions except those of the calf liver the load of lactate was cleared to preadministration levels within 1 hour. There was a similar increase in urea after the administration of ammonia in all the experiments except those using the lamb liver, where a marked increase occurred.

DISCUSSION

The results show that the isolated baboon liver perfused with either compatible or incompatible human blood does not provoke a significant thrombocytopenia, whereas perfusion of livers from calves, lambs, or pigs resulted in a marked fall in platelets within the first 30 minutes of perfusion. In addition, no obvious adverse biochemical, haematological, or immunological results were noted when the baboon liver was perfused with human blood. When livers from other species were used other evidence of liver damage was noted. Haemobilia occurred during perfusion of the calf liver and a major increase in aspartate transaminase was found during the perfusion of lamb livers. These detrimental effects taken in conjunction with the marked fall in platelets make the use of livers from these animals for clinical assist less desirable in our judgement.

The baboon has previously been used for cross-circulation (Saunders, Terblanche, Bosman, and Barnard, 1969; Hume, Gayle, and Williams, 1969) and no immunological reactions were observed. In addition, experiments in this laboratory have shown that baboons having a total volume replacement with human blood survive normally for 4 days. Only thereafter is there evidence of biochemical and haematological damage (Bosman, 1972). The use of the baboon liver for hepatic assist has been reported with no apparent immunological complication (Abouna and others, 1972).

Thus, in this unit clinical hepatic assist will again be offered as treatment for fulminant hepatic failure, but the livers will be taken from baboons rather than from pigs, calves, or lambs. Owing to the hazard of transmission of virus either to the patient or to personnel (Siegert, 1969) no animal will be used until it has been kept in isolation for 6 months and has been proved repeatedly negative to virological studies.

Acknowledgements.—We wish to acknowledg the continued interest and support of Professo J. H. Louw, Head of the Department of Surgery University of Cape Town. Expert technical assistanc was rendered by Mesdames M. Cox and J. Fourie Messrs. G. H. C. Engelbrecht and S. E. Abbott, an the staff of the J. S. Marais Surgical Laboratory Financial support was received from the Medica Research Council of South Africa, the Cape Provincia Administration, the Round Table Organization o South Africa, the Harry Crossley Foundation, an the C. L. Herman Bequest to the University o Cape Town.

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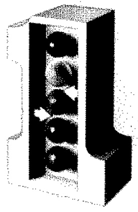

First in Bronchitis

double blockade of bacterial metabolism means resistance is unlikely to develop

ECTOPIC THYMIC TISSUE PRESENTING AS A LATERAL CERVICAL SWELLING

By D. R. A. FINCH and M. H. GOUGH
THE RADCLIFFE INFIRMARY, OXFORD

SUMMARY

Two infants presented with a swelling inferior to the angle of the mandible. At exploration both swellings were identified macroscopically and by frozen section as normal thymic tissue. In the light of present knowledge of the function of this gland in this age-group excision was not performed.

THE thymus is derived embryologically from the ventral outgrowths of the third, and possibly fourth, branchial cleft. As with the thyroid and parathyroid glands aberrations of migration may occur, and thymic tissue has been reported in situations as varied as the base of the skull and the mediastinum at the tracheal bifurcation (Hagens, 1932; Castleman, 1955).

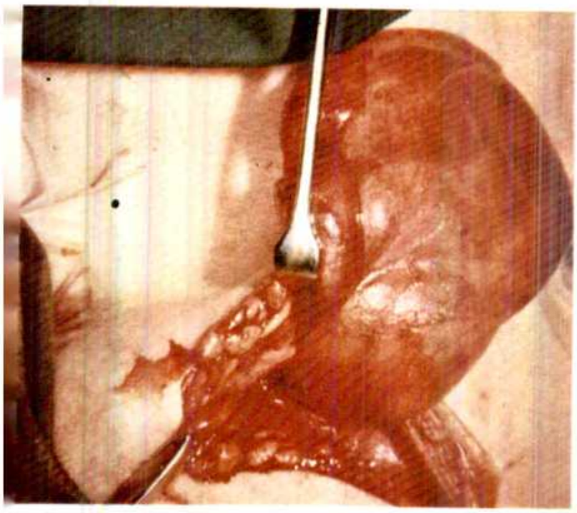
FIG. 1.—*Case* 1. The encapsulated fleshy mass at exploration.

In 1969 Barrick and O'Kell reviewed the literature relating to thymic tissue as a cause of swelling in the neck in childhood and found 43 cases, 40 of which were of thymic cysts and only 3 of normal thymic tissue.

We have recently seen 2 infants presenting with a mass inferior to the angle of the mandible and at exploration both masses proved to be normal thymic tissue.

CASE REPORTS

Case 1.—A. H. was noticed at birth to have a swelling 'the size of a grape' on the right side of the neck. At the age of 4 months the lump was more prominent and was explored under a general anaesthetic. An encapsulated fleshy mass approximately 7 × 5 × 2 cm. was found beneath the platysma, below the angle of the right mandible, and in front of the internal carotid artery, with a vascular pedicle running medially towards the thyroid cartilage (*Fig.* 1). Frozen section revealed normal thymic tissue. The lump was returned to the neck and the skin was closed. A subsequent chest radiograph failed to show a thymic shadow in the mediastinum (*Fig.* 2).

Case 2.—S. H. was noticed shortly after birth to have a swelling 'the size of a gooseberry' below the angle of the right mandible. This was explored at the age of 8 weeks, and a mass approximately 4 × 3 × 3 cm. resembling normal thymic tissue was disclosed (*Fig.* 3). Again, frozen section revealed normal thymic tissue and the lesion was returned to the neck. On this occasion, however, a chest radiograph taken postoperatively showed the presence of a thymic shadow in the anterior mediastinum (*Fig.* 4).

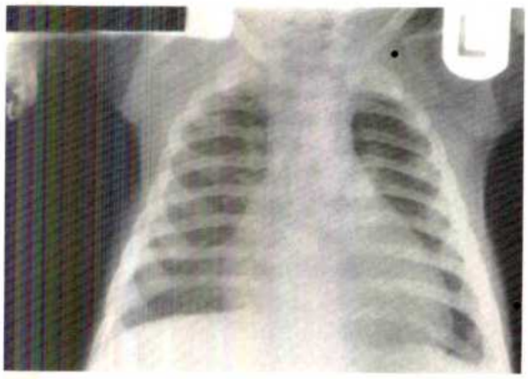
FIG. 2.—*Case* 1. Chest radiograph showing the absence of a thymic shadow in the mediastinum.

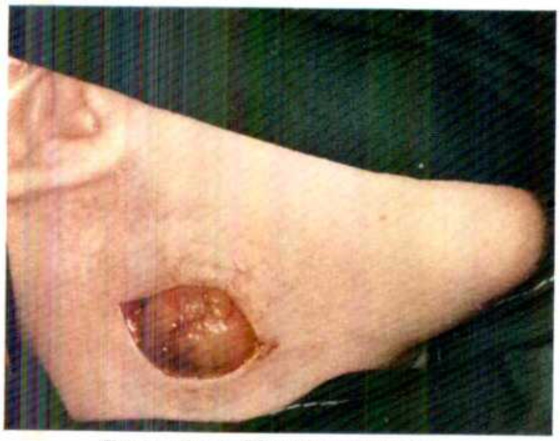
FIG. 3.—*Case* 2. The mass at exploration.

DISCUSSION

The differential diagnosis of a lump in the neck rests between a branchial cyst, a cystic hygroma, or possible malignancy. If there is any doubt on clinical examination exploration is justified at this early age.

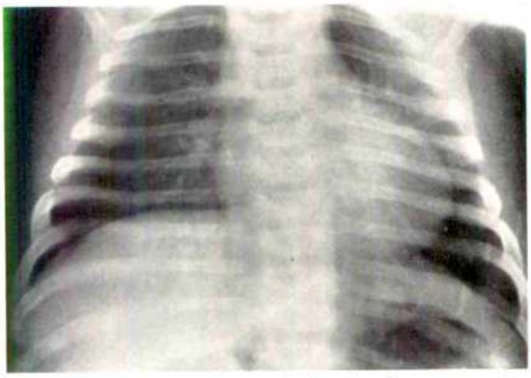

FIG. 4.—*Case* 2. Chest radiograph showing the presence of a thymic shadow in the anterior mediastinum.

It has been well established that the thymus plays an important part in the development of immunological competence. Goldstein and Mackay (1969) in *The Human Thymus* suggest that the stem-cell precursors of the lymphocytes are produced in the bone-marrow, enter the thymus and multiply, and there attain full immunological competence. Any cells which are reactive against the host's own tissues are recognized as such by the thymus and destroyed. The reminder leave the thymus and enter the general circulation through the efferent lymphatics.

Thymectomy in newborn mice results in a rapid reduction of the number of circulating lymphocytes and in depression of the cell-mediated immunological responses, as demonstrated, for example, by failure to reject a skin homograft (Miller, 1962). Thymectomy in other than the neonatal period produces less pronounced effects, but even in the adult mouse, although there is no immediate change, the circulating lymphocyte level and size of the lymph-nodes and spleen have been found to fall after 6 months, and an immunological deficiency develops as demonstrated by the antibody response to bovine serum albumin (Taylor, 1965).

It is not yet known whether these results also refer to man, but there is some evidence that the effects of thymectomy are less in species such as man and dog whose lymphatic system is better developed at birth (Fisher, Fisher, Lee, and Sakay, 1965).

As it is not possible easily to determine whether an ectopic thymic mass represents the whole or only part of the infant's thymic tissue we feel that it is important not to remove this tissue, and in this view we have been supported by the clinical immunologists with whom we have discussed the problem.

The prominence of the thymic swelling can be expected to diminish with growth of the facial skeleton and later with the normal involution of the thymus itself, and this reassuring information can be confidently imparted to the parents once a firm histological diagnosis has been made.

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TWENTY-FOUR-HOUR PRESERVATION OF CANINE KIDNEYS EXPOSED TO 45 AND 60 MINUTES OF WARM ISCHAEMIA

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SUMMARY

This investigation was designed to test the ability of a new hyperbaric organ preservation system to preserve canine kidneys for 24 hours after they had been subjected to significant periods of warm ischaemia. In group I (45 minutes of warm ischaemia) all the kidneys functioned well, and the mean maximum serum creatinine was 4·4 ± 1·7 mg. per 100 ml. In group II (60 minutes of warm ischaemia) 1 dog died on account of acute tubular necrosis. Th mean maximum serum creatinine was 5·4 ± 4·02 mg per 100 ml. The results indicate that hyperbari oxygen warrants serious consideration as an adjunc to organ preservation.

IT is now possible to preserve canine and porcin kidneys for 24–72 hours by a variety of means and t achieve consistent success, provided that the kidneys have been removed under optimal conditions (Belzer, Ashby, and Dunphy, 1967; Collins, Bravo-Shugarman, and Terasaki, 1969; Snell, Hopkinson, and Shepherd, 1972), but attempts to preserve kidneys that have been subjected to a significant period of warm ischaemia prior to preservation have been less successful. Simple surface cooling even for short periods has resulted in sporadic success (Pena, Millard, and Calne, 1971; Quin, Calman, Macpherson, Wood, Deane, McLaughlin, and Bell, 1972). Initial perfusion followed by surface cooling has been no more successful (Frost, Ackermann, Finch, and Manlove, 1970; Scott, Stephens, Keaveny, Kountz, and Belzer, 1971) except where the donor has been pretreated with vasoactive drugs (Løkkegaard, Bilde, Gyrd-Hansen, Nerstrom, and Rasmussen, 1971). Success has, however, been achieved using pulsatile hypothermic perfusion with oxygenated perfusate (Scott and others, 1971; Johnson, Anderson, Morley, Taylor, and Swinney, 1972).

MATERIALS AND METHODS

Mongrel dogs weighing 15–25 kg. were anaesthetized with thiopentone and intubated. Anaesthesia was maintained with an oxygen/nitrous oxide/halothane mixture. The right kidney was exposed through a subcostal incision and mobilized completely. After division of the ureter the renal artery and vein were ligated in continuity. The kidney was replaced in the abdomen and covered by bowel and omentum after which the wound edges were approximated. Forty-five minutes later (group I) or 60 minutes later (group II) the renal artery and renal vein were divided and the kidney was removed. The renal cortex temperature at the end of the ischaemic period was measured with a thermistor probe (Light Laboratories, Model 3GID) and found to be in the range 36–37° C. Phenoxybenzamine, 2·5 mg. in 0·5 ml. of physiological saline, was injected into the renal artery after cannulation. The kidney was placed in a bag surrounded by melting ice and perfused for 5 minutes from a height of 1 m. with a chilled Dextran 40/electrolyte solution (*Table I*). The kidney was then transferred to a Vickers' preservation unit.

Table I.—PERFUSATE COMPOSITION

Substance	*Quantity per litre*
KH_2PO_4	2·05 g.
K_2HPO	7·40 g.
KCl	1·12 g.
$NaHCO_3$	0·84 g.
Dextran 40	50 g.
Dextrose	25 g.
Procaine HCl	100 mg.
Chlorpromazine	16 mg.
Phenoxybenzamine	25 mg.
Heparin	5000 U.
Osmolarity adjusted to 320 ± 5 units with glucose	
*p*H at 20° C.	7·4

After 24 hours the dog was reanaesthetized and a midline abdominal incision was made. The contralateral kidney was excised and following a further injection of 2·5 mg. phenoxybenzamine into the right renal artery the kidney was reimplanted into the iliac fossa, anastomosing the renal artery end to end to the iliac artery and the renal vein end to side to the iliac vein. The ureter was implanted into the bladder using a simple cystotomy and fish-mouth technique.

During the nephrectomy operation 1 litre of dextrose saline was infused intravenously, less than 250 ml. being given prior to ligation of the vessels. In the implantation operation 1·5 litres of dextrose saline and 100 ml. of 10 per cent mannitol solution were infused. Postoperatively the dogs were allowed to drink water *ad libitum* and feeding was commenced on the second postoperative day. Dextrose saline was infused subcutaneously only if vomiting was profuse.

The serum creatinine was estimated daily for 14 days and three times a week thereafter until the dogs were sacrificed on the twenty-eighth postoperative day.

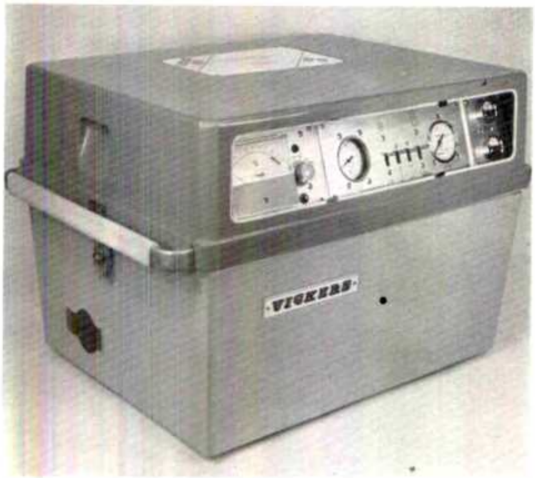

FIG. 1.—Vickers' portable renal preservation unit.

The Apparatus.—The preservation apparatus (*Fig.* 1) has been more fully described elsewhere (Hopkinson, Littlewood, and Snell, 1972). It is a portable device designed to hold a single human kidney and is approximately 60 cm. wide, 40 cm. deep, and 38 cm. high. It weighs approximately 32 kg. The perfusion circuit consists of a gas-driven pump, a 25-μ filter, a membrane oxygenator, and a pressure manometer. The pump is preset to give a predetermined flow rate (2 ml. per minute for canine kidneys) and a maximum output pressure of 80 mm. Hg. Cooling is by means of ice water circulated through a heat exchanger by a small pump. Both the pump and the temperature indicator and controller operate from a 12-V. d.c. dry cell. Supplies of oxygen for the perfusate and nitrogen to drive the perfusion pump are carried in small rechargable cylinders built into the apparatus. The ice reservoir has a capacity of 12–30 hours depending on the ambient temperature and the gas cylinders in excess of 24 hours' duration. The controls are preset to give optimal conditions for the preservation technique described.

Perfusate.—The perfusate is based on Collins's C4 solution (Collins and others, 1969). Magnesium sulphate has been omitted while Dextran 40 and chlorpromazine have been added (*Table I*). The electrolytes are made up in 500 ml. of de-ionized water and autoclaved. A few hours before use heparin, chlorpromazine, and phenoxybenzamine are added and the solution is filtered. Finally, 500 ml. of 10 per cent Rheomacrodex in 5 per cent glucose are added and the osmolality is adjusted with solid dextrose.

Storage Conditions.—In the preservation unit the kidneys were maintained at 5° C. under 310 kN per m.^{2} oxygen. For the first 4 hours the kidneys were perfused at a rate of 2 ml. per minute and thereafter no perfusion took place. During preservation no change in perfusate pH was observed and therefore no monitoring was required.

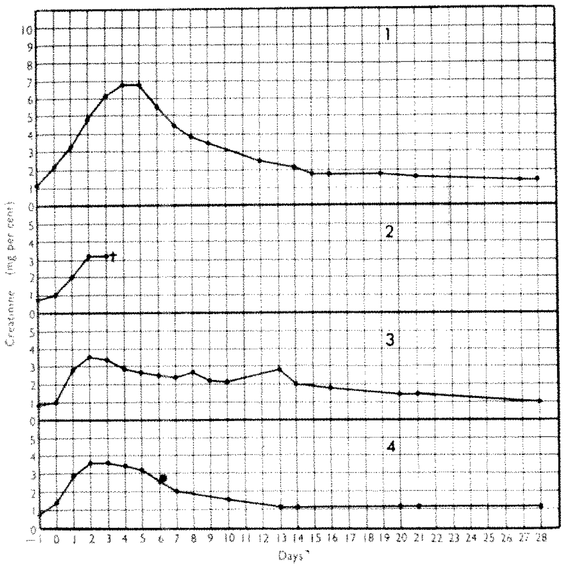

FIG. 2.—Renal function following 45 minutes of warm ischaemia and 24 hours' preservation.

Histology.—Tissue was obtained from all the grafted kidneys either at necropsy or when the dog was sacrificed at 28 days. A portion of each specimen was fixed in formol-saline, embedded in paraffin wax, and stained with haematoxylin and eosin, periodic-acid Schiff reagent, and Weingert's stain for elastic tissue. Another portion was immediately cut into small cubes, fixed in buffered glutaraldehyde, post-fixed in osmium tetroxide, and embedded in Epon 812. Sections, 0·5 μ thick, were cut from these blocks, stained with Azur II, and examined by light microscopy. Very thin sections for electron microscopy were stained with lead hydroxide and examined in a Philips' 200 electron microscope.

RESULTS

Group I: 45 Minutes of Warm Ischaemia.—Three of the 4 dogs in the group survived, with a transient rise in serum creatinine which returned to normal (*Fig.* 2). In 1 of these dogs (No. 4) the renal autograft appeared normal by both light and electron microscopy. No glomerular, tubular, interstitial, or vascular lesions were detected. The grafts from the other 2 dogs (Nos. 1 and 3) were also for the most part normal but both showed a few old, wedge-shaped, cortical scars which were probably caused by pyelonephritis. The scarring was more pronounced in dog No. 1 and had been noted at the time of transplantation. This pre-existing damage probably accounts for the rapid early rise in serum creatinine in dog No. 1 before the reimplantation of the kidney. The fourth dog (No. 2) developed extravasation of urine due to failure of the ureteric implantation and was killed. At the time of sacrifice the serum creatinine had ceased to rise and a return to normal renal function was anticipated. The transplant showed widespread interstitial oedema and dilatation of Bowman's spaces but was otherwise normal.

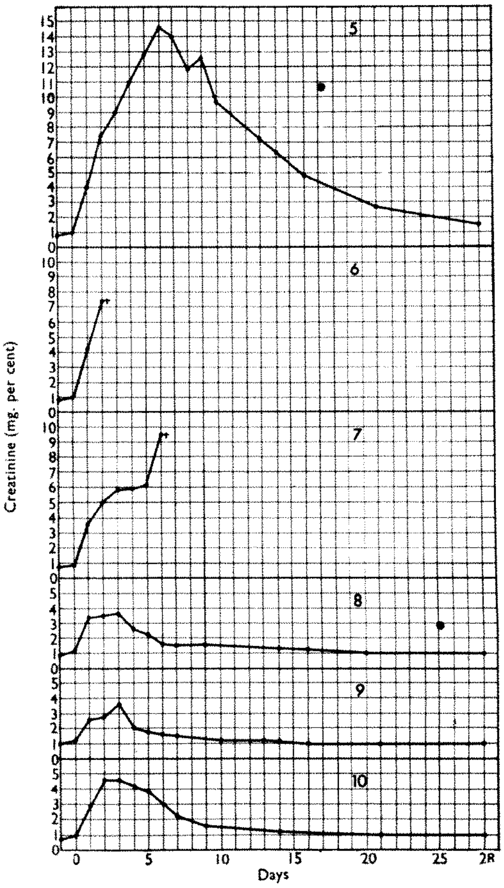

FIG. 3.—Renal function following 60 minutes of warm ischaemia and 24 hours' preservation.

Group II: 60 Minutes of Warm Ischaemia.—In 3 dogs (Nos. 8, 9, and 10) the transplanted kidney functioned well initially and the serum creatinine rapidly returned to normal (*Fig.* 3). All these grafts appeared normal by both light and electron microscopy. In dog No. 5 the kidney underwent torsion during preservation, leading to obstruction of the renal artery. In this animal the early renal function was poor but the serum creatinine had fallen to 1·7 mg. per 100 ml. by day 28. The renal transplant at this time showed many areas of infarction. Dog No. 7 developed a renal artery thrombosis on day 5, up to which time the renal function had been adequate to maintain life. At necropsy the kidney was completely infarcted. Dog No. 6 passed only very small quantities of urine and was killed on day 2. The graft showed widespread proximal tubular necrosis.

DISCUSSION

In cadaveric renal transplantation a period of warm ischaemia inevitably occurs between asystole in the donor and the onset of renal preservation. Wickham, Hanley, and Joekes (1967) demonstrated in the rabbit that increasing periods of warm ischaemia lead to progressively more severe impairment of renal function and that recovery is seldom complete if the period of warm ischaemia exceeds 60 minutes.

Table II.—PERFUSION CHARACTERISTICS OF THE KIDNEYS AND EARLY RENAL FUNCTION

DOG NO.	INITIAL PERFUSION VOLUME (ml.)	MACHINE PERFUSION PRESSURE (mm. Hg.)		MAXIMUM SERUM CREATININE (mg. per 100 ml.)
		Initial	Final	
45 minutes' ischaemia				
1	95	15	10	6·8
2	50	—	—	3·2
3	125	35	16	3·6
4	300	10	6	3·6
60 minutes' ischaemia				
1	92	25	10	14·6
2	85	10	6	7·4*
3	94	9	7	9·5†
4	72	12	11	3·6
5	78	11	10	3·7
6	85	10	6	4·6

* Sacrificed because of anuria.

† Sacrificed because of renal artery thrombosis.

Organ-sharing schemes designed to distribute kidneys on the basis of histocompatibility matching require reliable short-term renal preservation whilst tissue typing and transfer of organs are effected. The present investigation was carried out to test the ability of a hypothermic hyperbaric perfusion system to preserve kidneys subjected to periods of warm ischaemia similar to those encountered in clinical practice.

The initial gravity perfusion resulted in flow rates ranging from 300 to 50 ml. in 5 minutes but there was no correlation between flow rate and early renal function after reimplantation (*Table II*). However, there was a tendency for the flow to be less in the kidneys subjected to the longer period of ischaemia. In previous experiments (Hopkinson and others, 1972) with kidneys which had not been exposed to warm ischaemia the mean flow through 5 kidneys in 5 minutes was 265 ml., which is more than three times the mean volume which passed through the kidneys exposed to 60 minutes of warm ischaemia.

All the kidneys became pink rapidly after revascularization and began to pass urine within 5 minutes with the exception of the kidney of the dog that died of uraemia. After approximately 10 minutes some kidneys became mottled with blue patches but the phenomenon was transient and the kidneys appeared normal within half an hour.

Belzer and Kountz (1970) claim that kidneys which perfuse poorly during preservation function badly on reimplantation and that it is possible to select kidneys suitable for transplantation on the basis of their perfusion characteristics. In the present series we have found both the rate of initial perfusion and the machine perfusion pressure to be unreliable guides to subsequent function (*Table II*).

There have been no reports of repeatedly successful preservation of animal kidneys that had been subjected to 45 minutes or more of warm ischaemia without pretreatment of the donor.

Hartley, Collins, and Clunie (1971) showed in a series of human cadaver kidneys that initial perfusion followed by storage in iced saline slush resulted in immediate function in 24 out of 29 kidneys preserved for up to 12½ hours. In the dog, however, attempts to preserve kidneys after only 15 minutes of warm ischaemia have failed using this technique (Frost and others, 1970; Quin and others, 1972).

The hyperbaric system described here appears to offer an advantage over initial perfusion for the preservation of dog kidneys subjected to warm ischaemia and the results are at least comparable to those achieved with continuous hypothermic perfusion (Scott and others, 1971; Johnson and others, 1972), even though the ischaemic period in the series reported by Scott and others (1971) was only 15 minutes and constant success in the experiments described by Johnson and others (1972) was only achieved after 30 minutes of warm ischaemia. Better results have been reported (Claes and Blohmé, 1970) after 30 minutes of warm ischaemia, but the kidneys were implanted into the neck and kept cool during implantation which may account for the excellent early function. Certainly Dienst and Ansari (1971) have demonstrated that cooling the kidney during reimplantation has a beneficial effect on early postoperative renal function.

The results indicate that the technique described here is satisfactory for preserving kidneys that have been exposed to periods of warm ischaemia acceptable in clinical practice and a clinical evaluation is planned. Furthermore, the results of this investigation employing hyperbaric oxygen are not inferior to those achieved with continuous normobaric perfusion and suggest that hyperbaric oxygen warrants serious consideration as an adjunct to organ preservation.

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SECONDARY HAEMORRHAGE FROM THE ARTERIAL ANASTOMOSIS OF RENAL ALLOGRAFTS

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SUMMARY

Four cases of massive secondary haemorrhage from the arterial anastomosis of a renal allograft as a result of infection are described.

It is likely that the infections developed in the donors and that careful selection is necessary to prevent this. Immediate allograft nephrectomy is suggested as the treatment of choice. The external iliac artery may be ligated without necessarily embarrassing the circulation to the leg.

PATIENTS AND TECHNIQUES

THE donor kidneys were removed aseptically. The kidneys of the donors of *Cases* 1 and 2 were perfused by the method of Schalm (1968), and those of the latter 2 cases by the method of Brunius and Gelin (1966); the kidneys were preserved in ice until used. Renal transplantation was performed by a standard technique (Calne, 1965). Immunosuppression in *Cases* 1 and 2 was as described by Calne, Evans, Herbertson, Joysey, McMillan, Maginn, Millard, Salaman, White, Withycombe, and Yoffa, 1968). *Cases* 3 and 4 received 400 mg. prednisolone on day 1, 180 mg. on day 2, followed by a reduction of 20 mg. per day to 100 mg., and then 10 mg. per day to 50 mg.

The patients were maintained on twice-weekly dialysis and all except *Case* 2 had their own kidneys removed prior to transplantation.

CASE REPORTS

Case 1.—P. N., aged 25 years, was found to have proteinuria in 1960 which was shown on renal biopsy to be due to the nephrotic syndrome. He was treated with prednisone and diuretics. In 1963 his blood-pressure was 170/115 and he was given guanethidine. By 1966 he required haemodialysis. In November, 1966, he received a renal transplant from an 18-year-old male who had died following a road-traffic accident. The donor had been on a respirator for 8 days prior to death. Post-mortem examination revealed bilateral bronchopneumonia.

On the third day after receiving the transplant the patient developed a fever of 39° C. Blood cultures grew five organisms per ml. including *Escherichia coli* on two occasions, and he was treated with ampicillin and ceporin. The urethral catheter which was removed on the tenth postoperative day grew *E. coli* and this organism was also grown from his urine. He was given nalidixic acid and his temperature settled. By the seventh postoperative day he was producing over 1 litre of urine daily.

On the eleventh postoperative day the patient developed sudden pain at the transplant site, passed blood-stained urine, and had a fever. The pain increased and his blood-pressure started to fall. The transplant was explored under general anaesthesia. A massive haematoma was found surrounding the transplant and the arterial anastomosis was bleeding. The artery appeared friable and an attempt to reanastomose it to the external iliac artery was abandoned. The kidney was removed.

Histological examination of the arterial anastomosis showed a necrotic artery wall in which there were numerous Gram-positive cocci arranged in chains.

Postoperatively the patient was treated with chloramphenicol and colomycin and he made a slow recovery which was complicated by a transient mitral incompetence as a result of subacute bacterial endocarditis.

He became fit enough to receive a second transplant in March, 1967, but this contracted a nephrotic syndrome and he developed liver failure, possibly as a result of Imuran toxicity, from which he ultimately died.

Case 2.—R. H., aged 36 years, had a meningomyelocele closed in infancy. In 1966 he developed hypertensive renal failure due to chronic pyelonephritis and required dialysis.

A renal transplant was performed in December, 1966. The donor was a 16-year-old boy who had been involved in a road-traffic accident and who had then been on a respirator for 10 days prior to death. It was subsequently found that he had developed a *Pseudomonas pyocyanea* pneumonia.

A swab taken from the donor artery at the time of transplantation grew *P. pyocyanea* and urine passed on the second postoperative day grew the same organism. Blood culture was similarly positive.

On the thirteenth postoperative day the patient complained of pain and swelling at the transplant site and subsequently his blood-pressure fell. The wound was reopened when considerable clot was found and torrential haemorrhage was seen coming from the anastomosis. Cardiac arrest followed but the heart was restarted following standard resuscitative procedures. The kidney was removed and the defect in the external iliac artery was oversewn. The patient did not resume spontaneous respiration and consciousness did not return. He died 2 days later.

A swab taken from the arterial anastomosis grew *P. pyocyanea.*

Case 3.—P. P., aged 21 years, was a known case of Alport's syndrome (Alport, 1927), his mother having died from this disease and 1 brother also being affected. The patient presented in early 1971 with progressive renal failure and haemodialysis was therefore started.

Renal transplantation was performed in May, 1971. The donor was a 28-year-old female who had died following a drug overdose and who had been on a respirator for 8 days. Subsequently it was found that this donor had had pneumonia from which a *Klebsiella* sp. had been grown.

On the seventh postoperative day the patient complained of pain and swelling in the transplant area and his haemoglobin fell from 6·1 to 4·2 mg. per cent in 24 hours. The wound was explored and bleeding was seen coming from the arterial anastomosis. Arterial sutures were inserted and the bleeding stopped. The wound was closed. A swab taken from the wound at this time grew *E. coli* and urine taken on this day grew a *Klebsiella* sp. with the same sensitivities as that of the donor organism. Postoperatively the patient remained well but he developed a toxic epidermal necrolysis (Lyell's syndrome) and *Staphylococcus pyogenes*, Phage type 71, was grown from his nose and abdominal wound.

On the eleventh postoperative day he bled again and the wound had to be reopened. Bleeding was seen from the Carrel patch and the whole anastomosis was resutured. A wound swab and a specimen of urine again grew *Klebsiella* sp. and he was treated with gentomycin and vancomycin.

A further torrential haemorrhage occurred on the sixteenth postoperative day; the wound was reopened and haemorrhage from the anastomosis was controlled by pressure. The kidney was removed and the external iliac artery and vein were tied above and below the anastomosis. Cardiac arrest occurred, however, following the acute haemorrhage, but the heart was restarted after cardiac massage and standard methods of resuscitation.

Postoperatively the patient did not regain consciousness and he died from pneumonia 32 days after renal transplantation. His leg and foot remained warm at all times and there were no signs of oedema.

Cultures of the anastomosis grew a *Klebsiella* sp. and pyogenic staphylococci, and histology of the Carrel patch revealed a suppurative arteritis, with infection involving the perirenal, hilar, and periureteric tissues.

Case 4.—W. S., aged 45 years, presented with end-stage chronic glomerulonephritis which required haemodialysis from the beginning of 1971. Renal transplantation was performed as a 'double header' with *Case* 3 by another team of surgeons. Both the kidneys for *Cases* 3 and 4 came from the same donor, as described above.

On the nineteenth postoperative day the patient collapsed with acute pain in the transplant area and he became pulseless. He was resuscitated and then the wound was explored when it was seen that torrential bleeding was occurring from the anastomosis. Cardiac arrest occurred and immediate resuscitation was commenced. Normal cardiac function was restored after 20 minutes of cardiac massage. The kidney was removed and the external iliac artery and vein were tied above and below the anastomosis.

Postoperatively the patient made satisfactory progress and he recovered normal consciousness.

He remains alive and well and is back on the haemodialysis programme. Postoperatively he suffered paraesthesia in his left leg and the side of the transplant and the leg was swollen for 3 weeks. This has now resolved entirely, his foot is warm and pink, and he gets no claudication.

A profuse culture of a *Klebsiella* sp. was grown from the arterial anastomosis, the wound, and his urine prior to transplant nephrectomy.

DISCUSSION

Patients receiving standard doses of immunosuppression are particularly susceptible to infection. Fortunately, it is rare for the arterial anastomosis to be infected as described here, this having occurred in 4 out of 139 patients who received transplants in Cambridge between March, 1966, and July, 1971.

In 3 of the patients described here there was a definite relationship between the organism grown in the donor and that in the recipient. In the fourth case (*Case* 1) it was felt that a similar causal relation was likely. In *Case* 2 *P. pyocyanea* was grown from both the donor and the recipient. *Cases* 3 and 4 were transplanted with kidneys from the same donor. Cultures from the donor and both recipients grew a heavy culture of a *Klebsiella* sp. although *Case* 4 was also complicated by staphylococcal infection. All 3 donors had been on a respirator for a week or more. It is suggested that these donors are particularly likely to transmit infection and recipients of such kidneys should be watched carefully for early signs of haemorrhage.

When anastomosis is end to side of a donor Carrel patch to the external iliac artery of the recipient, infection threatens the external iliac artery. It has been known since the time of Astley Cooper (1813) and John Hunter that the external iliac artery or femoral artery can often be tied off in young people without serious nutritional impairment to the leg; this was confirmed in our last 2 patients.

Postoperative wound haematoma from general oozing is not uncommon in renal transplant patients who are undergoing regular haemodialysis involving heparin. Quite distinct from this is massive haemorrhage from the arterial anastomosis. Although rare, this is by far the most alarming complication of renal transplantation both to the patients and to the staff.

In all the 4 cases described here infection was thought to play the precipitating role and in 3 cases it was shown to have been transmitted from the donor.

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SURGICAL RESECTION OF RECURRENT CROHN'S DISEASE

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SUMMARY

The outcome of a group of 24 patients having multiple resections for Crohn's disease is presented by means of 'life charts'. These show that it is uncommon for a second resection to be the start of a downhill course and about half of the patients remain well over long periods of follow-up. Comparison with other series is difficult for various reasons, but where comparison is possible the results are similar, except that few patients in this series have so far come to a third resection.

THERE is continuing dispute concerning the place of excisional surgery in recurrent Crohn's disease. A review of the collected series (Kiefer, 1953; Brown and Daffner, 1958; Meyers, Ruble, and Ashley, 1959; Colcock and Vansant, 1960; Gump and Lepore, 1960; Davis, 1961; Stahlgren and Ferguson, 1961; Barber, Waugh, Beahrs, and Sauer, 1962; Barber, Waugh, and Sauer, 1963; Atwell, Duthie, and Goligher, 1965; Colcock and Fortin, 1965; Schofield, 1965; Lennard-Jones and Stalder, 1967; Banks, Zetzel, and Richter, 1969; Brill, Klein, and Kark, 1969) provides conflicting evidence on this question and comparison of one series with another is made difficult by different criteria for recurrence and varying lengths of follow-up, and by the series being selected in different ways in various parts of the world. The 'recurrence rate' in these series varies from 18 per cent (Schofield, 1965) to 73 per cent (Brown and Daffner, 1958), and there is very little comparable information on the patients who had multiple resections. One problem common to all follow-up investigations of Crohn's disease is that the effects of previous bowel excision may mimic recurrent disease:—

Diarrhoea and weight-loss may be due to either the effects of bowel resection or recurrence.

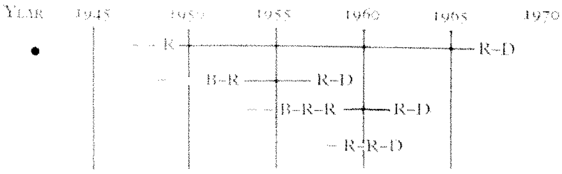
Attacks of abdominal pain and distension may be caused by either adhesion-obstruction or recurrence.

A swelling palpated under an old wound may be due to either scar tissue or recurrence.

A distorted bowel segment seen on barium study may be the result of either the previous resection or recurrence.

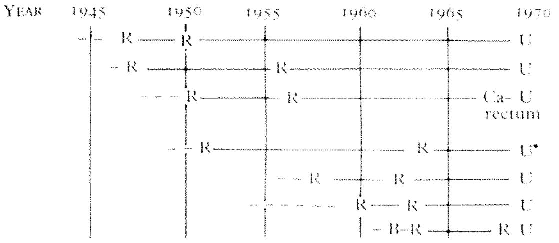
In an attempt to overcome this problem Lennard-Jones and Stalder (1967) classified their cases by the degree of certainty of recurrence; they also analysed their results by construction of life-tables, and a comparison with their results is made later in the Discussion. In the present series the uncertainty in diagnosing recurrence is reduced by case selection; this series concerns only those cases in which both the initial disease and the recurrence have been diagnosed by pathological examination of excised bowel.

Table I.—'LIFE CHARTS' OF 4 PATIENTS WHO DIED FOLLOWING MULTIPLE RESECTIONS



Key to abbreviations: B, by-pass; D, died; R, resection. The dotted lines indicate length of history before the first operation.

Table II.—'LIFE CHARTS' OF 7 PATIENTS WHO WERE 'UNWELL' FOLLOWING MULTIPLE RESECTIONS



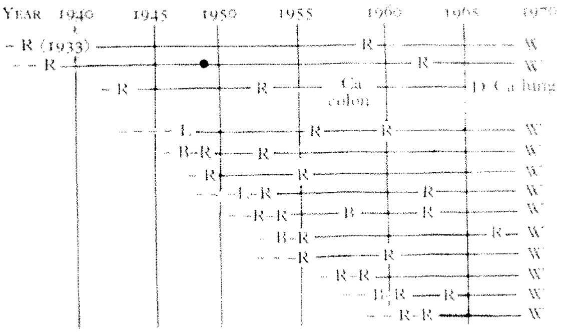
Key to abbreviations: B, by-pass; Ca, carcinoma; R, resection; U, unwell. The dotted lines indicate length of history before the first operation.

PRESENT SERIES

All the cases of Crohn's disease admitted to the London Hospital from 1946 to 1968 have been reviewed; equivocal cases have been excluded. In this series, numbering 152 cases, there were 24 patients who had two or more resections of bowel, with pathological confirmation of the diagnosis on each occasion. Patients in whom the first resection was undertaken less than 5 years previously have been excluded from this long-term study. The case histories of the 24 patients who had two or more resections are shown on 'life charts' (*Tables I–III*). In each of these the dotted line indicates the length of history prior to the first operation. *Table I* shows the histories of the 4 patients who died. All of these patients had enterocutaneous fistulae or complete obstruction (or both) in addition to their recurrent disease, and it is seen that death often followed soon after a surgical procedure in this deteriorating situation.

Table II shows the details of 7 patients remaining 'unwell'. The word 'unwell' reintroduces the uncertainties described earlier, but there is little uncertainty concerning the *initial* recurrence which was resected and the diagnosis confirmed pathologically. No attempt is made to classify these patients as regards the probability of recurrence. However, the 'life charts' show that all except 2 cases have already completed more than 5 years since the second resection without death or further surgery, and the symptoms making some of the patients 'unwell' might be entirely due to the multiple bowel resections. All are being managed as out-patients and only 2 are severely inconvenienced by their symptoms.

Table III.—'Life Charts' of 13 Patients who were Well (or Dead from Unrelated Causes) following Multiple Resections



Key to abbreviations: B, by-pass; Ca, carcinoma; L, laparotomy only; R, resection; W, well. The dotted lines indicate the length of history before the first operation.

Table IV.—A Comparison of the Outcome after a Second Resection for Crohn's Disease in Some of the Published Series

Author	First Resection	Second Resection			Third Resection
		Total	Well	Unwell/died	
Kiefer (1953)	118	28	10	7	11
Meyers and others (1959)	62	7	4	2	1
Barber and others (1963)	82	17	8	4	5
Schofield (1965)	95	18	5	1	12
Lennard-Jones and Stalder (1967)	73	16	5	5	6
Present series (1972)	108	24	12	10	2
Total	538	110	44	29	37
Percentage of second resections		100	40	26	34

Table III gives the histories of the 13 patients who are alive and well (or in 1 case dead from an unrelated cause). In this group all but 1 patient have completed 5 years since the second resection and all were entirely well without symptoms or signs of active disease at the time of the review.

Before discussing these results certain comments must be made on the process of case selection. The patients were selected solely by the common feature of having had multiple resections of pathologically confirmed Crohn's disease. All such cases which occurred in the larger series at the London Hospital are included in this study. However, there are several points which may introduce bias towards a 'favourable' outcome. First, resection of disease implies 'resectable' disease. Although it might seem likely that the 'worst' cases would be included in this study of multiple resections, a few of the most extensively involved cases are excluded by not being resectable, by-pass procedures or conservative treatment being undertaken instead. Secondly, the records are less complete for the patients who died early in the series whereas the notes of long survivors are well preserved. Although all the available records, including microfilmed notes, have been searched, it is easily possible that some early cases have been missed and amongst them a higher-than-average proportion of deaths. Thirdly, there is a source of statistical error in the inclusion of the first 3 cases in *Table III*. They are of particular interest because of the protracted nature of their disease, the average time between resections being 20 years and since the second resection 12 years, and they are included because one resection in each patient was performed during the period of study. Statistically, however, they should be regarded as part of a different population which is not currently reviewed and which includes all the patients having their first resection prior to 1946.

DISCUSSION

There is a sparsity of comparable information concerning the outcome of second resections for Crohn's disease. Even for first resections comparison between different series is difficult, for the reasons outlined earlier, and following second resections the uncertainties are increased. One particular difficulty is caused by the frequent grouping of 'by-pass' and 'resection' cases under a common heading (Brown and Daffner, 1958; Gump and Lepore, 1960; Stahlgren and Ferguson, 1961; Barber and others, 1962; Banks and others, 1969; Brill and others, 1969), and in these series a 'second operation for recurrence' is commonly a first resection, the original operation having been a by-pass procedure. These results are clearly not comparable with the present series; the relatively few series available for comparison are shown in *Table IV*. In view of the small individual numbers only the totals are expressed as percentages. It can be seen that about 1 in 5 of the patients who were subjected to a first resection for Crohn's disease came to a second resection. An exact comparison on this point is possible with the series of Lennard-Jones and Stalder (1967) using the same standard method of actuarial analysis (Hill, 1966). The calculated percentage chance of a second resection at various time intervals after a first resection is shown in *Table V*. This method of analysis is particularly suited to such comparisons since it makes full allowance for varying length of follow-up, patients 'lost sight of' during follow-up, and deaths. The two series are seen to have similar probability figures, as would be expected in generally similar series.

Table V.—Percentage Chance of a Second Resection by Actuarial Analysis in the Present Series compared with that in the Series of Lennard-Jones and Stalder (1967)

Author	Percentage Chance of a Second Resection at Various Times after the First Resection		
	2 yr.	5 yr.	10 yr.
Lennard-Jones and Stalder (1967)	10	16	26
Present series (1972)	6	16	31

The outcome following second resection is shown in *Table IV*, where it can be seen that one-third of the patients came to a third resection, but there are wide differences between series. These variations may be explained by differing surgical philosophies about patients with repeated recurrences, and the numbers are rather small for statistical analysis. The status at follow-up of all the second resection cases has been calculated by combining with the follow-up information of the third resections; it was found that 50 per cent were well, 30 per cent were 'unwell', and 20 per cent have died from complications of the disease or of its treatment. These figures accord with those of other large series which have not been included for lack of comparable information (e.g., Colcock and Vansant, 1960). The length of follow-up will clearly affect the results profoundly; however, long-term follow-up is common in the analysis of multiple resections as the various procedures are often spread over many years. In the present series the average time from the first operation to the review (or death) is 14 years and in most of the series cited the follow-up is at least 5 years.

The decision whether or not to operate for Crohn's disease is often difficult. In general, resection is reserved for patients with severe symptoms or complications and in recurrent disease this conservatism is increased. Some patients inevitably come to further surgery, for example, to relieve obstruction; conversely there are patients who remain entirely well despite recurrence for whom few surgeons would advise reoperation. Between these extremes are patients with 'symptomatic recurrence' in whom many factors will influence the decision. It is towards the management of this group that the present survey may be of some value. There is no evidence that further surgery is frequently the start of continuing complications; if the disease appears well localized and symptoms or complications are severe, then re-exploration with a view to second resection should not be withheld.

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THE MANAGEMENT OF CONGENITAL HYDRONEPHROSIS IN THE NEWBORN

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SUMMARY

Hydronephrosis due to pelvi-ureteric obstruction rarely presents in the neonatal period. When it does, the disease is advanced and it may be advisable to drain the obstructed kidney until the child is old enough and fit enough to withstand a pyeloplasty. In this paper 2 cases of neonatal hydronephrosis are reported and a satisfactory method of drainage is described.

CASE REPORTS

Case 1.—R. H. was admitted when he was 7 days old with pyrexia and oral thrush. A firm, smooth mass was palpable in the right side of the abdomen which was thought to be of renal origin. The blood-urea was 178 mg. per cent and his urine contained large numbers of pus cells and cultured a mixed growth of organisms. His condition improved with antibiotic therapy, the urine becoming sterile and the blood-urea falling to 52 mg. per cent. An intravenous pyelogram showed both kidneys to be functioning poorly. There was a huge pelvic hydronephrosis on the right side and very little excretion on the left. Under radiographic control right pyelostomy was performed using a large Intracath (*Fig.* 1). After this procedure his progress was very satisfactory (*Fig.* 2). The right kidney maintained a good urine output which was fortunate because little was excreted by the left. Prophylactically he was given rotating antibiotics but these did not prevent *Pseudomonas* organisms appearing in his urine cultures from time to time. During the ensuing 4 months the catheter was accidentally dislodged on two occasions. Each time the child became unwell after a few hours with high pyrexia. The Intracath was reinserted and he was given more powerful antibiotics specific against *Pseudomonas*—on the first occasion gentamycin and on the second carbenicillin. On both occasions he gradually improved over 48 hours. When he was 18 weeks old a Culp-flap pyeloplasty was performed through an anterior extraperitoneal approach. There was no scarring around the renal pelvis and the flap was fashioned without difficulty. It had been hoped to use the catheter to drain the kidney postoperatively but it was dislodged during the operation. The left kidney was found to be atrophic. His postoperative progress was uneventful and he has continued to do well.

Case 2.—A. C. was admitted when he was 4 weeks old for investigation of a left-sided abdominal mass which had been noticed since birth. The baby was otherwise well; the blood-urea was 50 mg. per cent and the urine was sterile. An intravenous pyelogram showed no excretion on the left with delayed excretion on the right outlining a large hydronephrosis (*Fig*. 3). Under radiographic

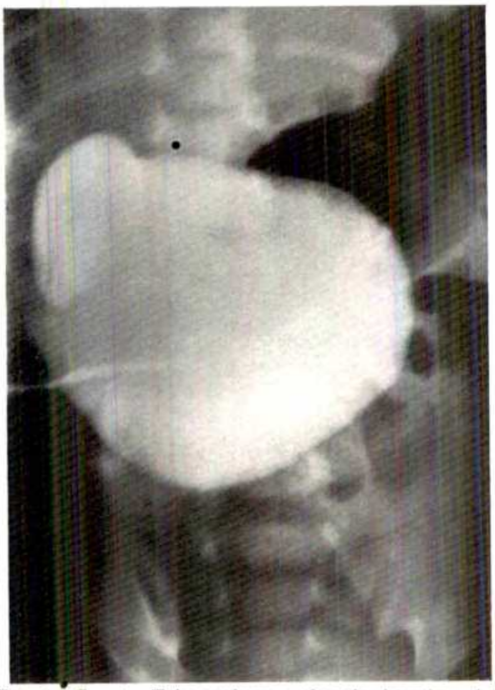

FIG. 1.—*Case* 1. Tube pyelogram after the insertion of the catheter, showing a grossly hydronephrotic right kidney.

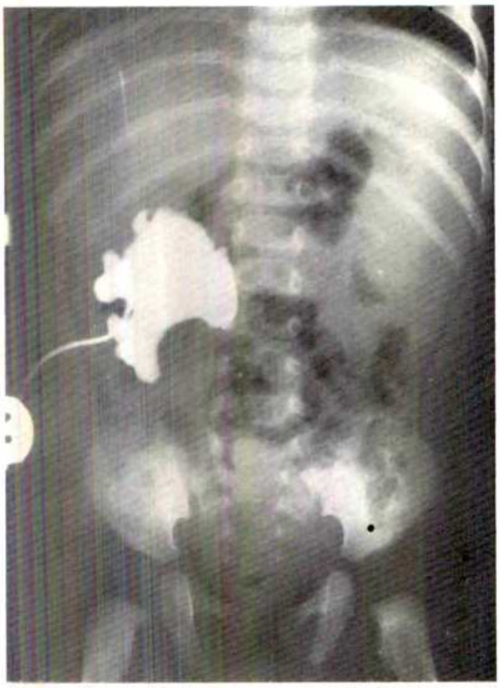

FIG. 2.—*Case* 1. Tube pyelogram 1 month after the insertion of the catheter, showing marked improvement in the degree of hydronephrosis.

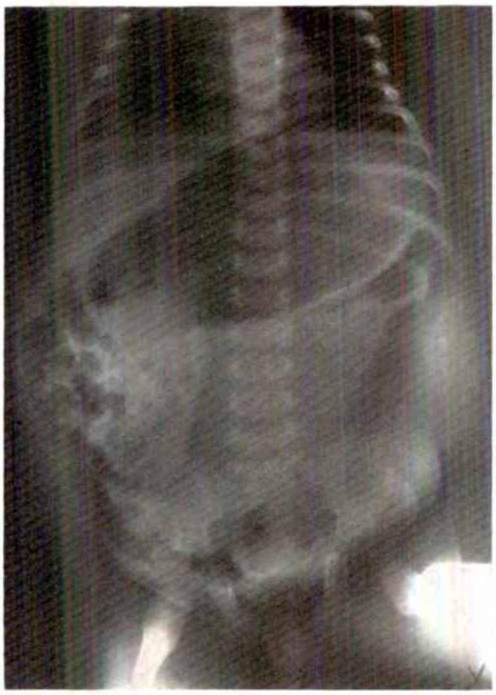

FIG. 3.—*Case* 2. Intravenous pyelogram, showing a large right hydronephrosis with no function on the left side.

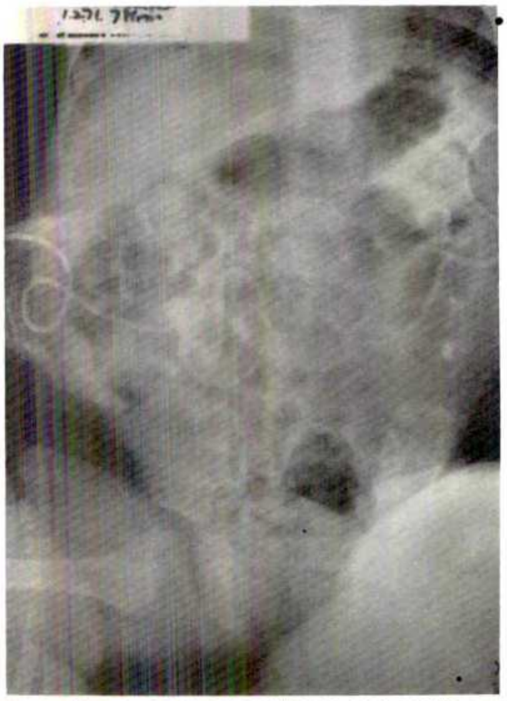

FIG. 4.—*Case* 2. Intravenous pyelogram at 6 months, again showing marked improvement after drainage.

control, an aspiration needle was inserted into the left-sided mass confirming the diagnosis of a large hydronephrosis, and therefore a large Intracath was inserted into each side. Prophylactic Septrin was prescribed. The child progressed very well and as the home circumstances were excellent he was allowed home. After 3 months one of the catheters partially fractured near the skin edge and had to be replaced. This was achieved without any difficulty by changing catheters along a guide wire. This was the only problem encountered with the child's pyelostomy tubes. On Septrin urinary infection was minimal although *Pseudomonas pyogenes* was cultured on occasions from the urine of both kidneys. At 6 months the intravenous pyelogram was repeated (*Fig.* 4). Both kidneys still showed hydronephrosis but there had been a marked improvement. Right Culp-flap pyeloplasty was performed shortly afterwards, using the anterior extraperitoneal approach. There was no scarring around the renal pelvis and the kidney had a reasonable cortex. The catheter was left undisturbed and acted as a drain postoperatively. His subsequent progress was without incident. When urine stopped draining via the catheter and passed all per urethra the tube was removed. The left side was operated on 3 months later using a similar approach and technique. There was a good thickness of renal cortex and again no fibrosis around the kidney. A Culp-flap pyeloplasty was fashioned and the catheter was used as a drain postoperatively. Postoperative progress was again uneventful.

DISCUSSION

Hydronephrosis due to pelvi-ureteric obstruction is relatively uncommon in the newborn. In a 30-year period Uson, Cox, and Lattimer (1968) report 16 neonatal cases out of a total of 130 in childhood. The younger it presents the more severe is the degree of obstruction and the common presenting symptom in the neonate is the presence of an abdominal swelling. Infection may supervene, resulting in further impairment of renal function and subsequent failure to thrive. Williams and Karlaftis (1966) report that 15 out of a series of 26 cases had a palpable mass in the renal area and 7 had urinary infection.

It is important that adequate drainage be instituted early in neonatal cases to conserve as much functioning renal tissue as possible. The disease is frequently bilateral or the unaffected kidney is congenitally abnormal in some other respect. Although initially the hydronephrosis may only be apparent on one side, in a high proportion of cases it subsequently develops in the opposite kidney. Infection in the obstructed kidney can lead to pyonephrosis with rapidly progressive destruction of renal parenchyma.

There is a definite anaesthetic risk attached to major operations in the neonatal period and the hazard to the child is greater if renal function is impaired or urinary-tract infection is present. A temporary drainage procedure would seem to be the treatment of choice, enabling the kidney to function without impediment until the child is old enough and fit enough to withstand a major operation without undue risk; this should be around 5 or 6 months of age. However, if a standard pyelostomy or nephrostomy is performed using a Malecot or similar catheter this involves a partial dissection of the renal pelvis almost as extensive as for a pyeloplasty, and postoperative fibrosis may make the subsequent plastic repair at the pelvi-ureteric junction much more difficult (Eckstein, 1968).

A simpler but equally effective method of drainage has been used successfully in the 2 cases presented here. The child is given a short general anaesthetic and then under radiographic control, using an image intensifier and television monitor a large Intracath is inserted through the flank into the enlarged renal pelvis. Once the pelvis is entered urine flows. Further information can be obtained at this stage by injection of a radio-opaque dye, which outlines the position of the catheter end. Once in a satisfactory position it is anchored to the skin by two silk sutures and also fixed with adhesive strapping. The proximal end of the catheter is connected to a Bardic bile-drainage bag using an intravenous extension tube. All the connexions are made watertight with waterproof adhesive strapping. A useful connexion piece between the catheter and the extension set has been found to be a Galbraith pyelography nozzle.

The subsequent management for the pyelostomy presents few problems. Care must obviously be taken to prevent accidental dislodgement of the catheter. It should be securely strapped to the child in such a position that it causes the minimum of interference with nappy changing, etc., and also where it is not easily accessible to the child's inquiring hand. Should it become dislodged 8–12 hours are allowed to elapse to permit the renal pelvis to fill up again as this obviously facilitates replacement. As the presence of a catheter in the kidney is a potential source of infection the child should have continuous prophylactic antibiotic cover. In this respect Septrin appeared to be the most effective with no side-effects. *Pseudomonas pyocyanea* is the most difficult organism to eradicate, and while normally the presence of this organism caused little concern should the catheter become blocked or displaced an acute fulminating pyelonephritis might ensue. This will produce a high pyrexia and toxaemia which requires treatment with more powerful specific antibiotics.

When the child is considered old enough to withstand the definitive plastic operation an anterior extraperitoneal approach can be used. It will be found that there is no fibrosis around the pelvis to interfere with the pyeloplasty and, whichever method is used, the catheter can be left in situ postoperatively to drain the kidney until the oedema around the suture line has settled.

CONCLUSION

In cases of neonatal hydronephrosis due to pelvi-ureteric obstruction it is important to conserve every nephron since in a high proportion of patients there are associated anomalies of the opposite kidney. The method of drainage described above has been found to be effective and is relatively simple to perform.

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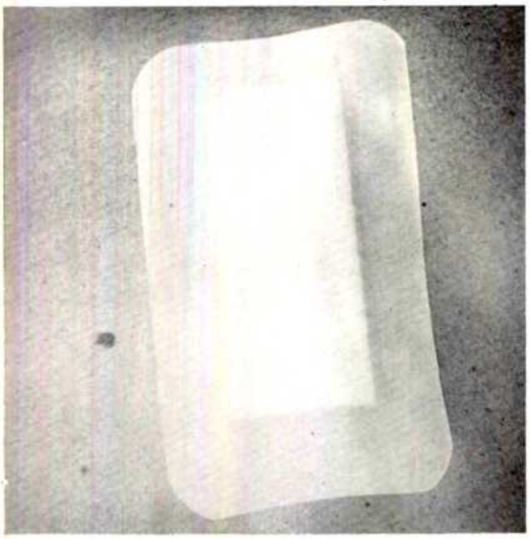

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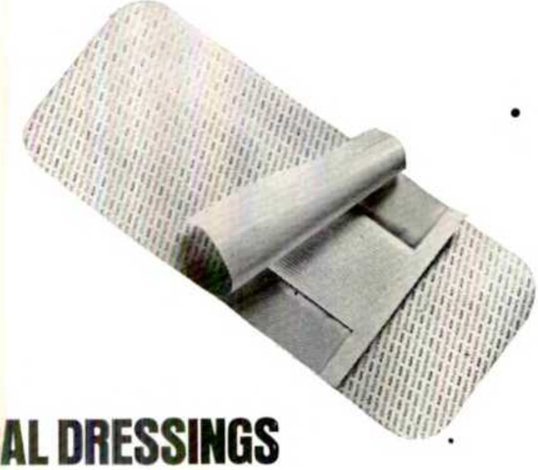

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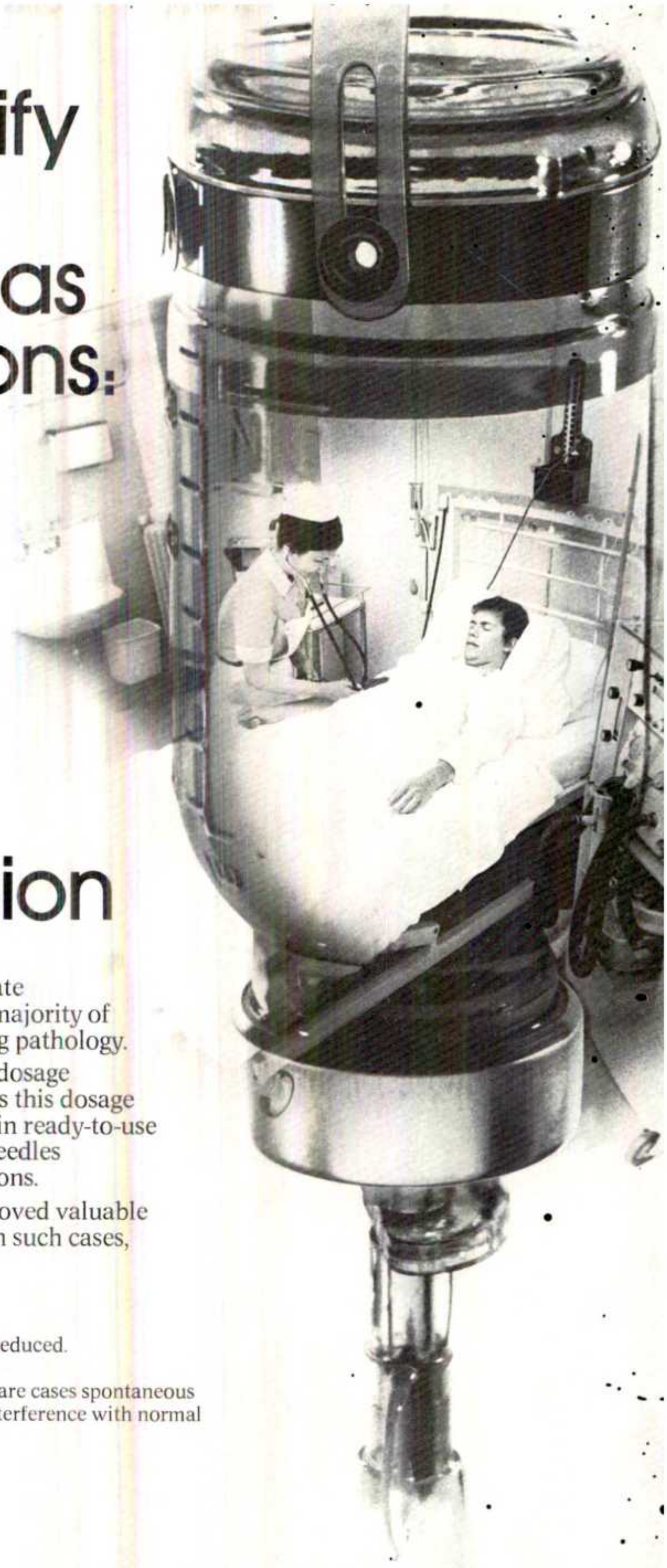

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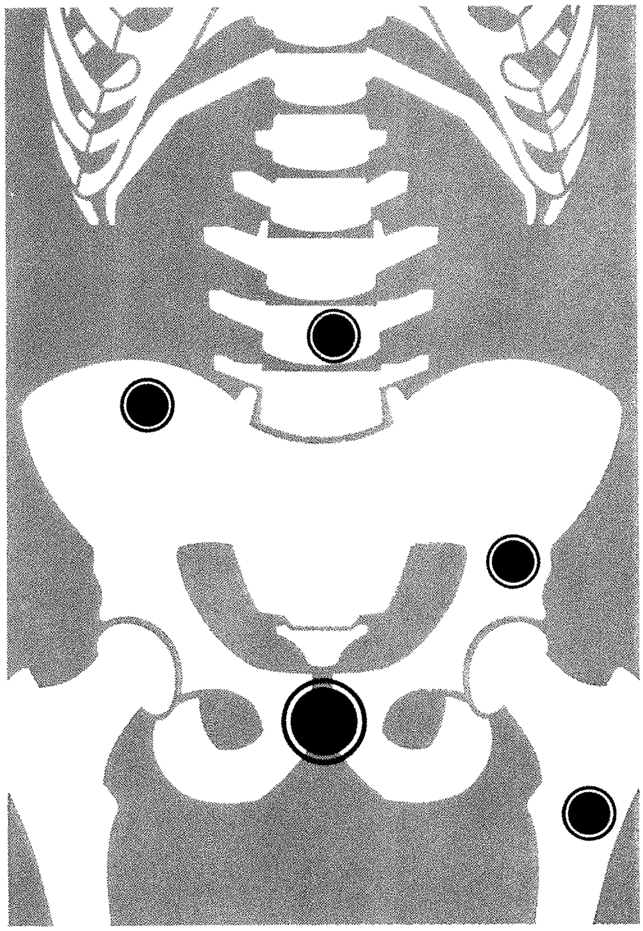

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SURGICAL RESEARCH SOCIETY

A meeting of the Surgical Research Society was held in the University of Liverpool on 14 and 15 July, 1972, with Professor R. B. Welbourn (President of the Surgical Research Society) in the Chair. The following papers were presented:—

1. Experimental Studies on the Influence of the Sympathetic Nervous System on Cerebral Blood-flow: V. D. Deshmukh, A. M. Harper, J. O. Rowan, and W. B. Jennett, Wellcome Surgical Research Institute, University of Glasgow; Institute of Neurological Sciences, Southern General Hospital, Glasgow; Department of Clinical Physics and Bio-engineering, Western Regional Hospital Board.

It is now well established that the cerebrovascular tree is accompanied by sympathetic nerve-fibres (Falck et al., 1968). The present study attempts to elucidate the function of these nerves.

Experiments were carried out in 30 baboons anaesthetized with N_2O, O_2, and phencyclidine and ventilated. Cerebral blood flow (C.B.F.) from the right fronto-parietal area was measured following the intracarotid injection of ^{133}Xe and calculated from the height/area equation (Høedt-Rasmussen et al., 1966). Bilateral cervical sympathectomy was performed about 2·5 cm. below the superior cervical ganglion. The cranial end of the right sympathetic chain was stimulated electrically.

Both sympathetic stimulation and intracarotid infusion of noradrenaline (40 ng. per kg. per min.) had minimal effects on the C.B.F. at normocapnia, but they consistently reduced the C.B.F. during hypercapnia by about 25 and 17 per cent respectively.

On morphological grounds and from physiological data it is argued that there is a dual control of the cerebral circulation, the extraparenchymal vessels being influenced by the sympathetic system while the intraparenchymal vessels are under local metabolic regulation. It seems that the sympathetic control may serve as a protective mechanism in acute episodes of elevated C.S.F. pressure and systemic hypertension.

Falck, B., Nielsen, K. C., and Owman, Ch. (1968), *Scand. J. clin. Lab. Invest.*, suppl. 102.

Høedt-Rasmussen, K., Sveinsdottir, E., and Lassen, N. A. (1966), *Circulation Res.*, **18**, 237.

2. Depression of Delayed Hypersensitivity and Abnormal Bone Scans in 'Early' Cancer of the Breast: D. S. Sumner, M. H. Edwards, and M. Baum (C. T. Howe), Department of Surgery, King's College Hospital Medical School, London.

Delayed hypersensitivity, which may be related to immunity to cancer, is depressed in patients with clinically advanced breast cancer (Mackay and Baum, 1968). Such depression has not been shown in patients with clinical Stage I or II disease, although over 20 per cent of these patients with apparently early cancer have occult metastases which can be detected by bone scanning (Galasko, 1971).

Using strontium 87^{m}, scans of the lumbar spine and pelvis were performed on 40 patients with breast cancer in clinical Stages I and II. Metastases were suggested by the presence of localized areas of increased uptake of the isotope. Delayed hypersensitivity was estimated pre-operatively by the response to an intradermal injection of 5 I.U. of old tuberculin (Mantoux test). A positive Mantoux test was recorded when a skin reaction of 3 mm. or more in diameter was seen at 48 hours.

Of 8 patients with abnormal scans, only 1 showed a positive Mantoux test. The remaining 32 patients had normal scans and the Mantoux test was positive in 16. This difference is significant ($P = 0·01$).

Thus, delayed hypersensitivity appears to be depressed seriously in patients with breast cancer before distant metastases become clinically overt.

Galasko, C. S. B. (1971), *Surgery Gynec. Obstet.*, **132**, 1019.

Mackay, W. D., and Baum, M. (1968), *Prognostic Factors in Breast Cancer*. Edinburgh: Livingstone.

3. Intravenous Caloric Requirements: A. O. B. Johnston and R. G. Clark, Department of Surgery, Royal Infirmary, Sheffield.

It has not yet been established whether there is a caloric intake at which there is optimal utilization of a fixed intake of intravenous nitrogen. In this study 26 patients under standard postoperative conditions received 0·23 g. nitrogen per kg. body-weight per day in a D-L-amino-acid mixture. The patients were randomized into four groups having 12, 25, 38, and 51 cal. per kg. body-weight per day. A control group of 5 patients did not receive either the extra calories or nitrogen. Fluid and electrolyte intakes were related to body-weight.

A linear relationship was found between the caloric intake and nitrogen balance ($P < 0·01$). The group receiving 51 cal. per day had a mean cumulative nitrogen balance of $-0·45$ g. nitrogen per kg. body-weight over 5 days as compared with $-1·18$ g. nitrogen per kg. body-weight in the controls. Urinary losses were 7–9 per cent of the infused free amino-acids and 10–13 per cent of the infused sorbitol. The caloric intake had no effect on these losses and it did not affect the cumulative sodium or potassium balances. Sorbitol is a good source of calories and it did not act significantly as an osmotic diuretic.

These results demonstrate that over the range studied nitrogen utilization improves linearly with increasing caloric intake. There was no level of caloric intake at which nitrogen utilization became maximal.

4. Computer-assisted Diagnosis of Abdominal Pain using 'Estimates' provided by Clinicians: D. J. Leaper, F. T. de Dombal, Jane C. Horrocks, and J. R. Staniland, Department of Surgery, The General Infirmary, Leeds.

This paper reports a comparison between two modes of computer-assisted diagnosis conducted as part of a prospective trial involving 472 patients suffering from abdominal pain of acute onset. In the first mode the computer used data collated from a large series of 600 patients. In the second mode the computer analysed each case using 'estimates' of probability provided by a group of 6 clinicians. The accuracy and reliability of the computer in each mode were compared with those of unaided clinicians in the same series of cases.

Using 'real-life' data the computer system was significantly more effective than the unaided clinician (91·1 versus 79·7 per cent accuracy). By contrast, when using the 'estimates' provided by clinicians the computer's overall accuracy (82·2 per cent) was relatively unimpressive and often the computer was *less* effective than the unaided clinician. When individual clinicians' 'estimates' were used the computer's accuracy fell even further.

It is suggested (*a*) that computer-aided diagnostic systems should use 'real-life' data and not clinicians' estimates, and (*b*) that clinicians cannot analyse patients in a probabilistic fashion, since in rarer diseases they have little idea of what the 'true' probabilities are.

5. **Lung Scans, Venograms, and Pulmonary Embolism:** J. J. Spindler, V. V. Kakkar, T. Corrigan, and D. Fossard (C. T. Howe), Department of Surgery, King's College Hospital Medical School, London.

Eighty-four patients with suspected pulmonary embolism were investigated in order to define the accuracy of lung scanning. An attempt was also made to assess whether peripheral venography, chest radiographs, electrocardiograms, and the clinical symptoms and signs could help in the analysis of the lung scans.

Forty-seven patients (56 per cent) had a normal lung scan. Only 5 of these cases had radiographic evidence of deep-vein thrombosis and these thrombi were confined to the tibial and soleal veins. Eighteen patients (21 per cent) had a slightly abnormal lung scan with a low probability of pulmonary embolism. Six of these patients had deep-vein thrombosis and 4 of these thrombi were in the femoropopliteal segment. Eleven patients (13 per cent) had a medium-to-high probability of pulmonary embolism, of whom 9 patients had deep-vein thrombosis and in 5 the femoropopliteal segment was involved. Eight patients (9·5 per cent) had lung scans which were diagnostic of pulmonary embolism. In 4 of these patients pulmonary angiograms confirmed the diagnosis and 2 patients required pulmonary embolectomy. Seven venograms were performed and all showed deep-vein thrombosis.

A lung scan with a perfusion defect of segmental distribution, venograms showing thrombi especially in the large veins of the leg, and a chest radiograph without evidence of an opacifying lesion indicate a diagnosis of pulmonary embolism.

A patient with normal venograms, a chest radiograph showing an opacifying lesion, and a lung scan with a perfusion defect which is not segmental in distribution is very unlikely to have pulmonary embolism.

Lung scanning is simple and reliable, can be repeated, and has no complications. Bilateral peripheral venography is also helpful in the diagnosis of pulmonary embolism.

6. **Absorbable Sutures. A Comparison between PGA and Catgut:** H. H. Wandall, Sv. Holm-Jensen, and Erik Agner, Institute for Experimental Research in Surgery, University of Copenhagen, Denmark.

An absorbable surgical suture has been developed from the synthetic material, polyglycolic acid (PGA).

A study was planned to evaluate the differences in biological behaviour between PGA and catgut with regard to tissue response and the loss of tensile strength during absorption. Different preparations of catgut (plain, chromic, and formalin hardened) were used in the experiments.

The results showed that catgut produces a chronic inflammation lasting for several weeks, a reaction which is absent in the case of PGA. PGA evokes early growth of granulation tissue which invades the thread and destroys it, while catgut becomes surrounded by a fibrotic membrane structure as the chronic inflammatory process subsides. PGA retains tensile strength with only a minor loss (10 per cent) within the first 6 days of implantation but from then on a rather rapid decrease takes place and no strength can be measured at 20–21 days. Catgut loses one-third to one-half of its initial tensile strength within the first 2 days but after this only a slight decline occurs with one-third of its initial strength remaining at 60 days. Great variation was observed. The type of suture preparation is not the decisive factor and the site of implantation determines to a greater extent the fate of the material. Repeated implantation of PGA at 6–7-week intervals causes a change in the cellular response and a massive infiltration of eosinophilic cells appears. Similar findings have not been observed with catgut. The disappearance rate in infected wounds was not significantly different from that observed in wounds without infection.

The new absorbable suture is thus not to be considered a mere substitute for catgut.

7. **A New Principle of Extracorporeal Respiration:** D. G. Melrose (R. B. Welbourn), Department of Surgery, Royal Postgraduate Medical School, London.

Extracorporeal respiration has up till now involved a direct contact between blood and gas in spite of evidence that this interface is responsible for a large proportion of the trauma generated by the method. Attempts to interpose a gas-permeable membrane have hitherto been relatively unsuccessful.

Although suitable membranes now exist (allowing an oxygen diffusion rate of more than 200 ml. O_2 per m.^{2} per min.) the difficulty lies in the geometry of the blood-film itself which may contribute as much as 90 per cent to the overall resistance to oxygenation.

A new device which consists of a number of silicone rubber tubes arranged about the periphery of a wheel relies on the generation of stable vortices within the blood flowing along these tubes when the system is set in oscillatory motion. These spiral vortices almost eliminate the boundary layers normal in axial flow (Melrose, 1972).

In a typical experiment the measured oxygen transport into a stationary tube was 21 ml. O_2 per m.^{2} per min. Oscillation of this tube to produce a movement of the wall relative to the blood within it, at a velocity of 210 cm. per sec., increased the transport to 200 ml. O_2 per m.^{2} per min. Similar considerations apply to carbon-dioxide transport.

A consequence of the oscillatory movement is that blood is induced to move in synchrony with the motion. When the system is equipped with one-way valves this pendulum motion is converted into forward flow and hence a pumping action is created.

Thus the inherent characteristics of the system lend themselves to the development of a self-contained pump oxygenator of simple geometry and very high efficiency.

Melrose, D. G. (1972), *Biomed. Engng*, **70**, 60.

8. **Non-invasive Test of Carotid Blood-flow: its Relevance to Transient Cerebral Ischaemic Attacks:** K. E. Britton, G. Duplock, G. Vaughn-Hudson, D. H. Keeling, and M. M. Bluhm (J. R. Kenyon), Department of Clinical Physics, St. Mary's Hospital Institute of Nuclear Medicine, Middlesex Hospital, London.

Aim: To demonstrate a screening test for abnormalities of carotid blood-flow in man; and whether turbulence of carotid blood-flow is atherogenic.

Method: Collimated scintillation detectors have been designed to view the left and right internal carotid arteries in the cavernous sinuses and to view the root of the aortic arch. Activity/time curves are recorded for 45 seconds after 10–15 mCi 99^{m} technetium is injected intravenously (Britton, 1969).

Results: 1. The activity/time curves determined from the left and right carotid detectors were compared in 89 patients, visually and numerically using a 'carotid index' derived from the take-off point, slope, and peak of these traces. The mean normal value was $0{\cdot}95 \pm 0{\cdot}23$ (1 S.D.); for right and left carotid stenoses values were $< 0{\cdot}49$ and $> 1{\cdot}41$ respectively. Differences ($P < 0{\cdot}02$) were found between 26 'normal' patients and 24 patients with evidence of cerebrovascular disorders. The 2 patients whose symptoms improved after surgery showed a return of the index to normal.

2. The common carotid–internal carotid transfer function has been determined by deconvolution of the output and the input activity/time curves determined from the aortic detector. This spectrum of transit times is used to indicate whether there is laminar or turbulent blood-flow. In turbulent blood-flow, eddying will aid deposition of material from blood and vortices will aid its embolization.

Britton, K. E. (1969), *J. Neurol. Neurosurg. Psychiat.*, **33**, 379.

9. Accelerometry in Gait Analysis: J. R. W. Morris (C. S. B. Galasko), Nuffield Department of Orthopaedic Surgery, University of Oxford.

A technique has been developed for studying normal or pathological movements by direct measurement of acceleration which avoids many of the disadvantages of cinephotography.

Five miniature accelerometers ($\frac{9}{16}$ in. × $\frac{7}{32}$ in. diameter) are mounted on a small Perspex platform. Their positions and sensitive axes are arranged so as to give output signals from which are derived three orthogonal translational accelerations, and two orthogonal angular accelerations. The data are recorded on a purpose-designed pocket cassette tape-recorder. This system allows data to be recorded for up to $\frac{1}{2}$ hr. from any limb segment on an ambulant subject. The recorded tape is played back into a computer for analysis.

Tests have been carried out on the mid-shank of normal subjects where anterior–posterior accelerations in excess of 1 *g* are quite usual in normal walking. Impulsive accelerations occurring at heel-strike are not measured as being significantly larger than those caused by other dynamic movements under muscular control. This situation is maintained during slow running where the foot articulations lengthen the duration of the impulse at toe-strike.

The technique incorporates complete portability and minimum disturbance to the subject.

10. Design Considerations in a New Knee Prosthesis: Paul Aichroth (H. Ellis), Orthopaedic Department, Westminster Hospital, London.

The prosthetic replacement of the knee has proved difficult in clinical practice. The use of large hinge prostheses is complicated by frequent postoperative problems and recently Gunston (1971) has shown encouraging results with a condylar replacement knee prosthesis.

This study explores the possibility of replacing joint surfaces at the knee with prosthetic materials.

The femoral condylar surfaces are replaced with metal components (stainless steel or titanium) and dowels are used to fix the surfaces to the underlying bony bed. Acrylic cement is used for the stabilization of the prosthetic components in bone. The tibial surfaces are replaced with high-density polyethylene components fixed again in a similar fashion with acrylic cement.

Both components are positioned accurately using a jig and the femoral and tibial surfaces are so arranged that rotation of the knee can occur. Other specific advantages are the relatively small size of the prosthesis, the rigid fixation, minimal joint disturbance with retention of the cruciate and collateral ligaments, and the low friction of the system.

Gunston, F. H. (1971), *J. Bone Jt Surg.*, **53**, 272.

11. Measurement of Metacarpophalangeal Joint Torque: A New Instrument: R. A. Dickson, R. Presswell, J. M. Thomas, and J. S. Calnan, Royal Postgraduate Medical School, Hammersmith Hospital, London.

Stiffness at the metacarpophalangeal joint has been measured using a portable arthrograph. This expensive apparatus can only record torque at the index metacarpophalangeal joint. A new instrument, the torque meter, has been developed to measure torque in all fingers of either hand in any position from full extension to 90° of flexion, so that torque can be investigated throughout the entire range of movement of the joint.

The instrument makes use of the principle of the torsion bar. By pressure of the finger on a horizontally attached extension bar, the torsion bar is wound up and the deflexion of the extension bar is registered on a Vernier dial gauge. The torsion bar pivots on the aluminium base and can be locked in any position of rotation, allowing a recording to be made in any position of the joint. Furthermore, the extension bar slides up and down so that any finger can be tested. By calibration against known weights, the movement of the torsion bar is shown to be Hookean.

Torque in normal metacarpophalangeal joints falls gradually in a linear fashion from full extension to 90° of flexion. In the rheumatoid joint with gross synovial proliferation, fall off to zero is rapid, while after synovectomy it returns to the gradual fall off of the normal hand.

12. The Effect of Composition on the Corrosion Resistance of Surgical Stainless Steel: D. F. Williams (D. Annis), Department of Dental Sciences, University of Liverpool.

A new design concept for corrosion-resistant orthopaedic implants has been presented previously (Williams, 1971). This was based upon observations that both design and materials selection controlled corrosion resistance. Further work has now been performed to determine optimum material specifications.

A study of *in vivo* corrosion occurrences has revealed two special features of the composition of stainless steel which influence the corrosion resistance. These concern carbon and nickel. Current specifications recommend a 0·07 per cent maximum for carbon and a range of 10–15 per cent for nickel. However, intergranular corrosion, which is critically controlled by carbon distribution, occurred in implants with less than this maximum. Only when the carbon content was less than 0·03 per cent were the implants immune to this corrosion.

Galvanic corrosion may occur between two components if their metallurgical structures are very different. Nickel has a marked influence on the structure and it was found that substantial structural changes in bone screws occurred when the content was less than 11 per cent.

It is concluded that revised specifications to give a maximum carbon content of 0·03 per cent and a range for nickel of 11–15 per cent will give significantly greater corrosion resistant surgical stainless steels.

Williams, D. F. (1971), *Br. J. Surg.*, **58**, 860.

13. Machine for Dynamic Load Testing of Internally Fixed Femoral Neck Fractures: M. A. Elloy (D. Annis), Bio-engineering and Medical Physics Unit, University of Liverpool.

Internal fixation is the usual treatment for femoral neck fractures. Good fixation permits joint function and holds the fragments in good apposition while osseous union proceeds.

Osteosyntheses have been tested under static load (Hackstock and Hackenbroch, 1969), but as bone deformation is time dependent, dynamic load testing is more appropriate.

A machine has been constructed which applies simulated walking or other physiological load cycles to femurs which are prepared with a 'standardized' transcervical fracture and internally fixed with the implant under test. The magnitude of loads, which are applied along three orthogonal axes, was derived from *in vivo* tests and supplied with air at 5·6 kg. per cm.^{2} pressure. The three pneumatically actuated loading units can produce forces ranging from 0 to 420 kg. with accuracy ±2 kg. and cycle at 0–3 Hz. A number of displacement transducers and a simple analogue computer deduce relative movement of the two fragments during load cycling, measuring up to ±2·54 mm. translation and ±2° rotation with an accuracy of better than 1 per cent. Continuous load cycling permits durability testing.

Dynamic testing will assist the surgeon in choosing an implant from the many available. Without this he must rely on information derived from clinical trials, which are time consuming and often unreliable.

HACKSTOCK, H., and HACKENBROCH, M. H. (1969), *Arch. orthop. Unfallchir.*, **66**, 72.

14. Isolation of Islets of Langerhans for Transplantation: D. R. THOMAS, A. A. GRIEVE, and M. FOX, The Royal Hospital, Sheffield.

The results of whole-gland pancreatic transplantation have been disappointing. Methods of separation using collagenase digestion of pancreas have been described for the isolation of islets for metabolic studies (Howell and Taylor, 1968). In the rat it has been shown (Lacy and Kostianovsky, 1967) that distension of the pancreas as a preliminary to collagenase digestion produced large numbers of islets. Difficulties have arisen over the harvesting of the liberated islets.

A method is described by which relatively large numbers of viable islets are harvested from rat pancreas.

Method: The animals are killed by cervical dislocation, the common bile-duct is identified, and a small polyethylene catheter tied in place. Ten ml. of Hanks's solution are injected to distend the pancreas prior to pancreatectomy. The pancreatic tissue is cut into small pieces and incubated with collagenase in a shaking water-bath. The digested pancreas is washed and transferred to a Petri dish. The vessel is gently agitated, allowing cellular debris to form a suspension which is discarded. The islets remain on the bottom, where they can be easily seen and can be harvested with the aid of a finely drawn Pasteur pipette under the dissecting microscope.

Results: (1) A yield of approximately 350 islets per rat pancreas may be obtained.

(2) Viability of the islets has been confirmed by successful transplantation beneath the renal capsule, and in the testis of the rat.

(3) Early experiments show that transplantation of isolated islets modify the course of streptozotocin diabetes in the rat.

HOWELL, S. L., and TAYLOR, K. W. (1968), *Biochem. J.*, **108**, 17.

LACY, P. E., and KOSTIANOVSKY, M. (1967), *Diabetes*, **16**, 35.

15. The Effect of Intravenous Prednisolone on Survival of Rat Heart Homografts: P. R. F. BELL, R. F. M. WOOD, R. O. QUIN, and K. C. CALMAN, Department of Surgery, Western Infirmary, Glasgow.

Since homograft rejection is initiated by lymphocytes, better immunosuppression following transplantation could conceivably be achieved by destruction of these cells at the time of grafting. Two agents are currently available which rapidly damage lymphocytes, namely large doses of intravenous steroids and anti-lymphocyte serum (A.L.S.). This study was undertaken to evaluate the importance of a single dose of these agents given at the time of transplantation alone or in combination with conventional immunosuppression.

Seven groups of 8 heterotopic rat heart transplants were performed, inbred A/gus rats serving as donors for inbred Wistar recipients. The groups, their immunosuppressive régimes, and the results are set out below.

(1) Controls—no treatment, rejected 7 ± 2 days. (2) Azathioprine and prednisolone (3 mg. per kg.) by daily intraperitoneal injection rejected 14 ± 3 days. (3) A single injection of intravenous prednisolone (15 mg. per kg.) at operation rejected 9 ± 3 days. (4) A single intraperitoneal injection of rabbit anti-rat A.L.S. rejected 16 ± 4 days. (5) A single injection of intravenous prednisolone (15 mg. per kg.) at operation followed by azathioprine and prednisolone as in (2) rejected 29 ± 5 days. (6) A single intraperitoneal injection of A.L.S. (1 ml.) at operation followed by azathioprine and prednisolone as in (2) rejected 33 ± 5 days. (7) A single injection of intravenous prednisolone (15 mg. per kg.) and one intraperitoneal injection of A.L.S. (1 ml.) at operation followed by azathioprine and prednisolone as in (2); all these animals were killed at 65 days without rejection.

These results suggest that large doses of intravenous prednisone or A.L.S. alone or in combination as a single dose immediately after surgery greatly enhance the immunosuppressive effect of conventional drugs. The use of a régime comparable to (5) in 33 human renal transplants has produced a 1-year survival of 85 per cent with 1 death.

16. Solutions for Short-term Organ Preservation: K. C. CALMAN, R. O. QUIN, R. F. M. WOOD, and P. R. F. BELL, Department of Surgery, Western Infirmary, Glasgow.

In the search for the ideal method of short-term organ preservation a variety of solutions has been devised. Of these solutions, the Collins C4 solution and the Gelin technique are widely used. The efficacy of these techniques for organ preservation has not been compared with each other nor have their advantages and disadvantages been defined clearly. The components of each method have been analysed and a solution, superior to both, devised.

The efficacy of the Collins and Gelin technique was assessed using the biologically perfused rat heart model (Calman et al., 1971). Groups of 20 rat hearts were flushed with either Collins's solution or a solution based on Dextran 40 containing 100 U. of insulin per litre (the standard solution). The hearts were stored for 17 hours and their viability assessed. The standard solution gave significantly better results than Collins's technique ($P < 0\cdot01$). The inferior results produced by Collins's solution were related to its high content of potassium.

When the standard solution was compared with the Gelin technique, however, the latter was found to be superior ($P < 0\cdot05$). Further analysis of the Gelin method into its three components showed that its superior performance was related to an initial flush with ½ per cent lignocaine and the addition of lignocaine to the solution. When the standard solution was preceded by lignocaine flush it gave results which were statistically superior to the Gelin technique ($P < 0\cdot05$).

Addition of magnesium to the modified standard solution again improved survival ($P < 0\cdot05$).

CALMAN, K. C., QUIN, R. O. MACPHERSON, S. G., and BELL, P. R. F. (1971), *Br. J. Surg.*, **58**, 865.

17. Effect of Different Preserving Media on the Level of ATP in Canine Renal Cortex:

T. Vincent Keaveny, Aidan O'Boyle, and P. Fitz-Gerald, Department of Surgery, University College, Dublin.

Changes in the energy metabolism of the canine renal cortex were studied during renal flush-out with Ringer's solution (0–4° C.) and with Collins's solution (0–4° C.) by following alterations in renal cortical ATP, ADP, and AMP levels.

Mongrel dogs (15–25 kg.) were studied. Five kidneys were flushed out with each flushing solution, the contralateral kidney in each case being used as a control. Renal flush-out was initiated within 50–55 seconds after nephrectomy and continued for a further 7 minutes.

Kidneys subjected to 55 seconds of warm ischaemia showed a mean fall of 28·9 per cent in the level of renal cortical ATP (resting level: 1·18 ± 0·10 μmol. per g. wet weight; level post-ischaemia: 0·84 ± 0·05 μmol. per g. wet weight).

A mean fall of 26·9 per cent in the level of renal cortical ATP was observed after flushing with Ringer's solution (resting level: 1·08 ± 0·01 μmol. per g. wet weight; level post-flush-out: 0·76 ± 0·05 μmol. per g. wet weight). This solution thus prevents a further breakdown in ATP after exposure of the kidney to 55 seconds of warm ischaemia.

A mean fall of only 1·7 per cent was observed in the renal cortical ATP level after flushing with Collins's solution (resting level: 1·16 ± 0·08 μmol. per g. wet weight; level post-flush-out: 1·14 ± 0·08 μmol. per g. wet weight). The ability of Collins's solution to maintain renal cortical ATP levels may explain its effectiveness as a preserving medium.

18. Hyperbaric Hypothermic Perfusion Preservation of the Ischaemically Damaged Dog Kidney:

R. O. Quin, R. F. M. Wood, S. G. MacPherson, K. C. Calman, and P. R. F. Bell, Department of Surgery, Western Infirmary, Glasgow.

Kidneys obtained in Britain from cadaver donors frequently have warm ischaemic injury in excess of 30 minutes. Most of these organs are stored in ice after an initial flush with a variety of different solutions and anuria from tubular necrosis is common after transplantation. This study was designed to compare the merits of initial infusion and cold storage with hyperbaric hypothermic perfusion of ischaemically damaged canine kidneys.

Dogs in all groups were starved for 12 hours then hydrated with saline (20 ml. per kg. over 30 minutes). No pretreatment of any kind was given prior to removal of the kidney, which was exposed to 40 minutes of warm ischaemia by immersion in a water bath at 37° C. After storage the kidney was transplanted and the opposite organ removed to assess immediate function.

Four groups of animals were studied. Simple surface cooling with ice storage for 6 hours at 40° C. preserved 1 out of 7 kidneys. The Gelin technique with 6 hours' storage at 4° C. preserved 2 out of 6 organs and an initial flush with a modified Perfudex solution successfully preserved only 3 out of 10 kidneys. The fourth group of dog kidneys was again exposed to 40 minutes of warm ischaemia followed by hyperbaric hypothermic perfusion for 24 hours. Using this technique 4 out of 6 organs were satisfactorily preserved with immediate function.

Initial infusion with widely used solutions followed by cold storage is not usually compatible with immediate life-supporting renal function. Hyperbaric hypothermic perfusion using a stable synthetic solution and a commercially available portable machine satisfactorily preserved function in dog kidneys exposed to combined warm and cold ischaemia times comparable to those encountered in human cadaver renal transplantation.

19. Dog Liver Preservation for 13–19 Hours with Collins's Solution and Isoproterenol:

L. Lambotte, J. B. Otte, and P. J. Kestens, Department of Experimental Surgery, University of Louvain, Belgium.

Previous experiments have shown that isoproterenol is of value in the preservation of the canine liver. This drug increases the membrane potential of the isolated perfused dog liver and improves the recovery of membrane potential after a period of anoxia. Addition of isoproterenol to the Ringer–lactate solution used to rinse the liver has extended the preservation of the canine liver from 90 to 180 minutes (Lambotte et al., 1971).

In the present experiments isoproterenol has been combined with Collins's solution (Collins et al., 1969). Two litres of Collins's C2 solution without heparin but with isoproterenol (0·2 mg. per litre) were used to rinse the liver which was thereafter kept in an ice-box. Small doses of isoproterenol were also given to the recipient during the operative period. Survivals longer than 5 days have been obtained in 5 out of 7 consecutive cases of orthotopic transplantation with a total ischaemia time ranging from 5 hours 13 minutes to 7 hours 50 minutes (mean ± S.E., 6 hours 15 minutes ± 24 minutes). The preservation period has been extended to 19 hours (7 dogs, mean ischaemia time 15 hours 30 minutes ± 58 minutes).

All the recipients survived the transplantation and were walking on the first postoperative day, and 5 of them survived more than 5 days. Similar results have never been obtained previously without a complicated perfusion technique. A common mechanism for the action of Collins's solution and isoproterenol is suggested. The reduction of the intracellular sodium concentration may result in a decreased activity of the sodium pump with a reduction in energy requirements.

Collins, G. M., Bravo-Shugarman, M., and Terasaki, P. I. (1969), *Lancet*, **2**, 1219.

Lambotte, L., Otte, J. B., and Kestens, P. J. (1971), *Gut*, **12**, 772.

20. Comparison of Function of *ex vivo* and *in vivo* Livers:

A. Cuschieri, P. R. Baker, and R. Shields, Department of Surgery, Liverpool University.

Assessment of function of the perfused liver prior to its use in hepatic assist or transplantation procedures is usually based on comparison with normal values. However, the 'normal' function of the *ex vivo* liver may not be the same as that of the *in vivo* one.

The function of the *ex vivo* (auxiliary) and *in vivo* (resident) porcine livers sharing the same circulation has therefore been compared in 6 experiments. The auxiliary livers were perfused with blood at physiological rates for 6 hours and function assessed in terms of bile volume and bromsulphthalein (BSP) excretion.

The mean volumes of bile (ml. per 15 min. per 100 g. liver) for the auxiliary and resident livers were 0·57 ± 0·22 (S.D.) and 0·92 ± 0·11 (S.D.) respectively, and this difference was significant ($P < 0{\cdot}01$).

Results from single injection experiments showed that excretion of BSP by the auxiliary liver improved with time. However, continuous infusion of BSP demonstrated that the increase in excretion occurred only during the first 2–3 hours of perfusion. After this a constant output was observed with mean BSP excretion rates (mg. per 15 min. per 100 g. liver) of 3·2 ± 2·0 (S.D.) and 5·6 ± 1·3 (S.D.) for auxiliary and resident livers respectively.

In conclusion, the *ex vivo* auxiliary liver does not function as well as the *in vivo* resident organ even when studied under optimum conditions.

21. Liver Perfusion with Human Blood. A Comparison of Pig, Calf, Lamb, and Baboon Livers: J. Terblanche, Rosemary Hickman, and S. J. Saunders, Departments of Surgery and Medicine, University of Cape Town Medical School, and the Liver Clinic, Groote Schuur Hospital, Cape Town.

The mortality of fulminant hepatic failure remains high despite exchange transfusion. Pig-liver hepatic assist was investigated but led to significant thrombocytopenia. This therapy was halted and reinvestigated in the laboratory, where the isolated pig liver perfused with human blood was shown to provoke a marked thrombocytopenia within 30 minutes. Because of the associated observations this was interpreted as a xenograft response (Hickman et al., 1972). As this phenomenon could not be prevented by pharmacological or physical means, livers from calves, lambs, and baboons were investigated.

All livers were perfused for 4 hours with heparinized human blood. Platelets were counted in hepatic inflow and outflow. Standard biochemical parameters, complement, and antibodies (cytotoxic, leuco-agglutinating, and heterophile) were measured in the hepatic vein blood.

Calf- and lamb-liver perfusions resembled the pig liver with a decline in platelets and a decrease in complement and antibody levels.

Baboon-liver perfusions were markedly different with minimal drop in platelets and no antibodies detected against baboon cells.

Hepatic assist should only be carried out with baboon livers, unless the thrombocytopenia associated with the use of the other livers can be prevented.

Hickman, R., Parker, J. R., Saunders, S. J., and Terblanche, J. (1972), *Transplantation*, **13**, 195.

22. Studies with a New Anti-secretory Drug (UK 5850) in Rats and Man: B. M. Hogbin, S. P. Cox, P. A. Johnson, R. D. Bugden, A. Bennett, L. G. Pullman, and E. A. Stevens (J. G. Murray), King's College Hospital Medical School, London, and Pfizer Ltd., Sandwich.

A new drug (UK 5850, Pfizer Ltd.) has been studied for its effect on gastric secretion in the anaesthetized rat (Rosenoer and Schild, 1962). UK 5850, 2·5–10 mg. per kg. i.v., caused dose-dependent inhibitions of acid-secretory responses to histamine, pentagastrin, carbachol, human gastrin I, and insulin i.v., and to electric vagal stimulation. Prolonged and sometimes complete inhibition of responses (histamine, pentagastrin, and carbachol only studied) could be obtained with 10 mg. per kg. UK 5850, although carbachol was usually inhibited less than histamine and pentagastrin. Studies in various species and tissues suggested that the activity of UK 5850 was not due to atropine-like activity or to a selective antagonism of gastrin. Administration of UK 5850 5–20 mg. per kg. s.c. to Shay rats produced a marked dose-dependent inhibition of gastric ulceration and acid secretion.

Submaximal gastric acid secretory plateaux were produced with pentagastrin or histamine infused i.v. in normal volunteers and duodenal ulcer patients giving informed consent. Aspiration of gastric juice was stopped for 1 hour when isotonic UK 5850 solution (250, 500, and 750 mg.) was given through the nasogastric tube. The average acid output in the two lowest consecutive 15-minute aspirates 1¼–2¼ hours after giving the drug were compared with the average pre-drug secretory plateau.

The combined results in 20 subjects showed percentage reductions of acid output (±S.E.) of 44±7, 34±7, and 42±8 with 250, 500, and 750 mg. UK 5850 (8, 6, and 6 experiments) respectively, due mainly to a fall in volume secreted. Responses to pentagastrin and histamine were inhibited similarly. These experiments show that orally administered UK 5850 is a weak antisecretory drug in man. Maximal inhibition was only about 40 per cent compared with up to 100 per cent with i.v. administration in rats, owing possibly to differences in secretory mechanism or in route of administration.

Rosenoer, V. M., and Schild, H. O. (1962), *J. Physiol.*, **162**, 155.

23. Studies with a New Gastric Secretory Inhibitor (UK 9040) in the Dog: D. B. Hamer, J. H. Baron, and J. Spencer, Department of Surgery, Royal Postgraduate Medical School, London.

Five dogs were each prepared with a fistula of the innervated main stomach (G.F.) and a denervated gastric pouch (H.P.), and 1 dog with a gastric fistula of a vagotomized stomach. Gastric secretion was stimulated by continuous intravenous infusions of pentagastrin (2, 8, and 16 μg. per kg. per hr.) and histamine acid phosphate (2 μg. per kg. per min.) or by single intravenous injections of insulin (0·2 μg. per kg.). Fifteen-minute collections of secretion were made for 3 hours and the volume, pH, and titratable acidity of the juice were measured.

Single intravenous injections of UK 9040, 2·5 mg. per kg., inhibited G.F. but not H.P. acid secretion in response to pentagastrin 2 μg. per kg. per hr. Doses of 5 and 10 mg. per kg. completely inhibited both H.P. and G.F. secretion, but the dogs vomited after 10 mg. per kg.

UK 9040 was given in capsules to the fasting dogs at various intervals before the injection of the stimulant. Doses of 15–30 mg. per kg. given 4–5 hours before the start of infusions of pentagastrin 2 or 8 μg. per kg. per hr., or histamine acid phosphate 2 μg. per kg. per min., produced complete inhibition of both G.F. and H.P. secretion, and there was similar 100 per cent inhibition of the acid response of the G.F. to insulin, 0·25 μg. per kg. There was less inhibition of acid secretion if the capsules were given only 1–2 hours or 18 hours before the secretory stimulants, or if a lower dose of only 8 mg. per kg. was used.

This new drug is a potent inhibitor of histamine-, pentagastrin-, and insulin-stimulated acid secretion in the dog.

24. The Effect of Burimamide on Gastric Secretion in Man: J. H. Wyllie, T. Hesselbo, and J. W. Black, Department of Surgery, University College Hospital Medical School, and Smith, Kline French Research Institute.

The anticholinergic drugs at present used to inhibit gastric secretion are not capable of suppressing secretion stimulated by histamine or pentagastrin given in maximal doses. For example, atropine in doses of 50 μg. per kg. has been estimated to produce only 22 per cent inhibition of pentagastrin-stimulated secretion (Konturek and Olesky, 1969).

Burimamide, defined as a histamine H$_2$-receptor antagonist, is virtually free from conventional antihistaminic activity but can completely inhibit histamine-stimulated acid secretion in animals (Black et al., 1972).

The action of burimamide has been studied in 6 normal volunteers. Gastric acid secretion was maximally stimulated by either histamine or pentagastrin. These experiments showed that burimamide is also effective in man and that 50 per cent inhibition of maximally stimulated secretion was produced by a blood-level of the order of 15 μmol. The effect on pentagastrin-stimulated secretion was the same as that on histamine-stimulated secretion. Thus, burimamide possesses properties which are not shown by any antisecretory agent previously reported.

In the doses used its effect on maximally stimulated acid secretion is similar to that of vagotomy.

Black, J. W., Duncan, W. A. M., Durant, C. J., Ganellin, C. R., and Parsons, A. M. (1972), *Nature, Lond.*, **236**, 385.
Konturek, S. J., and Olesky, J. (1969), *Scand. J. Gastroent.*, **4**, 13.

25. Secretin-induced Pyloric Reflux: Verification of the Mathematical Formula for Eliminating Reflux in Gastric Aspirate: R. G. Fiddian-Green, R. C. G. Russell, and M. Hobsley, Department of Surgical Studies, The Middlesex Hospital, London.

It has been claimed that the volume of duodenal contents refluxing into the stomach during gastric secretory studies can be calculated from the relationship between apparent rate of secretion and electrolyte concentration (Gardham et al., 1968). This hypothesis has been tested in 20 subjects: a plateau of maximally stimulated gastric secretion was achieved with intravenous histamine infusion (Lawrie et al., 1964), and reflux then induced by injecting Boots's secretin, 1·0 unit per kg. intravenously. In every study the 10-minute volumes of gastric aspirate increased, enabling reflux to be expressed as the difference between the observed volume and the mean pre-secretin plateau volume. Calculated reflux was obtained from the formulae

$$V_{\mathrm{R}}\,(\text{sodium}) = 7{\cdot}35\,Q_{\mathrm{Na}} - 0{\cdot}044\,V - 4{\cdot}05,$$
$$V_{\mathrm{R}}\,(\text{hydrogen}) = 0{\cdot}575\,V - 4{\cdot}29\,Q_{\mathrm{H}} - 4{\cdot}46 \text{ ml. per 15 min.},$$

where V is the volume and Q the ion output in mEq./10 min. sample. Both formulae gave equivalent results ($R = 0{\cdot}83$, slope $= 1{\cdot}1$, intercept insignificantly different from zero) and the sodium formula was shown to give a measure of the change in volume of pure duodenal juice refluxed. These results suggest that the calculation method is a valid approach to the estimation of reflux in gastric juice.

Gardham, J. R. C., Hassan, M. A., and Hobsley, M. (1968), *Br. J. Surg.*, **55**, 865.
Lawrie, J. H., Smith, G. M. R., and Forrest, A. P. M. (1964), *Lancet*, **2**, 270.

26. The Effect of Antral Denervation and Pyloroplasty on Gastric Emptying and 'Dumping': R. J. Clarke and J. Alexander Williams, The General Hospital, Birmingham.

To assess the effect of antral denervation and pyloroplasty on gastric emptying 40 male patients with uncomplicated duodenal ulcer had one of four operations: selective vagotomy without pyloroplasty (S.V.) or with pyloroplasty (S.V.+P.), or proximal gastric vagotomy without pyloroplasty (P.G.V.) or with pyloroplasty (P.G.V.+P.). It has been claimed that 'dumping' may be prevented by S.V. and by P.G.V. (Amdrup and Jensen, 1970).

Gastric food residue was measured after a 12-hour fast before operation and 3 months afterwards. The gastric emptying pattern of a hypertonic dextrose 'meal' was assessed by a dye-dilution technique. The occurrence of 'dumping' was noted.

All patients had a uniform gastric-emptying pattern before operation. After all operations more rapid initial gastric emptying occurred; the difference was highly significant after S.V.+P. and P.G.V.+P. Final gastric emptying was significantly shorter after P.G.V.+P. and was significantly longer after S.V.

Eight patients developed 'dumping', 7 of whom had pyloroplasties. Significantly more rapid initial gastric emptying occurred in patients with 'dumping'. Gastric food residue only occurred after S.V.

P.G.V. retains the most normal emptying pattern. S.V. leads to gastric retention. Pyloroplasty increases the gastric emptying rate. 'Dumping' is associated with rapid initial emptying and with pyloroplasty.

Amdrup, E., and Jensen, H. E. (1970), *Gastroenterology*, **59**, 522.

27. A Radio-isotope Method of Measuring Gastric Emptying, Reflux, and Secretion: R. A. Hinder, C. G. Bremner, and B. K. P. Horn (D. J. Du Plessis), Department of Surgery, University of the Witwatersrand, Johannesburg.

Existing methods of measurement of gastric emptying do not allow for the measurement of volume added by gastric secretion, duodenal reflux, or swallowed saliva, and thus do not accurately measure the total pyloric outflow.

A radio-isotope method of measurement of intragastric volumes has been devised by using the Volemetron, an apparatus usually used for the measurement of blood-volumes. A measured dose of RIHSA^{125} is introduced into the stomach, and the dilution factor of this dose allows for the estimation of intragastric volumes by the Volemetron. The test is carried out at 20-minute intervals following a milk or water meal. The method has been cross-checked with a dilutional dye technique (George, 1968) and found to be accurate.

Using a Packard gamma counter, the radioactivity of samples of gastric content is measured each time the intragastric volume is calculated.

These results are used in the following formulae to calculate the volume of fluid added to the original meal (A) and the total pyloric outflow (B) for each 20-minute period:—

$$A = -(V_1 - V_0)\frac{\log_e(C_1/C_0)}{\log_e(V_1/V_0)},$$
$$B = A - (V_1 - V_0),$$

where V_0 is the initial volume in the stomach; V_1, the final volume in the stomach; C_0, the initial concentration of isotope; and C_1, the final concentration of isotope.

In a group of 6 dogs, following a milk meal of 20 ml. per kg. body-weight (mean 307 ml.) the mean results per hour were as shown in the table.

	A (ml.)	B (ml.)	B AS PERCENTAGE OF ORIGINAL MEAL
Normal	75	207	73
After 3–5-cm. pyloroplasty	87	240	74

The increased volume of fluid added per hour in the post-pyloroplasty dogs is probably a reflection of marked duodenal reflux.

George, J. D. (1968), *Gut*, **9**, 237.

28. Liver Metastases—A Clinical Study: R. M. Grant and W. H. H. Garvie (J. N. Norman), Department of Surgery, University of Aberdeen, Scotland.

Studies in the rat (Garvie and Grant, 1971) have suggested that a carcinoma growing at a site remote from the liver can cause changes in hepatic glycogen metabolism. In order to determine whether this also occurs in man three groups of 9 patients were studied. The groups, which were of similar age and sex, consisted of (1) controls, (2) patients with colonic neoplasm and liver metastases, (3) patients with colonic neoplasm who had no evidence of hepatic metastases at laparotomy.

Fasting blood-sugar was estimated and 25 g. glucose given intravenously. Blood-sugar estimation was made

60 minutes later and then glucagon (0·01 mg. per kg. body-weight) was given intravenously. Further estimations of blood-sugar were made 10, 20, and 30 minutes later.

Fasting blood-sugar was similar in all groups. In the control group blood-sugar had returned to normal by the end of the first hour but it rose rapidly following glucagon. The group with hepatic metastases still had an elevated blood-sugar level at the end of the first hour and glucagon made little difference. The responses of the neoplastic group without evidence of hepatic metastases fell midway between the other two groups.

Glycogen metabolism in the liver is thus grossly affected by the presence of hepatic metastases. Even where there is no evidence of metastases the primary neoplasm itself appears to be able to influence the ability of the liver to metabolize carbohydrates.

Garvie, W. H. H., and Grant, R. M. (1971), *Br. J. Cancer*, **25**, 166.

29. Steroidogenesis in Human and Rat Mammary Adenocarcinoma: W. Miller, T. Hamilton, and A. P. M. Forrest, Department of Clinical Surgery, Edinburgh.

Human breast cancer tissue has been shown to act as a para-endocrine organ by virtue of its ability to transform steroids into physiologically active hormones (Jones et al., 1970). Mammary tumours induced in the Sprague-Dawley rat by dimethylbenzanthracene (DMBA) have also been used as an experimental model for human tumours (Huggins et al., 1961).

A direct comparison of the steroidogenic capabilities of the human breast cancer with the rat DMBA-induced adenocarcinoma has been made.

In vitro slices of two rat adenocarcinomata and two human breast cancers were incubated *in vitro* with dehydroepiandrosterone (DHA) ^{3}H and testosterone ^{14}C. The conversion of DHA to testosterone and of testosterone to 5-dihydrotestosterone and 16-hydroxytestosterone were determined by measuring the percentage incorporation of the appropriate radioactive label into the thin-layer chromatography.

The pattern of steroid metabolism was identical for both human and rat adenocarcinomata but the level of steroid conversion was greater in the rat tumours. This similarity is further evidence of the value of the DMBA tumour as an experimental model for human breast cancer.

Huggins, C., Grand, L. C., and Brilliantes, F. P. (1961), *Nature, Lond.*, **189**, 204.
Jones, D., Cameron, E. H. D., Griffiths, K., Gleave, E. N., and Forrest, A. P. M. (1970), *Biochem. J.*, **116**, 919.

30. Antibody Production in Breast Cancer: M. Maureen Roberts, Eleanor M. Bass, and I. W. J. Wallace (A. P. M. Forrest), Department of Clinical Surgery, Edinburgh.

Tissue extracts have been prepared from 14 benign and 35 malignant breast tumours. Normal breast tissue was available from 16 cancer patients. The total protein concentration (Lowry et al., 1951) and the immunoglobulins (Mancini et al., 1965) IgA, IgG, and IgM were estimated in all tissues and sera.

We have found a significant decrease in mean total immunoglobulin production in cancer tissue (86·8 mg. per cent) compared with benign tissue (119·3 mg. per cent). Although IgM was detected in only one-third of extracts, the mean absolute value was higher in tumour tissues (7·8 mg. per cent) than in benign tissues (2·9 mg. per cent). In 4 of the 8 cancer patients in whom control tissue was also studied, absolute values of IgM were consistently higher in the tumour tissue. Levels of IgM and IgG, but not IgA, correlated closely with the degree of round-cell infiltration of the tumour. Levels of IgM in tumours with marked round-cell infiltration were significantly higher than in benign tissues.

In 4 of 16 cancer patients tested we have found precipitating antibodies to tumour in the serum, whereas none could be detected in the serum to the 13 benign or normal tissues studied.

Lowry, O. H., Rosebrough, N. J., Farr, A. L., and Randall, R. J. (1951), *J. biol. Chem.*, **193**, 265.
Mancini, G., Carbonara, A. O., and Heremans, J. F. (1965), *Immunochemistry*, **2**, 235.

31. Protective Effects of Orchidectomy on Tumour Induction and Transplantation in Mice: J. E. Castro, M.R.C., Clinical Research Centre, Northwick Park, Harrow, Middlesex.

Females of most species are immunologically more competent than males. Orchidectomy causes potentiation of immunity as evidenced by accelerated skin-allograft rejection and increased response to some antigens (Castro and Hamilton, 1971). Orchidectomy increases the total number of thymus-dependent lymphocytes (O-positive) and slightly increases macrophage activity shown by increased clearance of carbon particles.

Balb C mice aged 3 months were used. Half were orchidectomized 6 weeks previously and sham-operated animals served as controls. Subcutaneous, dorsal sarcomata (which are not obviously hormone dependent) were induced by methylcholanthrene in oil. The rate of tumour induction was significantly slower in orchidectomized mice and the total number of them developing tumour was 23/36 (64 per cent) compared with 32/36 (89 per cent) in the controls.

Orchidectomized mice were slightly but significantly protected when challenged with a single-cell suspension of a methylcholanthrene-induced leukaemia (normally maintained in an ascitic form) given intraperitoneally. However, when the tumour was injected subcutaneously as a single bolus, so that it grew in a solid form, the protective effects of orchidectomy were increased.

These experiments suggest that orchidectomy by its immunopotentiating effects may have wider application to tumour therapy than the present role of treating 'endocrine-dependent' tumour alone.

Castro, J. E., and Hamilton, D. N. H. (1971), *Br. J. Surg.*, **58**, 870.

32. Macrophage Production in Response to the Growth of an Experimental Tumour: M. Baum and B. Fisher, Department of Surgery, University of Pittsburgh, U.S.A.

Tumours evoke a host response that resembles a delayed hypersensitivity reaction. The macrophage is recognized as playing a critical role in initiating and maintaining such reactions and may control immunoglobulin-mediated enhancement by clearing antibody antigen complexes from the circulation (Haughton, 1971).

The macrophages that populate the reticulo-endothelial system probably arise from rapidly dividing precursors in the bone-marrow. A method for studying this phenomenon is now available (Bradley and Metcalf, 1966).

C3H mice implanted with a syngeneic mammary tumour were killed at intervals from 24 hours to 21 days. Marrow cells were harvested from the femurs of each mouse, mixed with a semi-solid nutrient medium and plated out with 10^5 cells in each of a replicate series of 10 plates. These were then incubated for 7 days, by which time pure colonies of macrophage were found. The colony count was taken to represent the number of plated cells actively proliferating at the time of harvest.

Within 4 days of the tumour challenge there was a significant increase in macrophage production, but this response became exhausted after 2 weeks of progressive tumour growth. No such changes occurred in control mice implanted with kidney tissue.

These experiments suggest the presence of an as yet unexplored phenomenon relating to the host's response to a tumour.

BRADLEY, T. R., and METCALF, D. (1966), *Aust. J. exp. Biol. med. Sci.*, **44**, 287.
HAUGHTON, G. (1971), *Cell Immunol.*, **2**, 567.

33. Serum-mediated Impairment of Lymphocyte PHA Responsiveness by Gut Cancer:

A. J. EDWARDS, G. F. ROWLAND, MARGARET R. SUMNER, and C. M. HURD, St. Bartholomew's Hospital, London.

Whittaker and Clark (1971) showed depression of PHA-induced lymphocyte transformation in early breast cancer and, on the grounds that the effect was abolished on culture in control serum, claimed the presence of a depressant serum factor produced by malignancy. Al-Sarraf and Vaitkevicius (1971) dismissed this as a non-specific homologous effect.

PHA transformation was measured in 6 patients with gastro-intestinal cancer and in 6 patients undergoing laparotomy for other reasons. To test the possibility that a depressant factor is produced by the tumour and released into the circulation, each patient's lymphocytes were cultured in autologous peripheral or portal blood serum. In the cancer group the mean transformation index of peripheral lymphocytes in peripheral serum was 52·4 while these cells in portal serum gave 35·9. Each cancer patient showed an inhibition, the mean being 35·5 per cent ±9·5 (S.E.). No inhibition was observed in the control group, the mean indices being 19·5 and 18·7. Mean indices of portal lymphocytes from cancer patients were 41·6 in portal and 44·1 in peripheral serum, and in control patients they were 18·1 and 24·7.

It is concluded that tumour-effluent blood contains a factor inhibitory to lymphocyte transformation which becomes attached to the draining lymphocytes.

AL-SARRAF, M., and VAITKEVICIUS, V. K. (1971), *Lancet*, **2**, 314.
WHITTAKER, M. G., and CLARK, C. G. (1971), *Br. J. Surg.*, **58**, 717.

34. The Relationship between Pyloric Reflux and Gastric Ulcer:

R. C. G. RUSSELL, R. G. FIDDIAN-GREEN, M. A. HASSAN, C. M. S. ROYSTON, and M. HOBSLEY, Department of Surgical Studies, The Middlesex Hospital, London.

Pyloric reflux has been incriminated in the aetiology of gastric ulceration. To test this hypothesis, reflux has been determined indirectly by the use of mathematically derived formulae. Sixty-three subjects (20 control subjects, 20 duodenal ulcer patients, and 23 gastric ulcer patients) underwent a maximal histamine infusion test. When a plateau response had been obtained three 15-minute samples of gastric juice were collected. The average volume, the average sodium ion output, and the average hydrogen ion output were calculated. The average reflux for the three groups was control group 1·15 ml., duodenal ulcer patients 2·33 ml., and gastric ulcer patients 5·18 ml. There was significant difference between the gastric ulcer and the control groups, but not between the duodenal ulcer and control groups.

In gastric ulcer patients a positive correlation was found between reflux and the length of history ($P < 0{\cdot}001$), and the regression equation indicated that at zero length of history there was minimal reflux.

Whether the reflux is a cause or an effect of the gastric ulcer will depend on the relationship between the onset of symptoms and the appearance of the ulcer.

35. Patterns of Gastric Secretory Response to an Insulin Infusion in Vagotomized Patients:

R. R. DOZOIS, D. C. CARTER, and J. R. KIRKPATRICK, Department of Clinical Surgery, Edinburgh.

A 3-hour insulin infusion produces a steady state of acid secretion in response to a steady level of hypoglycaemia in healthy volunteers (Carter et al., 1972).

The insulin infusion test was performed in 38 vagotomized subjects. Three types of response were seen: (1) a sustained rise of at least 20 mEq./l. over basal values within 90 minutes of the start of infusion ('early positive response'); (2) a similar response occurring in the latter half of the test ('late positive response'); and (3) no significant elevation over basal values ('negative response').

The PAO_I (Baron, 1963) of subjects with an 'early positive response' (11 subjects, mean 10·6 mEq./hr. ± S.D. 8·2) and a 'late positive response' (9 subjects, mean 6·6 mEq./hr. ± S.D. 4·3) did not differ significantly ($P > 0{\cdot}05$), but these means both differed from that of the 'negative response' group (18 subjects, mean 0·66 mEq./hr. ± S.D. 1·0; $P < 0{\cdot}001$).

When the conventional insulin test and the insulin infusion test were performed in the same subjects, the timing of the response to both tests was almost identical. A close correlation between the PAO_I of each test was obtained ($r = 0{\cdot}89$; $P < 0{\cdot}001$).

BARON, J. H. (1963), *Gut*, **4**, 136.
CARTER, D. C. KIRKPATRICK, J. R., and DOZOIS, R. R. (1972), *Br. J. Surg.*, **59**, 305.

36. The Effect of Fat in the Duodenum on Gastric Secretion before and after Truncal Vagotomy (T.V.) and Highly Selective Vagotomy (H.S.V.) in Man:

P. J. LYNDON and D. JOHNSTON, University Department of Surgery, General Infirmary, Leeds.

It has been suggested that mechanisms responsible for inhibiting gastric secretion are preserved after H.S.V., but sacrificed in T.V. Inhibition of gastric secretion by fat in the intestine has been reported to be unchanged (Ward, 1972) or absent (Johnston and Duthie, 1969) after T.V. in man.

Fat-induced inhibition was studied in three groups of men: (1) 8 with duodenal ulcer (D.U.) before operation; (2) 8 after T.V. + pyloroplasty (parietal cell mass denervated, small intestine denervated); (3) 8 after H.S.V. (parietal cell mass denervated, small intestine innervated). Tests were performed more than 1 year after vagotomy, which was complete on insulin testing in each patient.

A low-dose pentagastrin infusion (0·20 µg./kg./hr.) provided the stimulus, and 60 ml. of olive oil were infused slowly into the duodenum after a plateau of gastric acid output had become established. The fat elicited the following decreases in acid output (mean ± 1 S.E.M.): (1) 5·3 ± 0·8 mEq./10 min. (76 per cent) in D.U.s. (2) 0·90 ± 0·2 mEq./10 min. (37 per cent) after T.V. + pyloroplasty. (3) 1·2 ± 0·3 mEq./10 min. (44 per cent) after H.S.V.

Fat produced significant inhibition ($P < 0{\cdot}02$) in all three groups, but inhibition was impaired after either type of vagotomy, compared with before operation. Inhibition was no greater in men whose intestine was innervated (H.S.V.) than in men whose intestine was vagally denervated (T.V.).

JOHNSTON, D., and DUTHIE, H. L. (1969), *Scand. J. Gastroent.*, **4**, 561.
WARD, A. S. (1972), *Br. J. Surg.*, **59**, 309.

37. Effect of Truncal Vagotomy (T.V.), Selective Vagotomy (S.V.) and Pyloroplasty, and Highly Selective Vagotomy (H.S.V.) without Drainage on the Response to Meat Extract in Man: C. S. Humphrey, R. B. Smith, P. J. Lyndon, and D. Johnston, University Department of Surgery, General Infirmary, Leeds.

Surgery for duodenal ulcer since 1943 has been based on the concept that vagal denervation of the antrum is essential (Nyhus et al., 1960). This was thought to diminish gastrin release, so providing protection against recurrent ulceration. An excellent stimulus to gastrin release in man is meat extract (Oxo solution) It has been shown previously that the acid response to Oxo is not greater after H.S.V. without drainage (antrum innervated) than after S.V. without drainage (antrum denervated) (Johnston et al., 1971).

Patients with duodenal ulcer (D.U.) were studied (1) before operation ($n = 26$) and more than 1 year after; (2) T.V.+ pyloroplasty (18); (3) S.V.+pyloroplasty (10); and (4) H.S.V. (25). Postoperative patients were in good health and insulin-negative. The mean peak acid output (± 1 S.E.M.) in mEq./hr. in response to the test meal were (1) D.U., 21·7 ± 2·2; (2) T.V.+pyloroplasty, 16·2 ± 3·0; (3) S.V.+pyloroplasty, 11·0 ± 2·9; and (4) H.S.V., 10·1 ± 1·5.

These results indicate that vagal denervation of the gastric antrum in man fails to diminish gastrin release n response to the chemical stimulus of a test meal. Indeed, acid outputs were considerably higher after T.V.+ pyloroplasty than after H.S.V. though the difference was not statistically significant. These results are in accord with recent studies in man of plasma-gastrin levels after vagotomy.

Johnston, D., Humphrey, C. S., Smith, R. B., and Wilkinson, A. R. (1971), *Br. J. Surg.*, **58**, 725.
Nyhus, L. M. Chapman, N. D., De Vito, R. V., and Harkins, H. N. (1960), *Gastroenterology*, **39**, 582.

38. Graded Vagotomy and Gastric Secretion in the Dog: S. Nundy and J. H. Baron, Department of Surgery, Royal Postgraduate Medical School, Hammersmith Hospital, London.

The current vagal operations for peptic ulcer, truncal vagotomy (T.V.), selective vagotomy (S.V.), and highly selective vagotomy (H.S.V.) all aim at complete denervation of the acid-producing area of the stomach, the assumption being that incomplete vagotomy does not alter acid production. We have tried: (1) to establish whether the stomach does respond in an 'all-or-none' fashion to vagal stimulation; (2) to compare the vagally (insulin) and chemically (pentagastrin) stimulatable secretion after graded division of the vagus nerve performed successively in the same animal.

The acid and pepsin responses to increasing doses of insulin and pentagastrin were measured in 3 dogs with chronic gastric fistulae after operations performed in the following sequence: (1) 'Half a highly selective vagotomy' (H.H.S.V.), dividing the nerves from the antral border to 1 cm. from the oesophagogastric junction; (2) H.S.V., dividing nerves in the remaining lesser omentum and around the lower oesophagus; (3) S.V., dividing the antral nerve; (4) Trans-thoracic truncal vagotomy.

Results.

1. *Insulin*: Peak outputs (per cent of control output ± S.E.M) were as shown in the table.

	Control (per cent)	H.H.S.V.	H.S.V.	S.V.	T.V.
Acid	100	45 ± 6	4 ± 1	4 ± 2	8 ± 4
Pepsin	100	30 ± 3	4 ± 1	3 ± 1	2 ± 1

2. *Pentagastrin*: Submaximal doses resulted in a lower acid output but the maximal response was unchanged.

The gastric secretory response after vagotomy is not an all-or-none phenomenon but is related to the extent of denervation of the acid-producing area.

After a highly selective vagotomy no further changes in secretory output to stimulation occurred when selective and truncal vagotomy were performed successively in the same animal.

39. Relationships between Acid Output to Pentagastrin, Gastric Pepsin Output to Insulin, and Lean Body Mass: J. B. Elder and I. S. Smith, University Department of Surgery, Manchester Royal Infirmary, and Gastrointestinal Centre, Southern General Hospital, Glasgow.

Gastric acid output has been related to parietal cell mass (Card and Marks, 1960) and to lean body mass (Hume and Melrose, 1967). Little is known of the relationship of pepsin output to gastric acid output and to lean body mass.

In assaying pepsin we found that insulin-stimulated peak pepsin output (mg. per 30 min.) correlated well with pentagastrin-stimulated peak acid output (mEq./30 min.) in 13 normal subjects ($r = 0{\cdot}89$, $P < 0{\cdot}001$).

Lean body mass was calculated and pepsin output to insulin was found to show good correlation with lean body mass ($n = 13$, $r = 0{\cdot}67$. $P < 0{\cdot}02$). It appears likely that peak pepsin output after insulin reflects peptic cell mass in normal subjects.

In 28 duodenal ulcer subjects there was no obvious correlation of individual acid and pepsin outputs with lean body mass. However, alternative analysis suggests the existence of separate subgroups. Mean peak pepsin output per kg. lean body mass for the ulcer subjects was significantly greater than normal ($P < 0{\cdot}001$), suggesting an increased number of peptic cells or alternatively increased sensitivity to insulin stimulation.

Card, W. I., and Marks, I. N. (1960), *Clin. Sci.*, **19**, 147.
Hume, R., and Melrose, A. G. (1967), *Br. med. J.*, **1**, 30.

40. Gastric Secretory Reduction after Vagotomy with an Innervated Antrum: R. J. Clarke, R. N. Allan, and J. Alexander Williams, The General Hospital, Birmingham.

A prospective randomized trial was conducted to show whether preservation of antral innervation by proximal gastric vagotomy (P.G.V.) produces adequate reductions of gastric secretion. Forty male duodenal ulcer patients had either a P.G.V. or a selective vagotomy (S.V.).

A combined insulin/pentagastrin test was used to assess gastric secretion (Baron et al., 1969). Estimations were made of the basal output of acid (B.A.O.) and pepsin (B.P.O.), the post-insulin maximal output of acid (M.A.O.$_{\text{I}}$) and pepsin (M.P.O.$_{\text{I}}$), and the post-pentagastrin peak output of acid (P.A.O.$_{\text{pg}}$) and pepsin (P.P.O.$_{\text{pg}}$).

The postoperative reductions of gastric secretion for P.G.V. and S.V. respectively were: B.A.O., 74 and 80 per cent; B.P.O., 75 and 50 per cent; M.A.O.$_{\text{I}}$, 96 and 92 per cent; M.P.O.$_{\text{I}}$, 94 and 87 per cent; P.A.O.$_{\text{pg}}$ 70 and 61 per cent; and P.P.O.$_{\text{pg}}$, 69 and 56 per cent.

There were no significant differences in gastric secretion before or after operation when P.G.V. was compared with S.T.V. Seven patients had a positive-acid response to insulin by the criteria of Hollander, 5 had S.V. and 2 had P.G.V.

Preservation of antral innervation is compatible with complete vagal denervation of the acid-and pepsin-secreting cells of the stomach.

Baron, J. H., Gutierrez, L. V., Spencer, J., Tinker, J., and Welbourn, R. B. (1969), *Gut*, **10**, 1046.

41. Studies of Gastric Acid Secretion after Small-bowel Resection:

J. H. Saunders, B. Buxton, and B. S. Bedi, University Department of Surgery, Western Infirmary, Glasgow.

Recent studies have shown that extensive small-bowel resection results in increased gastric acid secretion in dogs with denervated gastric pouches. The effect of small-bowel resection on acid secretion in dogs with innervated pouches was studied and the effect of antrectomy on gastric secretion defined.

Four dogs were prepared with vagally innervated pouches (group I). In another 4 animals an antrectomy was also performed at the time of pouch construction (group II). The adequacy of antrectomy was confirmed by histology. Both groups subsequently underwent a 75 per cent small-bowel resection.

Twenty observations of daily acid output in response to a standard meal were made before and after small-bowel resection.

The daily acid output in group I rose from 16·24 ± 0·68 mEq. before resection to 22·97 ± 1·23 mEq. after resection.

There was no increase in acid output following resection in group II. The results suggest that small-bowel resection in dogs results in an increased acid output from vagally innervated gastric pouches and that this can be prevented by antrectomy.

42. Radio-isotopic Investigation of Protein Synthesis and Reticulo-endothelial Activity following Partial Hepatectomy in the Rat:

S. J. Karran, K. G. Leach, and L. H. Blumgart, Departments of Surgery and Medical Physics, Welsh National School of Medicine and University Hospital of Wales, Cardiff Royal Infirmary.

Radio-isotopic scanning of the rat liver allows observation of the concentration of substances by different cellular systems within the liver both before and after partial hepatectomy (Croft, 1969; Karran et al., 1972). This paper reports quantitative investigation of the uptake and distribution of ^{75}Se-seleneomethionine (SM) and ^{99m}technetium-sulphur-colloid (TSC) to assess protein synthesis and reticulo-endothelial activity.

One hundred and twenty male Sprague-Dawley rats weighing 230–450 g. were studied using ether anaesthesia.

Uptake of the labelled amino-acid increased soon after partial hepatectomy, reaching a maximum at 6 hours and returning to near normal values by 3 days (80 animals). This increase was independent of the dosage below loading levels. Activity incorporated into liver protein was markedly raised at 12 hours ($P < 0{\cdot}001$).

Uptake of the colloid per g. reached a maximum immediately after partial hepatectomy, whereas total uptake decreased slightly. Normal levels were regained by 5 days (40 animals). The uptake of both compounds by each lobe of the liver was within ± 5 per cent of the mean value both before and after partial hepatectomy.

These results show that protein synthesis increases very soon after hepatic resection and suggest that there is an immediate increase in blood-supply to the remnant as shown by the uptake of the colloid.

Croft, D. N. (1969) in *Diagnostic Uses of Radio-isotopes in Medicine—Gastroenterology*. London: Hospital Medical Publications.

Karran, S. J., Leach, K. G., and Blumgart, L. H. (1972), *Br. J. Surg.*, **59**, 308.

43. Ovarian Implantation into the Spleen of Normal and Portacavally Shunted Rats:

Susan E. Seager, L. H. Blungart, and A. R. Boyns, University Departments of Surgery and Chemical Pathology, Welsh National School of Medicine and the Tenovus Institute of Cancer Research, Cardiff.

The original suggestion (Zondek, 1934) that oestrogens are inactivated by the liver was followed by investigations into changes in ovarian implants into the spleen of spayed rats. Granulosa-cell tumours and luteomas have been reported. Failure of such implants to undergo hyperplasia has been attributed to the presence of adhesions between the spleen and parietal peritoneum (Biskind and Biskind, 1949).

This paper reports an investigation of ovarian implants into the spleen of normal and rats with portacaval shunts.

Follicular development with luteinization was demonstrated in spayed rats after implantation and after 175 days masses of compressed corpora lutea were seen. Twenty animals with portacaval shunts, performed at the same time as implantation, showed markedly less luteal development but moderate follicular growth. Regression of hyperplasia was seen at 175 days after implantation, when portacaval shunts were performed in animals with hyperplastic implants. Hyperplasia only occurred when the implant effluent was allowed to pass through the liver.

No abnormal cells were seen in the implants at any stage.

Ovarian implants into the spleen offer a preparation for the study of ovarian–pituitary relationships.

Biskind, G. R., and Biskind, M. S. (1949), *Am. J. clin. Path.*, **19**, 501.

Zondek, B. (1934), *Skand. Arch. Physiol.*, **70**, 133.

44. Mucous Change in the Duodenum:

W. J. A. Patrick and D. Denham (A. P. M. Forrest), Department of Clinical Surgery, University of Edinburgh.

In 1935 Florey and Harding described the healing of artificial defects in the duodenal mucosa of cats by mucus-containing epithelium which they believed originated in Brunner's glands. Clumps of mucous cells have been described on the villi of the duodenal mucosa in the majority of patients with chronic duodenal ulceration and in a minority with chronic gastric ulcers or gastric cancer.

We have re-examined the significance of mucous change in the duodenum in upper gastro-intestinal disease in 62 patients with duodenal ulcers, gastric ulcers, or gastric cancer. Duodenal biopsies were obtained at operation and histological sections stained with periodic acid-Schiff reagent (PAS) for mucus.

The incidence of mucous change is high in patients with peptic ulcer disease, particularly of the duodenum. Contrary to what Rhodes (1964) suggested, there is no relationship between mucous change in the duodenum and the maximal acid output of the stomach.

The fine structure of the mucous cells in man has been examined with the electron microscope and the cells have been seen to arise from progenitor cells in the crypts.

Florey, H. W., and Harding, H. E. (1935), *J. Path. Bact.*, **40**, 211.

Rhodes, J. (1964), *Gut*, **5**, 454.

45. The Effect of Insulin on Canine Bile-secretion and Composition:

A. C. MacDonald, R. A. MacAllister, and C. MacKay, University Department of Surgery, Western Infirmary, Glasgow.

Gall-stone disease is associated with alterations in the lipid composition of bile (Admirand and Small, 1968), and is said to occur more commonly in vagotomized patients (Fletcher and Clark, 1968). It is important, therefore, to study the action of the vagus on bile-secretion.

We have studied the effect of insulin and atropine, separately and in combination, on bile-volume, bile-lipid (bile-salts, phospholipid, and cholesterol) secretion, and acid output on two occasions in 6 healthy dogs prepared with chronic biliary and gastric fistulae.

The maximum drug effects usually occurred in the second hour after injection. Insulin (1 unit per kg.) produced a significant increase in bile-volume (23·8 ± 2·2 to 47·6 ± 4·9 ml. per hr.) and bile-salt output (1·5 ± 0·2 to 2·2 ± 0·3 mmol. per hr.). Atropine (0·08 mg. per kg.) failed to block the choleretic action of insulin although it almost abolished its stimulatory action on acid secretion. This suggests that the choleretic action of insulin is mediated via non-vagal mechanisms. Atropine (0·08 mg. per kg.) itself caused a significant reduction in bile-volume (26·3 ± 2·6 to 16·8 ± 1·6 ml. per hr.) and in the secretion of bile-lipids, suggesting that there is a vagal component responsible for basal bile-secretion.

ADMIRAND, W. E., and SMALL, D. M. (1968), *J. clin. Invest.*, **47**, 1043.
FLETCHER, D. M., and CLARK, C. G. (1968), *Br. J. Surg.*, **55**, 895.

46. **Prophylactic Synovectomy is Therapeutic:** R. A. DICKSON and F. V. NICOLLE, Royal Postgraduate Medical School, London.

Synovectomy of the metacarpophalangeal joints of the hand may relieve pain and prevent the development of erosions. New information about hand function following synovectomy has been discovered using two new techniques of assessment—that of the measurement of individual digital forces (Dickson and Calnan, 1972), and that of the measurement of the density of the bones of the individual digits of the hand (Dickson et al., 1972).

The forces and bone densities of the hand were measured before and after prophylactic synovectomy of the metacarpophalangeal joints in 10 patients. The forces of the digits operated upon increased by approximately 100 per cent following surgery, while the forces of the remaining digits increased by about 10 per cent, presumably due to the increase in overall hand function resulting from surgery. Bone density increased in precisely the same manner following synovectomy.

Synovectomy leads to functional improvement in the hand and can reverse the general trend of osteoporosis. Prophylactic synovectomy therefore merits the prefix therapeutic.

DICKSON, R. A., BEALES, J. S. M., PETRIE, A., and CALNAN, J. S. (1972), *Br. J. Surg.*, **59**, 317.
— — and CALNAN, J. S. (1972), *Ibid.*, **59**, 316.

47. **A Three-phase Gas Exchanger for Blood Perfusion of Isolated Organs:** A. ZONTA, R. DIONIGI, L. DOMINIONI, and P. DIONIGI, Istituto di Semeiotica Chirurgica Laboratori di Chirurgia Sperimentale, Università di Pavia, Italy.

The results obtained with a gas exchanger designed for blood perfusion and based on a new principle of interposition of a phase of O_2-saturated water between blood and gas are presented. Oxygen uptake and CO_2 removal take place between blood and water separated by a silicone-rubber membrane.

Respiratory efficiency was tested determining: transfer of O_2 to blood and CO_2 removal at constant flow rate, with oxymetric determination of content; inlet and outlet Po_2 and Pco_2; and blood acid-base balance according to the Astrup method.

Plasma-protein degradation and R.B.C. damage were studied in recirculated blood for periods of 2–24 hours, determining: total and plasma Hb, plasma LDH, blood lactate, erythrocyte osmotic fragility, R.B.C. and W.B.C. and platelet counts, specific viscosity, and protein fraction β-lipoproteins.

The unit demonstrated a capability of saturating whole blood with a haematocrit of 40 from normal venous O_2 content to saturation at flow rates up to 100 ml. per min.

CO_2 elimination is slightly higher, requiring, for long-term perfusions, saturation of water with O_2–CO_2 mixtures. The low hydrosolubility of O_2 required high deliveries in water circuits (1000–1300 ml. per min.).

Plasma-protein degradation appears low. Significant viscosity changes and consistent lipoprotein alteration did not develop. The haemolysis is rather constant during the experimental period, resulting in an average plasma haemoglobin production of 0·76 mg. per m.^{2} per min.

48. **Peripheral Lymphatic Pressures in Normal Subjects:** R. D. QUILL and P. BYRNE (W. G. Fegan), Clinical Research Department, Sir Patrick Dun's Hospital, Dublin.

Pressures in lymphatic vessels on the front of the ankle in normal subjects have been measured on a tilt table.

The Pressures:—

In the horizontal position, at rest (6 subjects), ranged from 2 to 5 mm. Hg (mean 4·1).

During or immediately after plantar flexion of the ankle against resistance (5 subjects) there was a rise to between 5 and 12 mm. Hg (mean 7·8).

After tilting to between 45° and 75° (5 subjects), the mean pressures were: resting, 4·1 mm. Hg; during or immediately following plantar flexion of the ankle, 6 mm. Hg.

In 5 subjects spontaneous rises in pressure (by up to 3 mm. Hg) at intervals of 0·5 minute were observed. These were thought to be artefacts due to obstruction of the lymphatic by the proximally pointing recording needle, resulting in a slow build-up pressure below the needle, and a transient recorded pressure rise as lymph by-passed the obstruction. In 1 subject, however, a distally pointing needle was introduced and transient sharp rises in pressure were observed.

It appears that, unlike the venous system, there is no significant hydrostatic component in peripheral lymphatic pressures.

49. **Lung Scans using ^{131}I Human Plasminogen:** J. J. SPINDLER, V. V. KAKKAR, and M. SCULLY (C. T. Howe), Department of Surgery, King's College Hospital Medical School, London.

Abnormal lung scans using ^{99m}TcMAA are not specific for pulmonary embolism. Pneumonic consolidation, pleural effusion, and carcinoma will show as perfusion defects. An attempt was made to label pulmonary emboli with ^{131}I human plasminogen. It was hoped that the fibrin in the emboli would take up the radioactive plasminogen and an area of increased radioactivity would be seen on the lung-scan film.

An experimental model was set up. Venous thrombi were induced in greyhounds by a venotomy and scarifying the endothelium. Forty-eight hours later these thrombi were injected into the venous system and pulmonary emboli were thus established. Laboratory prepared and commercial plasminogen was labelled by one of three different techniques. The iodine monochloride iodination of MacFarlane was preferred. ^{131}I human plasminogen (500 ci) was injected i.v. and the lungs scanned with the gamma camera for about 10 hours.

Lung scans showed areas of increased radioactivity and pulmonary angiograms confirmed the presence of emboli. These pulmonary emboli were removed from the heparinized dog and the radioactivity was measured and compared with the radioactivity in the sample of blood. The concentration of ^{131}I plasminogen in the clot was 3–7·5 times that in the blood, showing an uptake of ^{131}I bovine albumin.

50. **Small-bowel Flora and Bowel Habit studied at Intervals following Vagotomy and Drainage:** G. G. BROWNING, K. A. BUCHAN, and C. MACKAY, Department of Surgery, Western Infirmary, Glasgow.

Post-vagotomy diarrhoea may be related to bacterial colonization of the upper small intestine. Eighty per cent of the patients have significant colonization of the upper small intestine in the first 7–10 days following truncal vagotomy and drainage (MacKay et al., 1969).

Twenty-five patients who had been studied in the immediate postoperative period were reassessed as regards their small-bowel flora and bowel habit on average 18 months (range 6–28) following surgery. Fourteen of these patients had a gastro-enterostomy and 11 a pyloroplasty. The incidence of significant colonization following gastro-enterostomy fell from 86 per cent (12 of 14) to 50 per cent (7 of 14), while the significant incidence of colonization following pyloroplasty fell from 100 per cent to 9 per cent (1 of 11). The difference between the two drainage procedures at follow-up is statistically significant ($P < 0{\cdot}05$). Of the 25 patients studied, only 2, both with a gastro-enterostomy, subsequently developed diarrhoea. Of these only 1 had a significant colonization of the upper small bowel.

The initial high incidence of colonization in pyloroplasty patients is not maintained.

In gastro-enterostomy patients, although there is a fall in incidence, 50 per cent of the patients are still significantly colonized on follow-up.

Owing to the low incidence of diarrhoea no aetiological connexion can be made between this symptom and colonization of the upper small bowel.

MacKay, C., Browning, G. G., and Buchan, K. A. (1969), *Br. J. Surg.*, **56**, 706.

51. The Effect of Potassium Loading on the Intestinal Handling of Electrolytes: Anne Hardy-Smith, Alma Birch, and R. Shields, Department of Surgery, University of Liverpool.

Controversy still exists concerning the effect of adrenal mineralocorticoids upon the intestinal handling of electrolytes. In most studies aldosterone has been administered or its secretion stimulated by inducing salt depletion. The effect of another stimulus of aldosterone secretion, potassium overloading, upon intestinal absorption of electrolytes was studied.

Thiry-Vella loops of ileum and colon were fashioned in 4 dogs and their ability to absorb water and electrolytes determined by established methods, following the intravenous load of 15 mEq. KCl, with and without dietary loading of 240 mEq. KCl and 120 mEq. NaCl. Changes in body electrolytes and extent of potassium overloading were monitored by measuring plasma, urinary and red blood-cell electrolytes, as well as total exchangeable sodium and potassium.

Acute intravenous loading produced increases of 2·1–4·2 mEq. K^+/l. plasma within 1 hour, with return to normal 6 hours later. Chronic dietary loading did not affect the plasma-potassium concentration despite profound E.C.G. changes.

Net intestinal transport of potassium was decreased largely as a result of increase flux of potassium from blood to lumen.

These results further define the action of mineralocorticoids upon the intestine and suggest that a protective mechanism may exist to reduce potassium transport from the gut when the body is being overloaded with potassium.

52. The Role of Peritoneal Lavage in Acute Intestinal Ischaemia: D. T. Caridis, Department of Surgery, University of Aberdeen, Scotland.

The usefulness of peritoneal lavage as a therapy for acute ischaemic injury of the gut was investigated on rabbits subjected to 1-hour transient occlusion of the superior mesenteric artery. The untreated controls ($n = 6$) died within 2 hours of release of the occlusion with a mean plasma volume loss of 30 per cent and endotoxaemia (mean 1·0 µg. per ml.). Intermittent lavage for 6 hours prevented endotoxaemia during the period of lavage, reduced plasma loss by 50 per cent, and prolonged survival of this group ($n = 10$) by 24 hours. In a further group ($n = 10$) replacement of plasma deficit did not improve the results from lavage alone. The gain from adding intra-intestinal kanamycin into the bowel after release of the occlusion was, however, considerable, for half of this group ($n = 10$) survived for 48 hours and the remainder had complete recovery. The amount of endotoxin recovered from peritoneal lavage fluid averaged 72·6 µg. per animal. The data demonstrate that this therapy by eliminating endotoxaemia can achieve survival from an otherwise uniformly lethal disorder.

53. Lymphocyte Transformation in the Mesenteric Lymph-nodes of Patients with Crohn's Disease: P. J. Guillou, G. R. Giles, and T. G. Brennan, University Department of Surgery, St. James's Hospital, Leeds.

The circulating lymphocytes of patients with Crohn's disease have a diminished transformation rate to phytohaemagglutinin (PHA) (Walker and Greaves, 1969). Six patients with ileocaecal Crohn's disease and 6 patients with non-inflammatory gastro-intestinal conditions were studied and the lymphocyte transformation rate (L.T.R.) to PHA compared in the peripheral blood and in mesenteric lymph-nodes.

The L.T.R. of blood lymphocytes in control subjects averaged 46·6 per cent (S.E. ± 1·7 per cent) compared with a mean of 35·8 per cent (S.E. ± 3·6 per cent) in patients with Crohn's disease ($P = 0{\cdot}01$). Similarly the mean L.T.R. of lymph-node lymphocytes was 41·1 per cent (S.E. ± 3·9 per cent) in the control subjects and 21·9 per cent (S.E. ± 3·6 per cent) in the patients with Crohn's disease ($P = 0{\cdot}002$). Cells obtained from lymph-nodes directly draining diseased bowel had the lowest L.T.R. (17·6 per cent S.E. ± 4·4 per cent) compared with cells in the nodes situated centrally at the root of the mesentery (28·8 per cent S.E. ± 4·8 per cent). In control subjects no such gradient existed. The diminished L.T.R. to PHA in patients with Crohn's disease was not increased by culture in pooled homologous AB serum. Likewise lymphocytes from control patients did not show reduced L.T.R.s when incubated in the serum of patients suffering from Crohn's disease.

These findings suggest that in patients with Crohn's disease the reduced L.T.R. in blood is the result of some local action at the site of disease.

Walker, J. G., and Greaves, M. F. (1969), *Gut*, **10**, 414.

54. Diverticular Disease treated by Methyl Cellulose Tablets: W. J. B. Hodgson (B. N. Brooke), Surgical Unit, St. George's Hospital Medical School, London.

Following animal experiments previously reported to the Society, 6 patients with diverticular disease were seen and examined and their rectosigmoid pressures were measured, using two fluid-filled open-tipped narrow-bore polythene tubes placed at 20 and 10 cm. from the anal margin through a sigmoidoscope. Pressures were measured for a resting period of 30 minutes, during feeding, and during a post-prandial period of 30 minutes. Results were expressed quantitatively using the colonic motility index (Chaudhury and Truelove, 1961). Activity was eight to ten times greater at the rectosigmoid than in the rectum.

The patients received a 6-month course of methyl cellulose (Celevac) tablets. No attempt was made to change their habitual low-residue diet. After this they were reassessed and examination and pressure measurements repeated as before. Results before and after methyl cellulose were compared.

All patients had become symptom-free; sigmoidoscopy had become technically much easier and activity at the rectosigmoid had fallen significantly to rectal levels, which remained the same. Since rectal pressures increase after colonic resection for diverticular disease (Parks, 1970) the bulk-forming action of methyl cellulose would appear to be rational and effective treatment and suggests that the acquired condition of diverticular disease is reversible.

CHAUDHURY, N. A., and TRUELOVE, S. C. (1961), *Gastroenterology*, **40**, 1.
PARKS, T. G. (1970), *Gut*, **11**, 121.

55. The Effects of Dietary Supplements of Wheat Bran and Cellulose upon Bowel Function:

T. HAMILTON, J. R. KIRKPATRICK, D. MITCHELL, and M. A. EASTWOOD, Departments of Clinical Surgery and Medicine, Edinburgh.

It has been suggested that diseases of the colon in Western society are related to a reduction in dietary 'fibre'; and high-residue diets have been advocated in the treatment of diverticular disease of the colon (Painter and Burkitt, 1971).

The effects of wheat bran and cellulose upon bowel habit and certain constituents of faeces have been investigated. Faeces were collected for 5 days from 8 healthy males before and during the ingestion of a daily dietary supplement of 16 g. unprocessed wheat bran over a 3-week period. Following a further 3-week control period the effect of a daily supplement of 16 g. cellulose was assessed in 4 of the subjects. Intestinal transit time was measured using radio-opaque markers (Hinton et al., 1971). Stools were weighed and faecal bile acids, faecal fat, and serum cholesterol measured.

Neither bran nor cellulose had a significant effect upon intestinal transit time or upon the frequency of stools. Wet weight of stool increased significantly but there was no change in total bile-acid excretion, faecal fats, or serum cholesterol. It is concluded that any therapeutic benefit from bran or cellulose results from increased water content of stool rather than from alteration in transit time.

HINTON, J. M., LENNARD-JONES, J. E., and YOUNG, A. C. (1969), *Gut*, **10**, 842.
PAINTER, N. S., and BURKITT, D. P. (1971), *Br. med. J.*, **2**, 450.

56. Urodynamic Assessment of Bladder Dysfunction following Spinal Injury:

D. G. THOMAS, R. H. SMALLWOOD, and D. W. GRAHAM (M. Fox), Spinal Injuries Unit, Lodge Moor Hospital, Sheffield.

Fifty patients with spinal injuries have been investigated by measuring urethral pressure profiles (Brown and Wickham, 1969) and pressure/flow values with synchronous radiological studies during bladder filling and voiding.

Standard methods of synchronous pressure/flow cystography (Bates and Corney, 1971) have been adapted for use in this study, employing double-lumen, nylon transurethral catheter (external diameter 1·5 mm.), slow filling of the bladder, and studying patients in the supine/oblique position.

The parameters recorded were: total bladder pressure, rectal pressure, intrinsic bladder pressure (cm. of water), voiding volume (ml.), voiding flow rate (ml. per sec.), and an integrated EMG of the external anal sphincter.

Fifteen spinal injury patients with returning reflex bladder activity were studied between 2 weeks and 9 months after injury.

The static urethral pressure at the level of the external urethral sphincter increased gradually during the post-injury period concomitant with increasing reflex somatic activity.

The external urethral sphincter is normally physiologically silent during micturition; in the paraplegic patient during a single act of voiding there is continuous and varying external sphincter activity. This incoordination between the detrusor and sphincteric mechanisms results in low flow rates often with intermittent voiding, and contributes to incomplete bladder emptying.

BATES, C. P., and CORNEY, C. E. (1971), *Br. J. Radiol.*, **44**, 44.
BROWN, M., and WICKHAM, J. E. A. (1969), *Br. J. Urol.*, **41**, 211.

57. The Effects of Early Experimental Cryptorchidism and Subsequent Orchidopexy on Maturation of the Guinea-pig Testicle:

P. M. ATKINSON (C. W. Jamieson), Surgical Unit, St. Mary's Hospital, London.

The results of orchidopexy for cryptorchidism in man are disappointing. The poor results and the underlying cause of cryptorchidism are not understood. Animal experiments have shown that intraperitoneal replacement of a mature testicle prevented spermatogenesis, and subsequent orchidopexy allowed it to recover (Wangensteen, 1927). However, the effects of orchidopexy upon immature experimentally cryptorchid testicles have not been investigated.

A group of 25, 7-day-old, guinea-pigs was made cryptorchid and a similar group was used as controls. Orchidopexy was performed at varying intervals until the post-pubertal age of 100 days. Testicular biopsies were taken at 7 days, at orchidopexy, at the post-pubertal age of 120 days, and at sacrifice in young adult life. The biopsies were studied histologically. The results indicated that early experimental cryptorchidism arrested testicular development, and later orchidopexy allowed it to continue to active spermatogenesis.

An experimental situation, which was comparable to the surgical treatment of natural cryptorchidism, has been used. This situation allowed an immature but initially normal testicle to achieve spermatogenesis after orchidopexy. This would suggest that the poor results following surgical treatment in man are due to an abnormality of the testicle itself. If this is true, the failure of descent might also be the result of that abnormality.

WANGENSTEEN, O. H. (1927), *Archs Surg., Chicago*, **14**, 663.

58. Changes in Serum Complement and the Immunoglobulins after Cardiopulmonary By-pass:

D. J. PARKER, G. CANTRELL, R. STROUD, R. KARP, and S. B. DIGERNESS, University of Alabama, Birmingham, U.S.A., and London Chest Hospital.

The relationship of organ dysfunction, particularly pulmonary dysfunction after cardiopulmonary by-pass, to changes induced in the blood remains speculative. Denaturation of plasma proteins at the gas–blood interface in oxygenators has been postulated as the cause but the biochemical pathogenesis remains unexplained.

Theoretically, activation of the complement system involving the release of anaphylatoxins and kinins causing an alteration in capillary permeability could be involved. Pruitt et al. (1972) recently showed aggregates of gamma-globulin produced in an oxygenator could combine and activate complement.

Eleven patients undergoing cardiopulmonary by-pass for aortic valve disease were studied preoperatively and serially to 8 days after surgery. Serum-complement levels reduced from preoperative values of $30{\cdot}7 \pm 5{\cdot}1$ to $18{\cdot}8 \pm 2{\cdot}7$ CH50 units per ml. at 4 hours ($P < 0{\cdot}001$) and $22{\cdot}2 \pm 4{\cdot}0$ units at 20 hours ($P < 0{\cdot}001$) after surgery. Immunoglobulins IgG and IgM also showed significant falls in the postoperative period, but IgA did not. Total protein and water content of blood estimations showed that the changes were not due to haemodilution itself.

A possible explanation is that the IgG aggregates produced during cardiopulmonary by-pass combine with complement before or after interacting with capillary membranes and lead to alterations in capillary permeability and hence organ function.

LEE, W. H., KRUMHAAR, D., FONKALSRUD, E. W., SCHJERDE, O. A., and MALONEY, J. (1961), *Surgery, St Louis*, **50**, 29.

PRUITT, K. M., STROUD, R. M., and SCOTT, J. W. (1972), *Proc. Soc. Exp. Biol. Med.*, in the press.

59. The Action of Autologous Lymphocytes against Colon Cells from Patients with Acute Ulcerative Colitis: *in vitro* Studies: P. S. HUNT (H. A. F. Dudley), Department of Surgery, Monash University, Melbourne, Australia.

Colon mucosal cells were obtained from operative specimens and by biopsy at sigmoidoscopy from patients with acute ulcerative colitis and controls with normal large-bowel mucosa. These cells were grown in multiple monolayer microcultures and also labelled in monodisperse suspension with chromium-51 (Perlmann and Holm, 1969). Lymphocytes were separated from blood by density-gradient centrifugation and multiple washings. The ability of lymphocytes from the same patient both to detach autologous cells in microculture and to release label from cells was quantitatively assessed. There was agreement between these two tests for lymphocyte reactivity. All patients with acute ulcerative colitis and none of the controls showed lymphocyte reactivity.

The results in patients who came to urgent colectomy differed from those who responded to steroids: the former demonstrated greater lymphocyte reactivity, which was unaffected by the addition of autologous serum; in the latter serological inhibition of lymphocyte reactivity was a uniform feature.

An additional finding in the serum of patients coming to urgent colectomy was the absence of immunofluorescent auto-antibodies to normal human colon.

These findings suggest an important role for the lymphocyte in the production of colonic damage in ulcerative colitis.

PERLMANN, P., and HOLM, G. (1969), *Adv. Immunol.*, **11**, 117.

60. Antilymphocyte Serum: An Investigation into the Decay Phenomenon: MARY PONSFORD (A. G. Riddell), University Department of Surgery, Bristol Royal Infirmary, Bristol.

Repeated immunization of animals producing immunosuppressive antilymphocyte serum results in the production of less potent material (Levey and Medawar, 1966; Ponsford and Symes, 1971).

Two series of rabbit anti-mouse thymocyte sera (R.A.M.T.S.) were prepared. Series I: Five weekly immunizations were followed, after an interval of 3 months, by three further weekly immunizations. Series II: Sixteen weekly immunizations were given. Animals were bled 7 days after each immunization.

The immunosuppressive potency of each serum was assessed by its ability to prolong the survival of C57B1 skin-grafts made to CBA mice. The potency of both series of R.A.M.T.S. declined after the third immunization.

The decline in potency of series II R.A.M.T.S. was paralleled by a fall in leuco-agglutinin and opsonin titres.

The administration of series I seven-pulse R.A.M.T.S. together with the three-pulse material significantly reduced the potency of the latter. In contrast later sera of series II were without effect on the potency of earlier sera.

It is suggested that, in series I, further immunization after an interval of 3 months resulted in the development of antibodies which inhibited the action of the immunosuppressive antibodies. However, in series II continuous immunization resulted in the absorption of immunosuppressive antibodies by the injected thymocytes.

LEVEY, R. H., and MEDAWAR, P. B. (1966), *Proc. natn. Acad. Sci. U.S.A.*, **56**, 1130.

PONSFORD, F. M., and SYMES, M. O. (1971), *Folia biol., Praha*, **17**, 227.

61. The Isolated Perfused Rodent Thymus as a Source of Lymphocytopoietic and Immunocompetence Promoting Factors: I. W. J. WALLACE and O. EKUEME (A. P. M. Forrest), Departments of Clinical Surgery, Royal Infirmary, Edinburgh, and Royal Infirmary, Cardiff.

Isolated perfusion *in vitro* of the rabbit and the rat thymus has been performed, and studies carried out on the ability of the perfusate to reconstitute neonatally thymectomized animals of these species in a manner comparable to the effect of thymus extracts (Goldstein and White, 1970).

The rabbit thymus was perfused with a saline-diluted rabbit medium in a closed circuit system, viability being maintained for at least 6 hours. The cell-free fraction of this perfusate administered to neonatally thymectomized rabbits enhanced significantly their susceptibility to sensitization to BSA as demonstrated by subsequent development of skin hypersensitivity. No such effect was obtained with unperfused control medium.

The rat thymus was perfused in open circuit with an acellular, protein-free, complex medium (Medium 199, Wellcome) and found to remain viable for at least 12 hours as assessed by glucose utilization. The cell-free effluent, given by repeated subcutaneous injection to 25 neonatally thymectomized rats, was found to raise the peripheral blood-lymphocyte count from $3{\cdot}8 \times 10^3 \pm 1100$ to $8{\cdot}6 \times 10^3 \pm 2000$ ($P < 0{\cdot}05$), and the differential count from 40 to 68 per cent. The unperfused medium had no such effect. Intact control animals treated with perfusate showed no significant rise in lymphocyte count.

GOLDSTEIN, A. L., and WHITE, A. (1970), in *Biochemical Actions of Hormones*, vol. I (ed. LITWACK, G.), p. 465. New York: Academic Press.

62. The Response of the Lower Oesophageal Sphincter to a Meat-extract Test Meal: G. R. GILES, A. ROSZKOWSKI, and P. J. GUILLOU, University Department of Surgery, St. James's Hospital, Leeds.

It has been suggested that gastro-oesophageal competence is largely determined by the pressures exerted by the lower oesophageal sphincter (L.O.S.) (Cohen and Harris, 1971). In an attempt to devise a test of sphincteric function L.O.S. pressures were assessed in response to a meat-extract test meal. Pressures were measured by a withdrawal technique repeated at intervals which results in a profile of the sphincter (10 normal subjects) or by continuously monitoring sphincteric pressures (8 normal subjects; 9 patients with hiatus hernia).

Almost all normal subjects showed increases in pressure following the test meal, reaching a peak after 30–60 minutes and then declining towards basal levels by the end of 2 hours. With the profile technique there was a mean percentage pressure increase over the basal levels of 20·0 per cent ± 9·0 by 30 minutes and 32·4 per cent ± 8·1 at 60 minutes. Continuous pressure monitoring was much more sensitive, with pressure increases of 86·7 per cent ± 24·9 at 30 minutes and 88·3 per cent ± 29·4 by 60 minutes. Patients with hiatus hernia showed diminished pressure increases of only 29·8 per cent ± 9·9 at 30 minutes and 36·8 per cent ± 11·7 by 60 minutes.

The meat-extract test meal demonstrates the poor sphincteric function in patients with hiatus hernia in a physiological manner and may prove useful in the clinical situation.

COHEN, S., and HARRIS, L. D. (1971), *New Engl. J. Med.*, **284**, 1053.

63. Diamine Oxidase and Histamine in the Small Intestine after Experimental Ischaemia: H. Richter, J. Kusche, K.-Th. Schumann, J. Schmidt, and W. Lorenz, Department of Experimental Surgery and Pathological Biochemistry, Surgery Clinic of the University Marburg/Lahn, Germany.

An altered balance of electrolytes and water and the formation and release of vaso-active substances can be observed in ischaemic gut. The concentrations of histamine and its inactivation by diamine oxidase (DAO) were measured in the small intestine of mongrel dogs before and following 10-hour ischaemia of the terminal ileum. Histamine was determined fluorometrically, the DAO activity by the spectrophotometric test with *o*-aminobenzaldehyde.

Before ischaemia the DAO activity and histamine concentration were 15·5 ± 5·7 mU. per g. and 17 ± 8 µg. per g. Following ischaemia the DAO activity was diminished in the ischaemic part of the ileum by 43 per cent ($P < 0·02$, $n = 8$), but increased in the non-ischaemic part by 75 per cent ($P < 0·01$). In the intestinal fluid the DAO activity was 21·7 ± 12·3 mU. per ml. in the ischaemic area and 61·3 ± 34·3 mU. per ml. in the non-ischaemic area ($P < 0·005$, $n = 10$). The histamine concentration remained unchanged in the ischaemic ileum, but decreased in the non-ischaemic ileum by 42 per cent ($P < 0·025$, $n = 8$). An inverse correlation existed between the DAO activity and the histamine concentration in the non-ischaemic small intestine before and after ischaemia ($r = -0·76$; $r = -0·99$).

Probably histamine released from the non-ischaemic gut was inactivated by DAO. This enzyme may protect the organism from histamine release into the circulation.

64. Glucagon in the Pathogenesis of Acute Pancreatitis: M. Knight (B. N. Brooke), Surgical Unit, St. George's Hospital Medical School, London.

There is evidence for the existence of a naturally occurring factor which retards the progression of acute pancreatitis by reducing pancreatic exocrine secretion. Glucagon decreases the volume and enzyme concentration of pancreatic juice, and hyperglucagonaemia has been noted in non-fatal experimental acute pancreatitis (Paloyan et al., 1966).

In this study plasma-glucagon levels were monitored during experimental pancreatitis induced in 6 dogs by the closed-duodenal-loop technique. This model produces oedematous pancreatitis at about 4 hours with sudden onset of fatal haemorrhagic pancreatitis and plasma-amylase elevation at about 10 hours.

An initial rise in plasma glucagon occurred which was maximal at a mean of 6¼ hours from operation. There then followed a fall in plasma glucagon maximal at a mean of 8¾ hours associated with hyperamylasaemia. A second rise in glucagon values occurred just before death. Average survival was 12½ hours. Six other dogs subjected to identical procedures received intravenous glucagon post-operatively. This treatment prolonged survival to a mean of 19 hours.

It is suggested that hyperglucagonaemia may be the factor which retards the progression of acute pancreatitis.

Paloyan, D. Paloyan, E., Wordbec, R., Ernst, K., De Ininger, E., and Harper, P. V. (1966), *Surg. Forum*, **17**, 348.

65. The Role of Vagal Release of Gastrin in Pancreatic Enzyme Secretion: W. H. Beesley, R. Orahood, P. Dutta, and M. M. Eisenberg (W. G. Fegan), Dublin and Minneapolis.

The vagal control of pancreatic enzyme secretion is known to be mediated by (1) direct extragastric vagal innervation of the pancreas, (2) vagal release of gastri from the stomach, (3) pancreozymin release consequer upon duodenal acidification. The relative importance these factors is uncertain.

Eight dogs were prepared with chronic gastric (G.P and pancreatic fistulas (P.F.).

A dose of 200 mg./kg. 2-deoxy-D-glucose was give intravenously as a vagal stimulus. Pancreatic juice wa collected every 15 minutes and gastric juice every 3 minutes for 4 hours. Pancreatic protein, bicarbonat and gastric HCl output were measured.

Four dogs underwent selective extragastric vagotom removing only direct extragastric pancreatic innervatio leaving intact vagal innervation to the stomach, an resulting in unaltered gastric acid production and vag release of gastrin. Four dogs underwent selective gastr vagotomy, removing vagal innervation to the parietal cel and gastric antrum, resulting in an almost zero vagal relea of acid, while preserving extragastric vagal innervation the pancreas.

The 4-hourly pancreatic protein output fell by 77 p cent following selective gastric vagotomy and by 15 p cent following selective extragastric vagatomy compar with control levels.

The reduction in output following elimination of vag release of gastrin, and of only 15 per cent when the gastr mechanism is intact, demonstrates that the vagal relea of gastrin is the major element in vagally stimulat pancreatic enzyme production and that direct extragastr vagal fibres are relatively unimportant.

66. Lysolecithin: A Factor in the Path genesis of Gastric Ulceration?: A. G. Johnso Charing Cross Hospital Medical School, London.

The regurgitation of bile-salts into the stomach has be proposed as a cause of gastric ulceration. The phosph lipid, lysolecithin, which is formed in the duodenum wh phospholipase A in pancreatic juice hydrolyses t lecithin in bile, is also a strong detergent and highly to to cell membranes. This study was designed to determi whether during the night lysolecithin occurs in sufficie concentration in the gastric juice of gastric ulcer patie to cause mucosal damage.

A nasogastric tube was positioned at 9.30 p.m. by t water-recovery method, 3 hours after a normal hospi supper, and 10-ml. samples taken at 2-hourly interv throughout the night. Lysolecithin was measured silicic acid chromatography (Borgstrom, 1957) and purity confirmed by thin-layer chromatography.

Twenty-seven patients were studied. The mean of t peak concentrations (483 µg. per ml.) and mean of samples (212 µg. per ml.) for gastric ulcer patients w significantly higher ($P < 0·001$) than for normal cont patients (36 µg. per ml. and 23 µg. per ml. respectivel Duodenal ulcer patients had normal or slightly rais levels. The values found in gastric ulcer patients similar to those causing mucosal damage under expe mental conditions (Davenport, 1970) and it is conclud that lysolecithin may be as important or more import than bile-salts in the aetiology of gastric ulceration.

Borgstrom, B. (1957), *Acta chem. scand.*, **11**, 749.
Davenport, H. W. (1970), *Gastroenterology*, **59**, 505.

67. Effect of Secretin on Pentagastri stimulated Myoelectrical Activity of t Stomach: B. S. Bedi, I. H. Khan, and K. Kelly, University Department of Surgery, Weste Infirmary, Glasgow, and Mayo Clinic, Rochest Minnesota.

There is evidence that secretin inhibits spontane electrical activity of the stomach. The purpose of t study was to investigate the effect of secretin on pen gastrin-stimulated gastric myoelectrical activity.

Three dogs were prepared with chronically implanted Ag–AgCl electrodes on the serosal surface of the stomach. Electrical recordings were made in fully conscious dogs. Pentagastrin and secretin, alone or in combination, was given by continuous intravenous infusion over 20 minutes. Dose–response studies to both pentagastrin and secretin were first made; the doses used ranged from 0·0015 to 0·048 μg. per kg. per min. for pentagastrin, and from 0·025 to 0·39 unit per kg. per min. for secretin. The effect of combined pentagastrin and secretin was studied at maximal and submaximal doses. Four observations were made on each dog using each dose of secretin and pentagastrin.

There was a dose-related increase in the frequency of pace-setter potentials with pentagastrin infusion. Secretin by itself had no influence on the frequency of the pace-setter potential. Small doses of secretin inhibited pentagastrin-stimulated action potentials but did not affect the frequency of the pace-setter potentials. The kinetics of the dose–response relationship between secretin and pentagastrin suggest that secretin blocks the action of pentagastrin on gastric myoelectrical activity in a non-competitive manner.

68. Histamine Release from the Liver by Trypsin: R. Tauber, R. Uhlig, G. Mann, A. Schmal, and W. Lorenz, Department of Experimental Surgery and Pathological Biochemistry, Surgery Clinic, University of Marburg/Lahn, Germany.

Histamine release is probably involved in various pathophysiological processes observed in the abdomen, such as stress ulcers, acute pancreatitis, ileus, or during liver transplantation. Proteolytic enzymes, such as trypsin, kallikrein, and trypsin-like lysosomal proteases mainly, are considered to cause this histamine release.

As a model for these processes the quantitative aspects and the site of histamine release by trypsin (5 mg. per kg. i.v. into the femoral vein) was investigated in 9 male anaesthetized mongrel dogs (14–25 kg.) by the fluorometric determination of histamine in plasma and whole blood of the ventral aorta, portal vein, hepatic veins, and inferior vena cava. In the plasma of the inferior vena cava the histamine concentration rose from 0·5 ± 0·3 to 16·2 ± 12·2 ng. per ml. ($P < 0{\cdot}02$), and in the whole blood from 42 ± 32 to 102 ± 74 ng. per ml. at the time of maximum hypotension following the injection of trypsin. Since only plasma histamine, but not whole-blood histamine, is free and vasoactive, the majority of released histamine was very rapidly inactivated by an uptake into the erythrocytes.

In the hepatic veins the histamine concentration of the whole blood rose from 44 ± 30 to 835 ± 620 ng. per ml., in the ventral aorta from 45 ± 37 to 340 ± 280 ng. per ml., and in the portal vein from 43 ± 30 to 114 ± 84 ng. per ml., indicating that histamine release by trypsin occurred preferably in the liver.

It is assumed that the erythrocytes play an important role in the rapid inactivation of histamine released by proteolytic processes, and that the liver is one of the target organs for this release.

69. Effect of Renal Revascularization by Splenic Artery Implantation on Experimental Renovascular Hypertension: J. F. O'Grady and F. A. Reichle (J. P. McMullin), Saint Vincent's Hospital, Philadelphia.

Recently prolonged patency of experimental splenic artery implants (S.A.I.) into the ischaemic renal cortex has been demonstrated. Conflicting data regarding the effect of such implants on renovascular hypertension in the dog have been reported (Lanier et al., 1970).

The effect of S.A.I. on blood-pressure in a large number of rats with renal artery stenosis (R.A.S.) was tested. Left R.A.S., S.A.I. into the renal cortex, and contralateral nephrectomy were performed on forty 150-g. male Holtzman rats. Forty additional animals had left R.A.S., right nephrectomy, and no S.A.I. Prolonged patency of the S.A.I. was confirmed in some animals by angiography or at post-mortem examination.

Over 800 individual systolic blood-pressure determinations were performed by Doppler auscultation over the ventral aspect of the rat tail distal to a sphygmomanometer cuff. Significantly less hypertension was noted beginning 30 days postoperatively and throughout the extent of follow-up (90 days) ($P < 0{\cdot}01$ or $P < 0{\cdot}02$ at every 10-day interval).

Extrarenal arterial implantation into the ischaemic renal cortex of the rat does exert a significant anti-hypertensive effect.

Lanier, V. C., Van Way, C. W., Tyree Finch, W., Manlove, A., Michelakis, A. M., and Foster, J. H. (1970), *Surg. Forum*, **21**, 175.

70. The Production of Experimental Chronic Myocardial Infarction leading to Left Ventricular Failure in the Dog: W. Lloyd Jones, S. Smith, J. Serur, E. H. Sonnenblick, and F. H. Ellis, jun. (D. Annis), Lahey Clinic Foundation, Peter Bent Brigham Hospital, Boston, and Liverpool Royal Infirmary.

Chronic myocardial infarcts were produced in 18 adult dogs by a two-stage coronary artery ligation and agar injection technique.

At the first operation the anterior descending branch was ligated near its origin from the left coronary artery and plain agar (1·5 per cent) at 37° C. was injected distally. Four weeks later, through a second thoracotomy, one or more of the left circumflex apical branches was ligated and injected distally with agar.

Immediate mortality was 5 per cent (1/18) following the first operation, 15 per cent (3/18) following the second operation, and 15 per cent during the convalescent period. The surviving 11 animals showed decreased exercise tolerance with increased heart size and pulmonary congestion on chest radiographs.

Left ventricular catheterization under morphine sedation 5–8 weeks after the second infarction revealed a marked elevation of the left ventricular end diastolic pressure (mean 40 mm. Hg) with a reduction in cardiac output and ejection fraction. Left ventricular cine-angiography performed concurrently in all dogs showed akinetic areas on the antero-apical cardiac surface involving 25–35 per cent of the end diastolic perimeter.

Post-mortem examinations revealed changes of transmural infarction involving 20–35 per cent of the left ventricular surface area, whilst the lung tissue showed evidence of long-standing pulmonary congestion.

71. Contractility and Compliance-elasticity Studies in Arterial Vein Autografts: W. G. Waddell, I. J. Vogelfanger, V. Moonje, K. U. Malik, M. MacConaill, and G. Ling, Department of Surgery, Faculty of Medicine, University of Ottawa, Ottawa, Ontario.

The right lateral saphenous vein was used as an arterial autograft in the ipsilateral femoral artery in 28 unselected mongrel dogs. Four animals were studied immediately after operation. Three groups of 8 dogs were studied 2, 5–7, and 13–15 months postoperatively.

In each instance the vein autograft was compared with the normal lateral saphenous vein and the normal femoral artery from the contralateral hindlimb. Helically cut strips of the vessel wall were placed in suitably maintained muscle-baths and contractility was measured isotonically by recording the change in length induced by increasing doses of noradrenaline (10^{-9} to 5×10^{-5} mg. per ml.). The vessel strips were placed under slight tension and compliance and elasticity were determined by recording the change in length and recoil in response to changes in tension (500 mg. to 2·0 g.).

There is an approximately sixfold decrease in contractility in the arterial vein autografts 5–7 months postoperatively and about 35 per cent reduction in compliance and elasticity over 1 year after operation in comparison with normal lateral saphenous veins. If the latter observation proves to be progressive with longer periods of follow-up, stiffening of the vein-grafts may explain late graft failure, particularly in situations where continued flexibility is required.

72. **Prolonged Left-heart By-pass without Anticoagulation:** C. R. W. GRAY, J. S. BAILEY, and C. E. DREW (H. Ellis), Cardiothoracic Department, Westminster Hospital, London.

During the past 5 years a ventricular-type pump has been developed which is unique in that the ventricle, valves, and cannulae are formed from a single silicone-rubber moulding. The surface presented to blood is smooth, making anticoagulation unnecessary.

The drive system is hydraulic so that in the event of rupture of a silicone part, blood can only mix with normal saline. The control system is pneumatic and permits independent variation of systolic and diastolic duration and stroke volume.

Thirty-five experiments have been performed on calves. By-pass from left atrium to aorta was attempted for 24 hours. The by-pass was then discontinued and the animal allowed to survive. Monitoring of blood-pressures, blood-gases, and haematological and biochemical parameters was performed throughout by-pass. Post-mortem histological studies were carried out.

The action of the pump during by-pass was examined on cine-film.

73. **Low Doses of Heparin in the Prevention of Postoperative D.V.T.—A Double-blind Trial:** D. P. FOSSARD, T. CORRIGAN, J. J. SPINDLER, and V. V. KAKKAR (C. T. Howe), Department of Surgery, King's College Hospital Medical School, London.

It has been suggested that low doses of heparin reduce the incidence of postoperative venous thrombosis (Kakkar et al., 1971). All these papers are open to criticism on the grounds that the diagnosis of D.V.T. was made clinically or that the trial was not controlled.

Sixty-three patients over the age of 40 years undergoing major elective surgery were studied, using the ^{125}I-fibrinogen uptake technique to diagnose venous thrombosis. Patients received either calcium heparin, 5000 units subcutaneously, 2 hours before operation and then twice daily for 7–10 days, or a placebo administered similarly. Selection of patients for treatment or placebo was randomized and neither the physicians in charge of the patients nor those concerned with diagnosis of D.V.T. knew which 'drug' the patients had received.

Thirty-four patients received the placebo, of which 14 (41 per cent) developed venous thrombosis, and 29 patients received heparin, of which 2 (7 per cent) developed venous thrombosis. These results are statistically significant ($P < 0.005$).

KAKKAR, V. V., FIELD, E. S., NICOLAIDES, A. N., FLUTE, B. J., WESSLER, S., and YIN, E. T. (1971), *Lancet*, **2**, 671.

74. **Soleal Veins and Local Fibrinolytic Activity:** A. N. NICOLAIDES, C. T. CLARK, R. D. THOMAS, and J. D. LEWIS (C. W. Jamieson), Surgical Unit, St. Mary's Hospital, London.

Recent studies have demonstrated that practically all postoperative thrombi start in the soleal veins where stasis occurs (Nicolaides et al., 1971). It has been suggested that diminished local fibrinolytic activity may be an additional local factor predisposing to thrombosis (Brown et al., 1971). The purpose of the present study was to compare the fibrinolytic activity present in the soleal veins with the activity of the popliteal and femoral veins using a histochemical technique.

Samples of soleal, popliteal, and femoral veins were obtained from 6 cadavers within 36 hours from death. Cryostat sections were mounted on slides with fibrin films and incubated for 5, 10, 20, 30, 40, 60, and 90 minutes at 37° C. Sections from all three veins from the same cadaver were mounted on the same slide. The time at which lysis first occurred was determined.

The results showed that the incubation times required to produce lysis by the popliteal and femoral veins were always the same for each set of veins. However, there was always delay in the appearance of lysis in the soleal veins. This delay was 5 minutes in 1, 20 minutes in 3, 30 minutes in another, and 70 minutes in the remaining specimen.

In a separate experiment with veins obtained at operation it was determined that storing the vein in serum at 4° C. (to simulate cadaveric conditions) for 36 hours did not alter its fibrinolytic activity.

These preliminary results suggest that there may be diminished fibrinolytic activity in the soleal veins and this may be an additional local factor predisposing to the initiation of thrombi and their subsequent extension.

BROWN, I., DOWNIE, R. J., HAGGART, B., LITTLER, J., MURRAY, G. H., ROBB, P. M., and SAUTER, G. H. (1971), *Lancet*, **1**, 774.
NICOLAIDES, A. N., KAKKAR, V. V., and RENNEY, J. T. G. (1971), *Br. J. Surg.*, **58**, 307.

75. **Small Doses of Subcutaneous Heparin preventing Deep-vein Thrombosis in Major Surgery:** A. N. NICOLAIDES, P. DUPONT, N. DOUGLAS, J. D. LEWIS, S. DESAI, and C. W. JAMIESON, Surgical Unit, St. Mary's Hospital, London.

It has been demonstrated recently that small doses of subcutaneous heparin can prevent deep-vein thrombosis in surgical patients (Kakkar et al., 1971). Previous studies involved small numbers of patients undergoing minor operations. The purpose of the present study was to determine the effectiveness of subcutaneous heparin in preventing venous thrombosis in a large series of patients undergoing major general and thoracic operations which carry a high risk of deep-vein thrombosis.

All the patients were over the age of 40 and were scanned with the ^{125}I-fibrinogen test. Two hundred and twelve patients have been studied to date. They were classified as general surgical or thoracic and then randomly allocated to a control or test group. Both groups received the routine preventive measures practised in this hospital (elastic stockings, supervised leg exercises, and early mobilization). In addition, subcutaneous sodium heparin (5000 units in 0·2 ml.) was administered to the test group 2 hours before operation and then 12-hourly for 7 days. Twenty-three (22 per cent) out of the 105 in the control group developed deep-vein thrombosis, while 1 of the 107 patients in the test group did. This is highly significant (Fisher's exact test $P = 0.000036$).

The preliminary results of this trial indicate that small doses of subcutaneous heparin are most effective in preventing deep-vein thrombosis in patients undergoing major general and thoracic operations.

KAKKAR, V. V., FIELD, E. S., NICOLAIDES, A. N., FLUTE, P. T., WESSLER, S., and YIN, E. T. (1971), *Lancet*, **2**, 669.

76. Turbulence as a Factor in the Aetiology of Varicose Veins: A. L. KLINE and P. BYRNE (W. G. Fegan), Department of Clinical Surgery, Sir Patrick Dun's Hospital, Dublin.

Although patients with marked symptoms and signs of calf-muscle-pump dysfunction have varicose veins they are almost insignificant especially when compared with the gross varicosity displayed by many asymptomatic varicose patients.

The flow characteristics in superficial veins of two groups of ambulatory patients were studied.

Group I: Ten asymptomatic patients with gross varicosity of the long saphenous vein and its tributaries.

Group II: Ten patients with marked symptoms and signs of muscle-pump dysfunction with minimal varicose veins.

The results obtained were compared with those of 10 normal students.

In both pathological groups reverse flow was demonstrated but was absent in normal patients. Although the velocity and duration of this reverse flow were far greater in group I, the most significant difference between the two groups was the fact that turbulence was present in the flow of the asymptomatic patients with gross varicosities. Turbulence was detected with an accelerometer (Gosling and King, 1969) and also by analysis of the audio signal from the Doppler ultrasound equipment. Turbulence was not found in the symptomatic patients (group II or the normal patients).

Turbulent retrograde flow may be responsible for vessel-wall changes resulting in sacculation and tortuosity.

GOSLING, R. G., and KING, D. H. (1969), *J. appl. Physiol.*, **27**, 1, 106.

SHORT NOTES OF RARE OR OBSCURE CASES

BILATERAL TRAUMATIC RENAL ARTERY OCCLUSION WITH SURVIVAL AFTER LATE RECONSTITUTION OF ARTERIAL FLOW

BY W. E. BIRKENSTOCK, R. RABKIN, AND D. P. STABLES

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SUMMARY

Survival after bilateral traumatic renal artery occlusion is uncommon. A patient is described who recovered useful renal function despite a 12-hour delay in reconstitution of arterial flow. Postoperative oliguria lasted 45 days, necessitating prolonged haemodialysis.

TRAUMATIC renal artery occlusion is being detected with increasing frequency (Steiness and Thaysen, 1965; Grablowsky, Weichert, Goff, and Schlegel, 1970; Evans and Mogg, 1971). The occasional attempt (Steiness and Thaysen, 1965; Grablowsky and others, 1970) at restoring blood-flow to the kidney has failed and the usual treatment is nephrectomy. As there is experimental evidence (Hamilton, Phillips, and Hiller, 1948; Steuber, Kouvacs, Koletsky, and Persky, 1958) that after 3 hours of total arterial occlusion the normothermic dog kidney may, and after 8 hours will, lose viability it might seem futile to attempt operation in traumatic arterial occlusion if there is considerable delay. We therefore report a case of complete bilateral traumatic renal artery occlusion to emphasize that useful renal function can be salvaged even 12 hours after injury.

CASE REPORTS

A 16-year-old coloured girl was brought to hospital between 1½ and 2 hours after a motor-vehicle accident. Physical examination revealed fractures of the pelvis, left loin tenderness, absence of bowel-sounds, and severe hypotension. The bladder contained less than 30 ml. of blood-stained urine. Cystography excluded bladder rupture. Because of difficulty in the correction of her hypotension and delay in the performance of excretion urography, which showed no excretion of contrast medium, abdominal aortography was performed 9 hours after injury. This demonstrated occlusion of both renal arteries within 2 cm. of their origins with irregular contours suggestive of intimal tears (*Fig.* 1).

At operation 10½ hours after injury bilateral renal artery occlusion was confirmed. The right renal artery was thrombosed from approximately 1½ cm. from its origin to its bifurcation (*Fig.* 2 A).

This was explored first through a longitudinal arteriotomy and thrombus was extracted. The intima and media were found to be disrupted and folded up distally causing complete occlusion. These were teased back, sutured to the adventitia, and the arteriotomy closed with a Dacron patch (*Fig.* 2 B). Good distal pulsation was palpable.

The left renal artery was avulsed except for a thin strand of adventitia posteriorly (*Fig.* 2 A). Thrombus was extracted from both ends of the vessel and 1–2 cm. of damaged artery were excised prior to mobilization of the kidney and end-to-end anastomosis (*Fig.* 2 B). Pulsatile flow was restored and a left renal biopsy produced brisk bleeding. A tear in the left renal vein was sutured.

Bilateral retroperitoneal haematomas were present. Small bowel which had been rendered ischaemic by a mesenteric tear was resected.

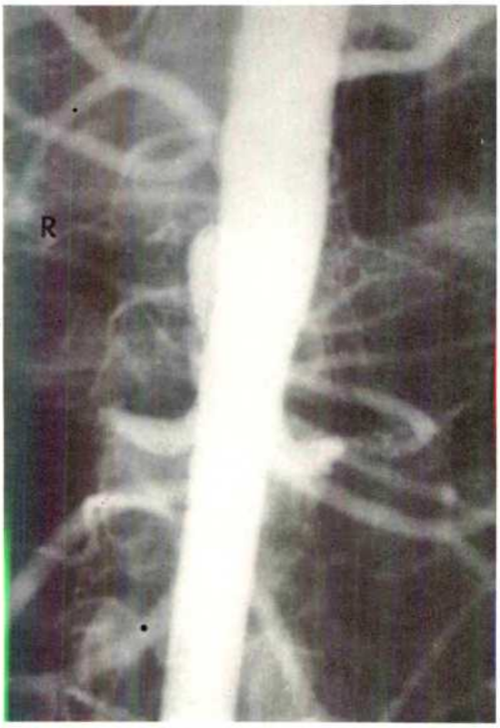


FIG. 1.—Preoperative arteriogram.

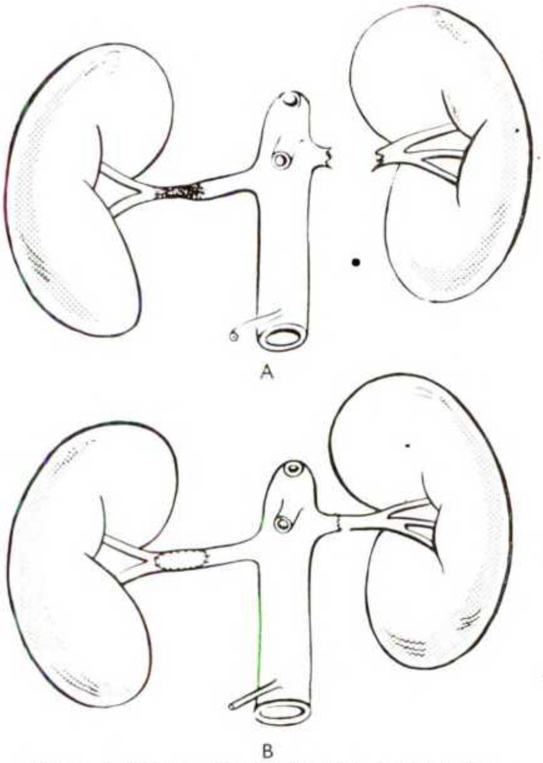
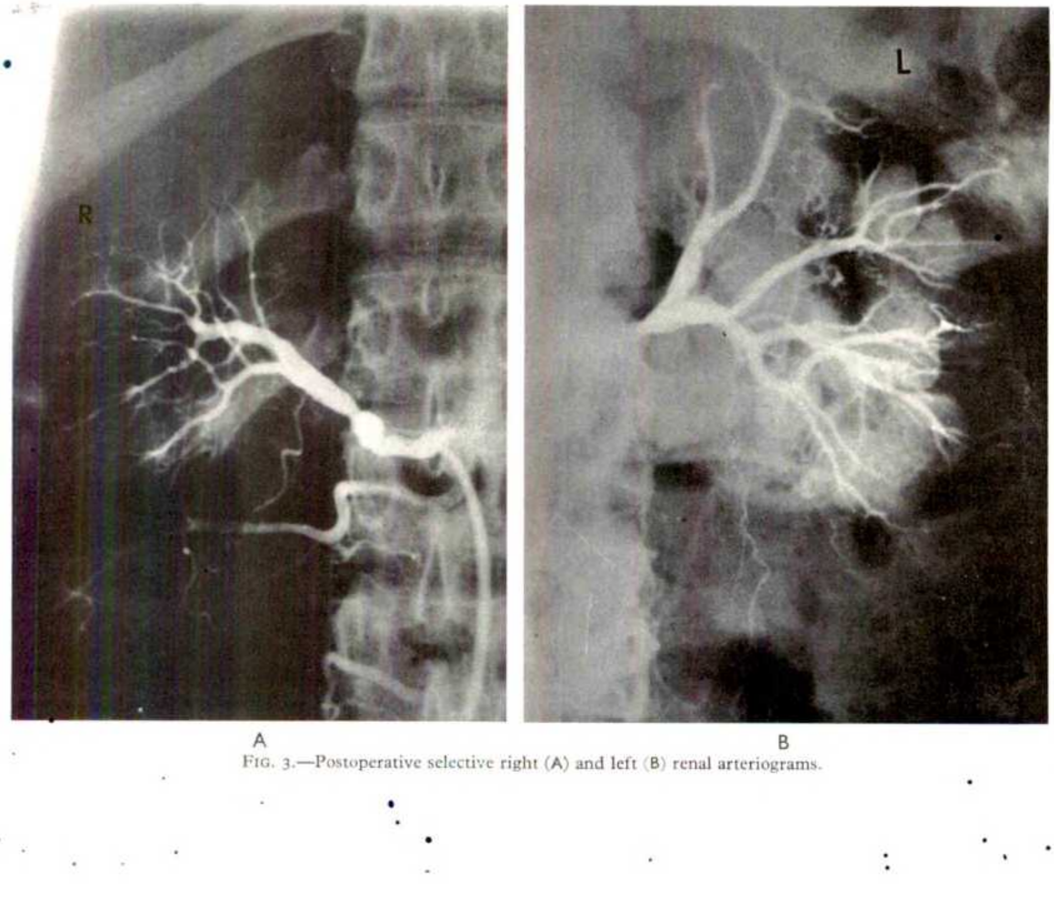


FIG. 2.—A, Diagrammatic appearance of operative findings. B, Postoperative appearance.



A B

FIG. 3.—Postoperative selective right (A) and left (B) renal arteriograms.

Histology of the left renal biopsy specimen showed capillary congestion, interstitial and tubular oedema, and some tubular necrosis.

Selective renal arteriography 36 days after operation showed patent renal arteries with moderate stenoses at their sites of repair (*Fig.* 3). All of the right renal segmental arteries were patent but the posterior division of the left renal artery was occluded. Two subsequent excretory urograms showed excretion of contrast medium by the right kidney only. This finding was confirmed with an isotope renogram.

The postoperative course was complicated by recurrent infections of a thigh wound, a pulmonary infarct, and a urinary-tract infection. The oliguric phase lasted 45 days, being particularly severe for the first 11 days, daily urine output being less than 100 ml. (*Fig.* 4). Haemodialysis was repeated frequently to control uraemia and hyperkalaemia and to allow a 40-g. protein intake from the eighth day onwards. The last haemodialysis was performed on the sixty-fifth day and thereafter the patient was maintained on the same diet with unrestricted fluids. She returned to a reform school for juvenile delinquents, and as she is extremely uncooperative it is likely that her protein intake has increased. Four months after injury menses returned; at that time the creatinine clearance was 6 ml. per minute per 1·73 m^2., serum creatinine, 8·8 mg. per 100 ml.; and the blood-urea, 230 mg. per 100 ml. When last seen 186 days after the accident she was fully active, looked well, was normotensive, and her urine was sterile. The serum creatinine was 7·1 mg. per 100 ml.; the blood-urea, 203 mg. per 100 ml.; and the haemoglobin, 10 g. per 100 ml.

DISCUSSION

The operation on this patient was life-saving since her uncooperative behaviour and psychopathic personality would have prevented her acceptance for a renal transplantation or a chronic dialysis programme. Despite a 12-hour delay in the restoration of main arterial flow she recovered sufficient renal function to leave hospital and resume her normal activities. This result is all the more remarkable because the postoperative urograms indicated that the right kidney is responsible for most, if not all, of her renal function.

The explanation for the recovery of function must lie in the perfusion of some nephrons through collateral vessels (Brest, Bower, and Heider, 1964; Perkins, Jacobsen, Feder, Lipchik, and Fine, 1967) during the period of complete artery occlusion. Failure of the preoperative aortogram to demonstrate this collateral circulation in no way excludes its presence. The potential collateral pathways through capsular, adrenal, and ureteric arteries are small and these vessels are difficult to define on good-quality aortogram films in normal subjects, let alone those obtained after severe abdominal trauma. Relatively little blood-flow need be postulated as arterial pressures below the levels required for glomerular filtration are adequate to maintain viability of renal parenchyma (Morris, Heider, and Moyer, 1955).

Recovery of renal function after even longer delays in surgical correction has been described in spontaneous renal artery occlusion by emboli (Morris and others, 1955; Brest and others, 1964). In such cases it is likely that an extensive collateral circulation had been stimulated by a previously compromised renal circulation. The capacity of the collateral pathways to widen in chronic renal ischaemia has been emphasized by Brolin and Stener (1966), who described a patient in whom one renal artery was occluded and yet the kidney excreted contrast medium normally and was normal in size.

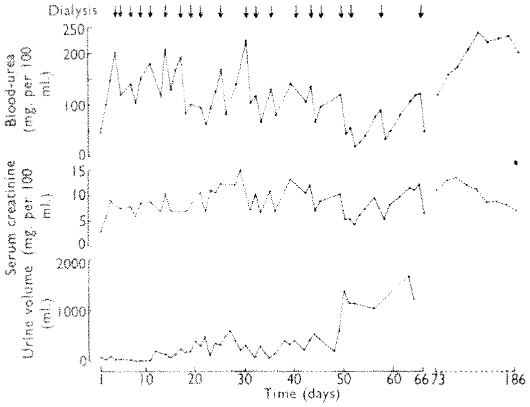


FIG. 4.—Postoperative course.

In the present case once patency of the renal arteries had been confirmed by postoperative arteriography a prolonged period of intermittent haemodialysis was necessary. Equally long or longer oliguric phases have been described in patients recovering from acute cortical necrosis (Walls, Schorr, and Kerr, 1968). Also described in acute cortical necrosis (Rieselbach, Klahr, and Bricker, 1967; Walls and others, 1968) is the slow improvement in renal function noted in our patient. This improvement has been attributed to functional adaptation of the surviving nephrons rather than to an increase in the functioning nephron population (Rieselbach and others, 1967). Further improvement in our patient's renal function is possible so long as she remains normotensive.

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ACUTE MYELITIS PRESENTING AS SPASTIC COLONIC ILEUS

By H. T. WILLIAMS and D. T. L. TURNER

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SPASTIC ileus of the large bowel is seen occasionally in surgical practice and reports have been published of a variety of causes (Caves and Crockard, 1970; Watkins, 1970). We wish to record a further example of this condition which was due, we believe, to an acute viral myelitis and which preceded the onset of other neurological signs by 11 days.

CASE REPORT

R. T., a Civil Service clerk aged 57 years, was admitted with a 4-day history of abdominal pain. The pain had been of gradual onset, was constant, and was situated in the left iliac fossa. There had been no bowel action since the onset of the pain but he had passed a little flatus. He had previously been in good health.

On examination the patient was moderately obese with a pyrexia of 37·5° C. There was some abdominal distension with tenderness in the left iliac fossa but no masses were palpable. Rectal examination revealed moderate benign prostatic enlargement only. No abnormality could be detected in the cardiovascular, respiratory, or central nervous systems.

Plain abdominal radiographs showed gas in the proximal colon with slight distension of the small bowel. A provisional diagnosis of acute diverticulitis was made and the patient was treated with nasogastric suction, intravenous fluids, and antibiotics. During the ensuing 8 hours his pain became more severe, central, and colicky. There was increasing abdominal distension and obstructive bowel-sounds were heard. A repeat abdominal radiograph showed distension of the large bowel down to the sigmoid colon with fluid levels in the proximal colon; there was also some distension of the small bowel with a few fluid levels. Enemata failed to relieve the distension and therefore a laparotomy was performed.

At operation the large bowel was found to be uniformly distended but there was no evidence of any mechanical obstruction. The bowel wall was not inflamed and there were no signs of an ischaemic episode. A flatus tube was passed up from the anus, and the left colon was partially decompressed manually. A decompression needle was used in an attempt to deflate the caecum but this was only partially successful. Owing to the spasticity of the wall the bowel did not deflate normally. The flatus tube was left in situ and the abdomen was closed.

Post-operatively the patient remained chronically distended but this gradually improved after 2 days when he began to pass small amounts of flatus spontaneously. On the eighth day he developed painless retention of urine and this was followed a few hours later by a progressive flaccid paralysis of his lower limbs. Sensation was also impaired below D.V.10. Myelography revealed no block in the subarachnoid space, but the cerebrospinal fluid was found to contain the following: white blood-cells, 640 per c.mm. (mainly polymorphs); red blood-cells, less than 1 per c.mm.; protein, 20 mg. per 100 ml. No organisms were seen on film or were subsequently cultured.

During the next week there was a gradual return of power and sensation in the lower limbs and after 2 weeks the patient was able to stand with assistance although he was unable to walk. A cystometrogram showed normal bladder sensations but the tone was reduced. There was no abdominal distension but bowel action was achieved only with the aid of enemata. He continued to improve over the following 3 weeks. A further cystometrogram showed normal bladder tone and after the removal of the catheter he passed urine spontaneously with good control and little residue. Spontaneous bowel action had also returned and the patient was walking with the aid of a frame. A repeat lumbar puncture 4 weeks after the first showed clear fluid with normal pressure. The fluid now contained: white blood-cells, 9 per c.mm.; red blood-cells, less than 3 per c.mm.; protein, 150 mg. per 100 ml.; a Lange's test was negative. The patient was discharged 11 weeks after admission, having normal bladder and bowel function and walking with the aid of one stick only.

DISCUSSION

Spastic ileus or pseudo-obstruction of the large bowel is seen infrequently. Since Ogilvie first described the syndrome in 1948 it has been noted in association with intra-abdominal inflammation, retroperitoneal disease, cardiac failure, coronary thrombosis, systemic infection, and following traumatic lesions of the spinal cord. There has also been a number of cases where no aetiological factor has been demonstrated. The present case was initially placed in the idiopathic category until the development of paraparesis. This, however, did not occur until 11 days after the onset of bowel symptoms. Cord decompression having been excluded by the myelogram, the diagnosis lay between spinal artery thrombosis, acute myelitis, and multiple sclerosis. Acute myelitis now seems the most probable because of the protein and polymorphs in the cerebrospinal fluid and because of the subsequent recovery of function. We have been unable to find any previous record in the literature of acute myelitis presenting initially as a large-bowel ileus.

Acknowledgements.—We are most grateful to Mr. R. P. Rosswick for permission to publish this case and for advice in the preparation of this report. Miss C. F. Steptoe rendered invaluable secretarial assistance.

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RUPTURED SOLITARY CYST OF THE LIVER

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SUMMARY

A further case of a ruptured solitary cyst of the liver is described. A brief review of the 7 previously described cases is given. The management of the condition is discussed, and surgical treatment by either total excision or excision of the roof of the cyst is recommended.

SIR BENJAMIN BRODIE in 1846 described seeing a young lady with a cystic tumour of the right upper abdomen which disappeared after aspiration of 2 pints of clear watery fluid. This case has been considered to be the earliest report of a solitary cyst of the liver, but as it was not authenticated by operative or post-mortem findings the first definitive report is said to be that of Michel in 1856.

Table I.—DETAILS OF THE PREVIOUSLY REPORTED CASES OF RUPTURED SOLITARY CYST OF THE LIVER

CASE	AUTHOR	AGE AND SEX	CLINICAL FEATURES	OPERATIVE FINDINGS
1	Davis (1937)	67 F.	10-day history of severe abdominal pain, with mass palpable in the abdomen for many years On examination distended abdomen with generalized tenderness	Tan-coloured fluid in the peritoneal cavity; large cyst in the right lobe of the liver. Cyst excised; satisfactory postoperative recovery
2	Lulenski (1948)	42 F.	Recurrent epigastric pain for 3 years; sudden severe pain with nausea and vomiting On examination generalized abdominal tenderness	100 ml. grey-green fluid with moderate peritoneal reaction; 4 × 4 × 6-in. cyst in posterior inferior surface of left lobe. Cyst deroofed with satisfactory recovery
3	Horton (1954)	44 F.	Continuous aching abdominal pain for 3 days after striking abdomen On examination generalized abdominal pain with mass palpable	Laparotomy revealed ruptured liver cyst. No procedure, but later enucleation of cyst performed with satisfactory result
4	Morgenstern (1959)	56 F.	Sudden epigastric pain On examination moderately shocked with diffusely tender abdomen	3–4 litres dark greenish fluid; 35-cm. cyst in left lobe of liver. Left lobectomy performed; recovery satisfactory
5	Johnston (1960)	82 F.	Right-sided abdominal pain with vomiting On examination ill with tense abdomen, maximum on the right side	Reddish-brown fluid; 15-cm cyst in the right lobe of liver. Catheter drainage; died on third postoperative day
6	Sachs and Robbins (1967)	81 M.	Known case of liver cyst being treated by aspiration. Presented with vomiting and generalized guarding. Treated conservatively. Died on thirteenth day after admission	Post-mortem examination showed a ruptured liver cyst in the inferior surface of liver with fistulous tract into a duodenal ulcer
7	Govostis (1969)	70 M.	Known case of liver cyst. Presented with abdominal pain and generalized guarding	Chocolate-brown fluid; a large cyst in the right lobe treated by drainage. Recovery satisfactory

Since then about 350 cases have been described in the English literature, the condition having been reviewed by Davis in 1937, Geist in 1955, and Flagg and Robinson in 1967.

The term 'solitary cyst of the liver' is specific. It should not be confused with retention, degenerative or other distinctive cysts found in the liver, or with polycystic disease of the liver. Geist (1955) in his review limited the term to single cysts, or at the most not occurring in more than two or three isolated portions of the liver, with typical gross and microscopic appearances. The cyst although solitary may be multilocular. Macroscopically the cyst has a smooth wall, up to 7 mm. thick, is greyish or greyish-green in colour, and contains a clear and serous or dark and viscid fluid. Microscopically three layers are recognized, namely an outer collagenous layer containing muscle-fibres, bile-ducts, and compressed hepatic cells, a middle layer containing vascular elements, and an inner layer of tall, columnar epithelium, mucus-producing epithelium, ciliated epithelium, or squamous epithelium.

The solitary cyst of the liver is usually asymptomatic, but the following complications do occur: bleeding into the cyst (Ackman and Rhea, 1931); jaundice which according to Flagg and Robinson (1967) occurs in 9 per cent of cases; secondary infection of the contained fluid (Greig and Stinson, 1961); hepato-cysto-enteric fistula (Sachs and Robbins, 1967); torsion of the cyst (Orr and Thurston, 1927); rupture of the cyst. Rupture is a rare complication, only 7 cases being recorded in the English literature. An account is given of a further case.

CASE REPORT

Mr. L. A., aged 68 years, was admitted as an emergency on 21 Sept., 1969, with severe abdominal pain. One week prior to admission he had had a sudden severe epigastric pain which had lasted for 2 hours, leaving a dull ache in the epigastrium for a period of 4–6 hours. He had then been well and at work until the day of admission, when after a light lunch he had felt severe pain in the lower sternal region which had radiated to the epigastrium and to the back. He had vomited twice. On admission he was in considerable pain and had a pyrexia of 37·8° C., a tachycardia of 110, and a normal blood-pressure of 130/90 mm. Hg. The abdomen was tender throughout with maximum tenderness in the upper epigastrium. No mass was palpable. Investigations showed a normal white blood count, a normal serum amylase, and radiographs of the chest and abdomen were within normal limits.

A diagnosis of a perforated duodenal ulcer was made and a laparotomy was performed. A ruptured solitary cyst of the liver was found, with a greenish-brown fluid in the peritoneal cavity. The cyst was situated in the left lobe of the liver, measured 12 cm. in diameter, and was thin-walled, being covered on the left lateral side by omentum which was adherent to the site of the perforation. A left lobectomy flush with the falciform ligament was performed. Pathological examination confirmed this to be a solitary cyst of the liver with many bile-ducts in the outer layer of the cyst wall.

Postoperative recovery was uneventful apart from wound dehiscence on the ninth postoperative day. When seen at follow-up 6 months later the patient was well and there was no abnormality on abdominal examination.

DISCUSSION

A summary of the previously reported cases of ruptured solitary cyst of the liver is given in *Table I*. Each presented as an acute abdomen. In *Cases* 6 and 7 the presence of a liver cyst was known and therefore rupture of the cyst was strongly suspected. In *Cases* 1 and 3 a mass was palpable, but in the remaining 3 cases there were no features to aid diagnosis, hence the need for laparotomy to determine the diagnosis.

At laparotomy the diagnosis is obvious but the main problem is to determine the correct surgical treatment for the ruptured liver cyst. The following measures have been advocated for treating solitary cysts of the liver: simple aspiration, total excision, marsupialization, external drainage, internal drainage into either the stomach or a Roux-en-Y loop of small bowel, and excision of the dome of the cyst with oversewing of the edges.

The general consensus has been that the cyst should be totally excised, whenever possible, by lobectomy or enucleation. Enucleation of the larger cysts, particularly if intrahepatic, is dangerous as the deeper part of the cyst may be adherent to the hilar structures which may be damaged if enucleation is attempted. For those cysts which lend themselves to total excision, namely those in the left lobe of the liver and those which are superficial on the anterior inferior surface of the right lobe, total excision is the procedure of choice. In all other instances excision of the roof of the cyst with oversewing of the edges is recommended, and this operation is particularly applicable to the ruptured liver cyst as it presents little technical difficulty and gives rise to few complications; these factors are of considerable importance as rupture of a liver cyst presents as an emergency when the full resources necessary for more major procedures may not be available. Belcher and Hill (1969) had no complications with this treatment in 3 cases which were followed up for 18, 15, and 1 year, respectively. Longmire, Passaro, and Joseph (1966) warn that on the rare occasion when bile is present in the cyst external drainage should be performed. Whatever method of treatment is undertaken care must be taken to break down all the loculi of the cyst otherwise there will be a recurrence (Rosenberg, 1956).

The operative mortality is low. Clark, Marks, Bernhard, and Bunfeldt (1967) estimated a mortality of 2·1 per cent for the surgical treatment of the uncomplicated solitary liver cyst. Despite the low mortality, Sanders and Garrett (1968) urge conservative treatment for solitary liver cysts which have been diagnosed clinically with compatible radiological signs and liver scans. Caplan and Simon (1966), in a review of the radiological signs, stress the inaccuracy of diagnosis and the need for surgical confirmation. There are, therefore, two reasons for urging surgical treatment of all suspected liver cysts, namely confirmation of the diagnosis and prevention of complications, as is illustrated by *Case* 6 in *Table I*. Complications undoubtedly increase the morbidity and mortality, 2 out of the 8 recorded cases having died as a direct result of the rupture of the cyst.

Acknowledgement.—I wish to thank Mr. W. W. Slack, under whose care this case was admitted, for permission to publish the case and for his useful criticism during the preparation of this paper.

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CONGENITAL OESOPHAGO-BRONCHIAL FISTULA IN AN ADULT

By D. G. HILL

THORACIC UNIT, GUY'S HOSPITAL, LONDON

SUMMARY

A case of oesophago-bronchial fistula presenting in adult life and treated successfully by surgical excision is reported. Unusual features were severe halitosis and the downward direction of the fistula from the oesophagus to the lung.

FISTULOUS communication between the oesophagus and bronchi may be congenital, traumatic, inflammatory, or neoplastic. Fistulae which are muscular, epithelial lined, and clearly congenital, yet present in adult life, are rare and have been described only 29 times in the literature. This paper reports a further example of such a lesion (Belsey, 1966).

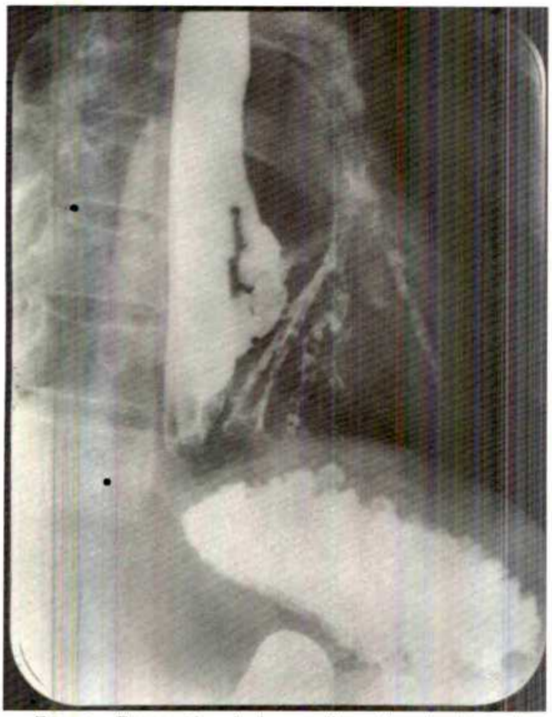

FIG. 1.—Preoperative barium-swallow film detailing the fistulous communication between the oesophagus and the left lung.

CASE REPORT

A 29-year-old Arab male presented to the Thoracic Unit, Guy's Hospital. He had a 16-year history of retrosternal burning pain after meals (especially with spicy meals), water brash, and postural oesophageal reflux, and a 3-year history of breathlessness, wheezing, and coughing up small particles of food on eating meals, especially related to spicy foods. He had had a tonsillectomy in Cairo 6 years previously with partial relief of symptoms for 3 years.

Severe halitosis was the only significant physical finding.

INVESTIGATIONS.—A chest radiograph was normal. A barium-swallow examination detailed an oesophago-bronchial fistula communicating with the posterior basal segment of the left lower lobe (*Fig.* 1). Oesophagoscopy showed free oesophageal mobility, and biopsy of the mouth of the fistula was reported as normal squamous epithelium. Bronchoscopy revealed a normal bronchosegmental anatomy and no sign of inflammation. Some barium was sucked out of the left common basal bronchus.

OPERATION.—At operation the fistula was located in the left inferior pulmonary ligament immediately below the pulmonary vein. There was no related fibrosis or inflammation. The fistula, which measured 1 cm. in diameter, led directly from the oesophagus in a downward direction into the posterior basal segment of the lower lobe. As the fistula entered the lung it became cystic. Segmental resection with excision of the fistula was performed, the oesophageal defect being closed by a double-suture line. The defect in the lung was oversewn.

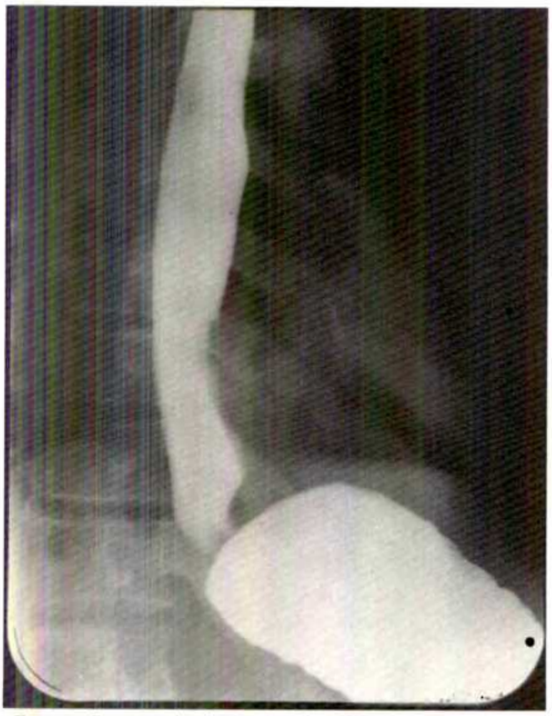

FIG. 2.—Postoperative barium-swallow film showing a normal oesophagus and no trace of the fistula.

Histological examination of the fistula revealed squamous epithelium with ciliated mucous glands embedded in the outer muscle layers.

The patient made an uneventful recovery. Postoperative barium swallow showed a normal oesophagus (*Fig.* 2).

There was a small encysted effusion at the left base which subsequently cleared (*Fig.* 3).

A year later at follow-up the patient had fully recovered with complete relief of symptoms.

DISCUSSION

Braimbridge and Keith (1965) classified 23 cases of congenital oesophago-bronchial fistulae collected from the literature. They divided the cases according to the manner in which they terminated at the respiratory end of the fistula. This is most commonly a single tract running to a lobar or segmental bronchus. However, the tract may first become cystic and then run into a bronchus (26 per cent) or occasionally it is in communication with a sequestrated segment of lung (17 per cent). The case reported here was clearly seen to be cystic at its bronchial end.

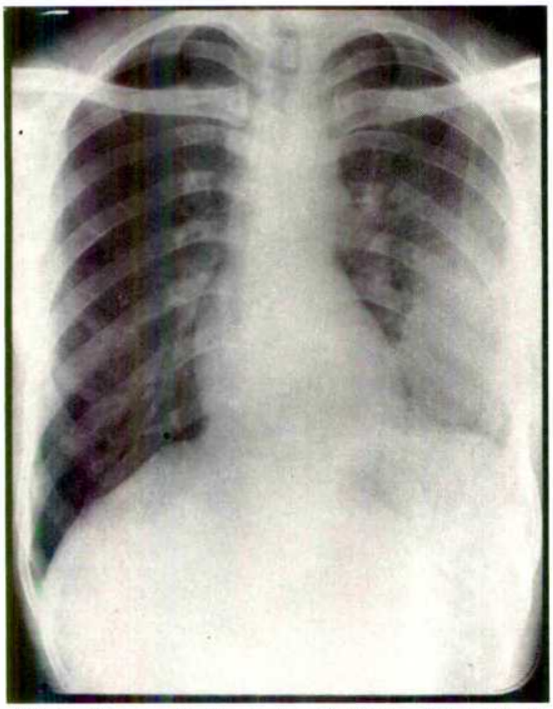

FIG. 3.—Postoperative chest radiograph showing the left pleural effusion.

Histology of the fistulous tract usually shows a muscular tube lined by either squamous or columnar epithelium. The congenital nature of the lesion is supported by the absence of inflammation.

Symptoms may begin in childhood but are often intermittent and not noticed. At presentation, usually in adulthood, chronic respiratory infections are the most frequent complaint. A cough is a consistent feature. Haemoptysis is not uncommon and may be massive (Kinley and Lang, 1969).

Alimentary symptoms are less common, but symptoms such as choking on swallowing or food particles found in the sputum can be diagnostic. Halitosis which was an important feature of the case presented here has not previously been noted.

The reason for the late onset of symptoms has been variously attributed to:—

1. A membrane in the tract which breaks down with age.
2. An operculum of mucosa which may intermittently cover the oesophageal end of the fistula and close it during swallowing.
3. The usual upward direction of the tract.

In the case reported late 'presentation' was due to incomplete investigations of the patient's symptoms previously. (He had had a tonsillectomy for the same symptoms 6 years before the diagnosis was made.) In fact he had had relevant symptoms for 16 years which may fit in with the downward direction of the fistula. The diagnosis is most convincingly made by barium swallow (65 per cent; Braimbridge and Keith, 1965). Bronchograms show the damage that has occurred in the lung but do not usually show the fistula. Endoscopy may reveal the orifice of the tract but this is usually only possible if the diagnosis has already been made (Le Roux and Williams, 1968).

Management is by resection of the fistulous tract alone or together with lobectomy, segmental resection, or pneumonectomy. There have been no operative deaths in any of the reported cases.

Acknowledgement.—I wish to thank Mr. A. K. Yates for his help in preparing this paper.

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REVIEWS AND NOTICES OF BOOKS

The Shoulder and Neck. By JAMES E. BATEMAN, M.D., F.R.C.S., Toronto. 10½ × 7½ in. Pp. 615 + xiii. Illustrated. 1972. London: W. B. Saunders Co. Ltd. £13·85.

THIS is a most comprehensive work in which every facet of the surgery of the shoulder and neck is considered in a very practical manner.

This large volume is divided into seven sections. Section 1 deals with the basic sciences as related to the shoulder and neck. Developmental defects and anomalies are considered in some detail. The surgical anatomy of this large region is discussed and the principles of shoulder and neck function are considered.

In Section 2 the problems of investigation and diagnosis of various conditions and lesions are set forth.

Section 3 is devoted to a consideration of clinical syndromes. Degenerative tendinitis, ruptures of the rotator cuff, and frozen shoulder are well described.

Section 4, a large section, is dedicated to trauma of the neck and shoulder. There is a very comprehensive review of the common injuries to this region which occur in road accidents and in sports. As one would expect, nerve injuries are frequent and are described in some detail.

Section 5 deals with systemic disorders of the shoulder and neck; section 6 considers the many and varied tumours which are found in this part of the body, while in section 7 disability evaluation of the shoulder and neck come under review.

Throughout this volume the illustrations are of a high order, especially the line drawings which are original and convincing. The radiographs have been well chosen and are clear.

An excellent reference volume on an important region in the human body.

Spezielle pathologische Anatomie. Volume 2, Part 1: Oesophagus und Magen. By Professor Dr. WILHELM DOERR, Heidelberg, Professor Dr. GERHARD SEIFERT, Hamburg, and Professor Dr. ERWIN UEHLINGER, Zürich. 9¾ × 6½ in. Pp. 1077 + xvii. Illustrated. 1971. Berlin: Springer Verlag. DM.380.

IN the past continental textbooks on pathology showed a tendency to concentrate on the purely morphological aspects. Thus, pathology was usually identical with and was actually named pathological anatomy. In the present volume dealing with the systemic pathology of the oesophagus and the stomach the authors have broken the strings that traditionally bound them and have included a good deal of functional pathology. As they have not given up an inch of their morphological territory this means that the actual text runs to 850 pages. Another trend in this book is to include material that is of interest to the clinician—gastro-enterologist or abdominal surgeon—so that he will hardly ever look in vain for even the most specialized details. This gigantic handbook is all that it should be: a masterly review of the pertinent literature, blended with personal observation, illustrated with good photographs, and spiced with useful diagrams. All aspects of the subject are extensively covered, as can be easily proved by randomized checks on obscure or rare conditions. Of course, the book is primarily of importance to him for whom it was written: the pathologist; but surgeons engaged in research will certainly do well to consult it. The first section on the sequelae of gastric operation has a wider appeal and could fruitfully be consulted by the practising surgeon. The final 170 pages comprise an impressive list of references, extending from the dawn of pathology to 1969. It is a pity that the authors, who obviously have read a great many of these articles, have not annotated this bibliography. It might have been helpful in selecting articles for further reading because reading them all would probably take a lifetime.

Acute Cholecystitis. By CLARENCE J. SCHEIN, M.D., New York. 10 × 7 in. Pp. 309 + xv, with 179 illustrations. 1972. New York: Harper & Row, Publishers, Inc. $17.50.

A WHOLE book devoted to the subject of acute cholecystitis—is this possible? Yes, because this is simply a phase of the obstruction of the cystic duct.

This book covers the whole pathology of cholecystitis and includes the aetiology, diagnosis, treatment, and results of treatment.

The first chapter discusses the historical background to the condition, and presents biographical sketches of the surgeons of the past who have written about acute cholecystitis. It is pleasing to see photographs of Lord Moynihan and Rutherford Morrison as pioneers of the English school.

Cholecystectomy is the treatment of choice in this condition, and the author has discussed in considerable detail the complications which may occur following surgical intervention. Stones in the cystic duct remnant are common.

There is a most extensive list of some 629 references at the end of the book.

Bacterial Infections. Changes in their Causative Agents. Trends and Possible Basis. Edited by M. FINLAND, W. MARGET, and K. BARTMANN. 10 × 7 in. Pp. 231 + viii, with 53 illustrations. 1971. Berlin: Springer Verlag. DM.48.

THIS book comprises the papers read at the third Bayer symposium. The first symposium was devoted to problems of immunology, and the second to catecholamines.

The twenty-two contributors come from America, Great Britain, Germany, Sweden, France, and Switzerland. Every facet of this important subject is discussed at length.

Infections in hospital wards, in operating theatres, and elsewhere in hospital buildings are tabulated and comparisons are made between different groups of hospitals. The changing pattern of infecting organisms is described in some detail.

Sensitivity to various types of antibiotics is set out in an interesting manner.

This book should be of interest to surgeons, as the biological, epidemiological, and therapeutic points of view are portrayed in a very practical way.

This is an important reference volume on an important subject.

Resistance to Trauma. By Zdenek Hruza, M.D., Ph.D., Sc.D., New York. 9 × 6 in. Pp. 97 + xiv, with 13 illustrations. 1972. Springfield, Ill.: Charles C. Thomas. $7.

This monograph written by a pathologist seeks to investigate the important problems of shock and trauma. By the use of animal experiments the effects of repeated trauma on the various organs of the body have been studied. Therapeutic approaches, such as adrenergic blockage, treatment with novocaine, depot epinephrine, and norepinephrine, and increase of saturation of the portal blood with oxygen by insufflation of oxygen into the bowels are all critically reviewed.

The author has made a complete review of the literature on trauma and has included a very extensive bibliography at the end of the book.

Neonatal Emergencies and Other Problems. By John Black, M.D., F.R.C.P., Sheffield. 8½ × 5½ in. Pp. 282 + v. 1972. London: The Butterworth Group. £3·75.

This is an important book for the clinician, for it sets out the facts and figures concerning the day-to-day care of the newborn infant. Birth trauma is considered at length, and the list of complications which may result from forceps delivery is a long one. Such problems as maternal diabetes and the pre-diabetic state are dealt with in a very comprehensive way.

An interesting chapter on maternal addiction to alcohol is impressive. Another very practical chapter is devoted to the difficult problem of talking to parents—the author is at his best here.

There are some very useful appendixes at the end of the book.

This book will appeal to house-surgeons and practitioners alike, while senior students and nurses will find it a useful reference volume.

La Chimiothérapie regionale des Cancers de l'Appareil digestif. By P. Kissel, M. Bessot, A. Duprez, and G. Mauuary, Nancy. 9½ × 6 in. Pp. 216 + x, with 15 illustrations. 1971. Paris: Masson et Cie, Editeurs. 46F.

This most fascinating monograph deals with chemotherapy of gastro-intestinal malignancy. A group of scientists of various disciplines has been collaborating in Nancy for more than 10 years. They have borrowed widely from other workers but have also added many original ideas and techniques of their own. The quintessence of their method is regional perfusion after synchronization of the cell kynetics. When the proliferative cycle is synchronous all the cells will be affected by a drug active in a specific phase as soon as this phase is reached. In this way a maximum effect can be obtained with relatively small amounts of antimitotic substance. To prevent a deleterious effect on the remainder of the body chemotherapy is given through the nutrient artery of the tumour.

The book is made up of five chapters. The first gives an account of basic cellular physiology, explaining DNA metabolism and how autoradiography is derived from it. The second chapter summarizes the currently used antimitotics and their mode of action. The introductory part is closed by a third chapter on how to regionalize chemotherapy, discussing the various routes that can be used and the complications to be expected. In the second part of the book the knowledge acquired in the introduction is applied to three specific tumours: carcinomas of the liver, the stomach, and the rectum. As wide experience has already been gained in Nancy this section, giving overall results and illustrative single case histories, is most important. For anyone actually engaged in using this sort of therapy this book is obviously compulsory. It seems, however, to have a much wider appeal, for it can be unreservedly recommended to beginners who want a lucid and authoritative introduction to this rapidly expanding field that seems so full of promise.

Modern Trends in Orthopaedics—6. Edited by A. Graham Apley, M.B., B.S., F.R.C.S., Pyrford, Surrey. 8½ × 5½ in. Pp. 273 + x. Illustrated. 1972. London: The Butterworth Group. £7·50.

Orthopaedic surgery covers an ever-expanding branch of surgery and these 'Modern Trends' volumes are invaluable to the postgraduate who is studying for higher degrees or diplomas in surgery. This series is also of real use to the young orthopaedic surgeon who wants to keep abreast of this specialty.

The range of subjects covered in this book is very wide. A comparison of postgraduate training in Great Britain and the United States of America is made. Total hip replacement and total replacement of the elbow-joint are discussed at length. Other important chapters deal with coxa plana, arthroplasty of the knee-joint, and epidurography in a very practical way.

This book is a great credit to the 'Modern Trends' series.

The Elephant Man. By Ashley Montagu, Princeton, New Jersey. 8¾ × 5½ in. Pp. 140 + x, with 28 illustrations. 1972. London: Allison & Busby. £2·10.

This book, written by a well-known American anatomist and anthropologist, concerns a very bizarre man called by Sir Frederick Treeves the 'Elephant Man'.

The book is dedicated to the memory of Charles S. Sonntag, an anatomist who worked at University College in London.

Although much has been written about John Merrick, the Elephant Man, by Sir Frederick Treeves and others, never before has such a complete account been presented. Ashley Montagu, an author of some forty books, always showed a great interest in this patient of Treeves. The author also gives a very interesting short account of the life of Sir Frederick Treeves.

This book is a mixture of a detective story and a warm portrait of an apparently ugly figure who is likely to capture the affection of every reader.

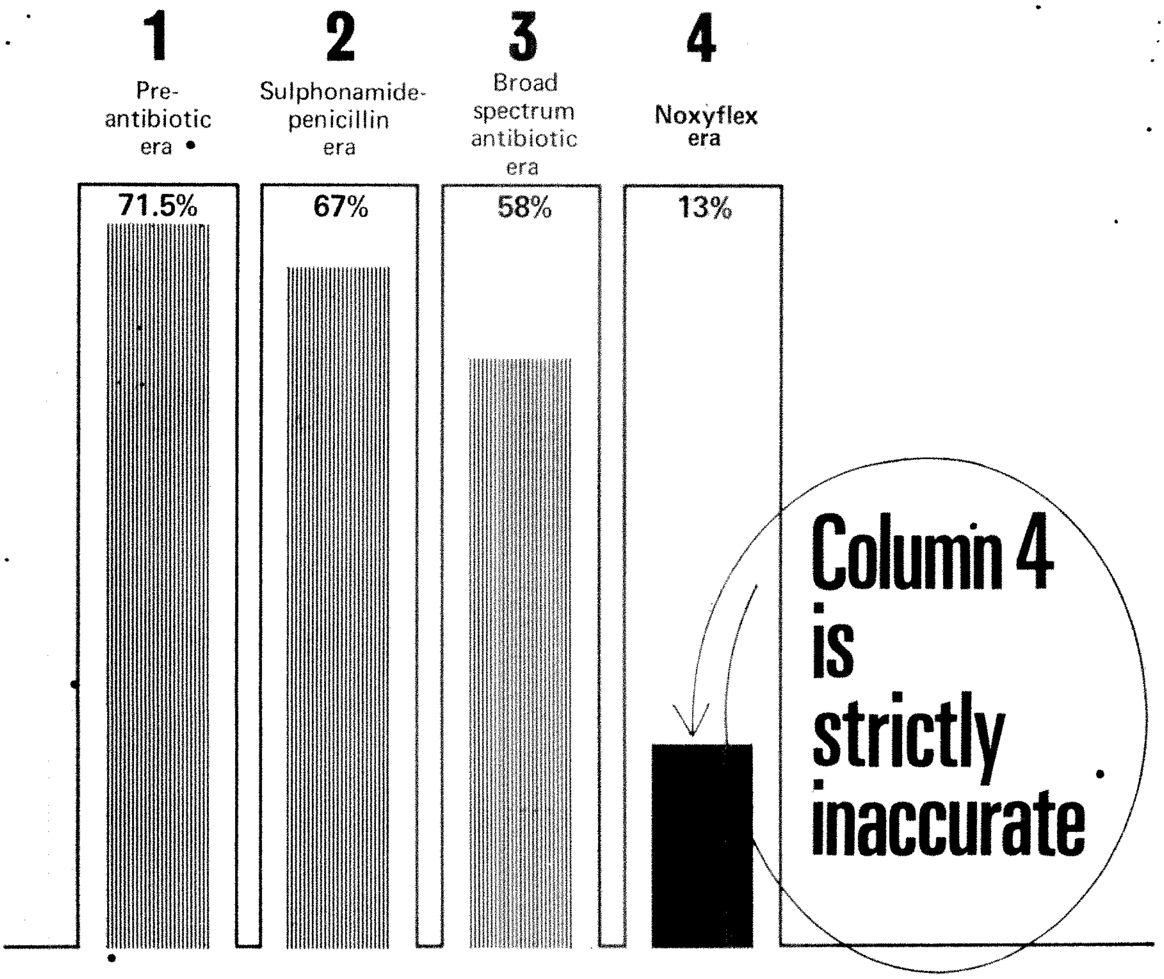
A book which will interest doctors, students, and nurses, as well as the lay public.

Handbuch der medizinischen Radiologie. Volume 5, Part 4. Edited by L. Diethelm, Mainz. 10½ × 7½ in. Pp. 824 + xx. Illustrated. 1971. Berlin: Springer Verlag. No price given.

This volume of the 'Encyclopaedia of Medical Radiology' deals almost entirely with juvenile osteochondritis. The disease process is discussed and illustrated in relation to virtually every bone in the body but of course the hip-joint gets more attention than the rest.

A section on congenital coxa vara is included. This mammoth work has been produced by a single author and contains a vast number of up-to-date references, most of these relating to the German rather than the English literature. Undoubtedly this volume will become a standard reference book for this particular condition.

The graph below compares mortality rates due to faecal peritonitis, era by era.
It is not pedantically accurate because its sources differ. But the point is fairly made.



Why inaccurate? Because column 4 refers to 23 cases of faecal peritonitis which were treated successfully with Noxyflex. But the *3 deaths which occurred were due to causes other than peritonitis - as post-mortem revealed. **The mortality rate due to peritonitis can therefore be regarded as zero.**

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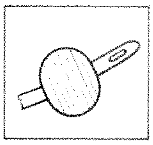

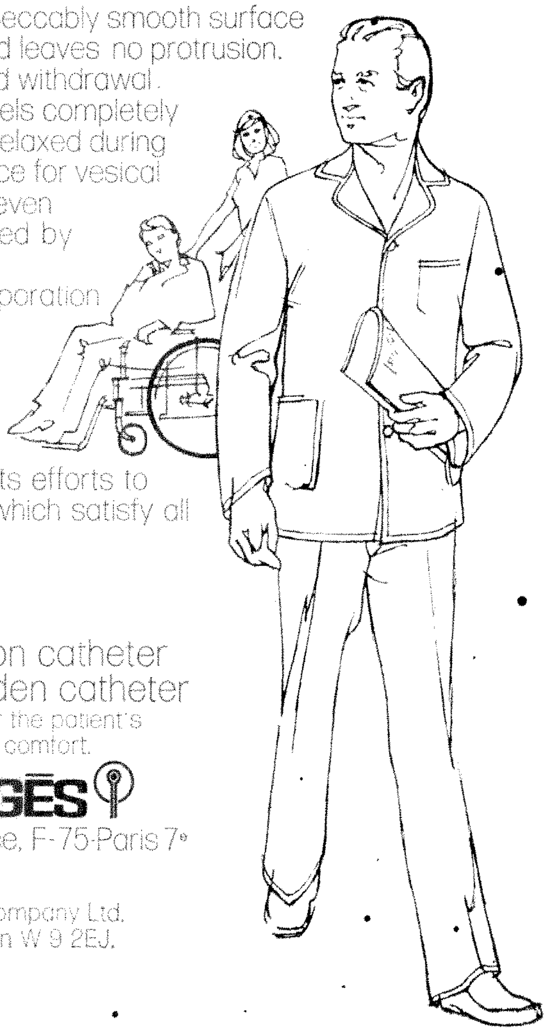

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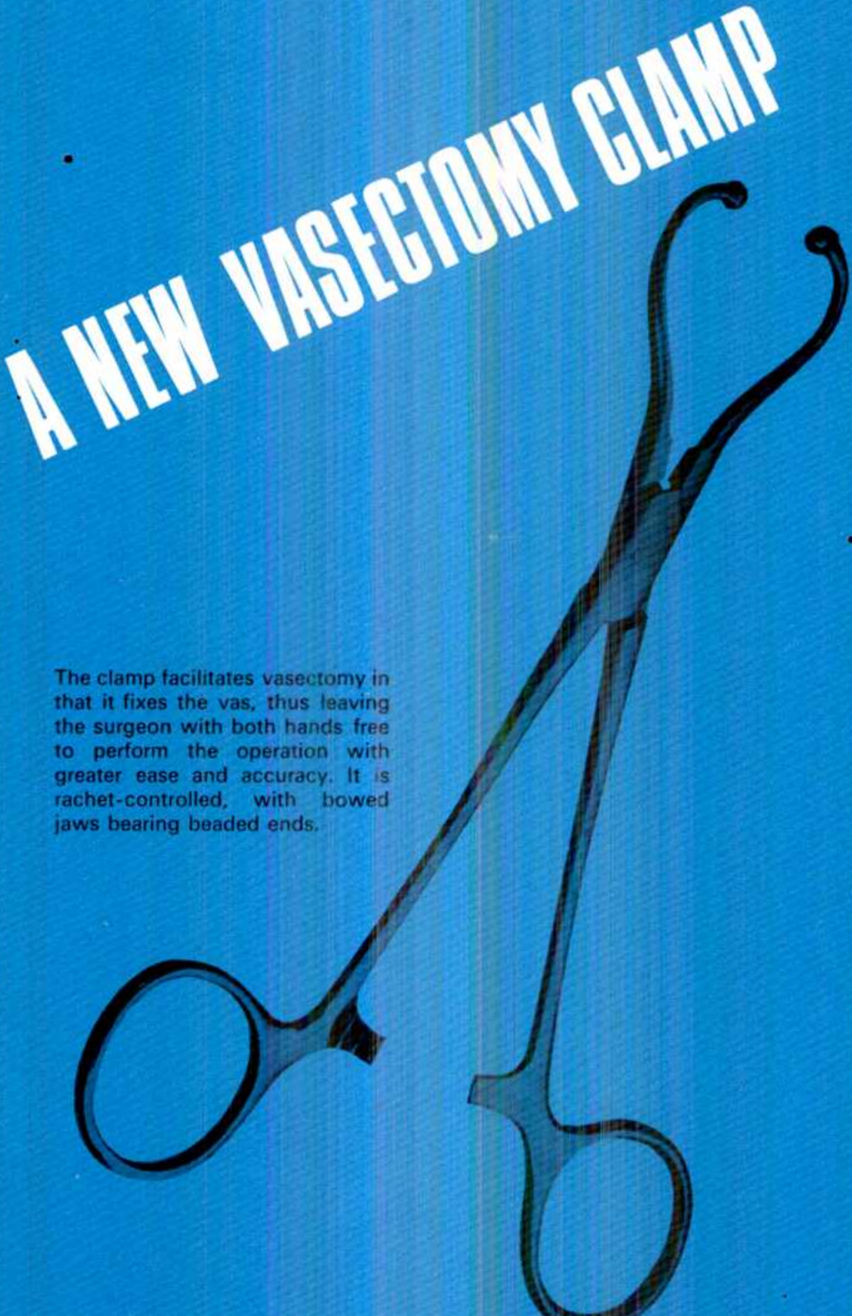

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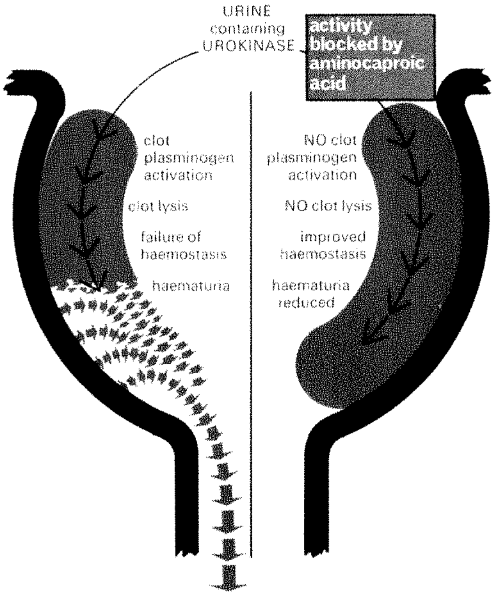

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CONTENTS

ORIGINAL PAPERS

PAGE

METABOLISM AFTER INJURY. I: EFFECTS OF SEVERITY, NUTRITION, AND ENVIRONMENTAL TEMPERATURE ON PROTEIN POTASSIUM, ZINC, AND CREATINE *D. P. Cuthbertson, G. S. Fell, Catherine M. Smith, and W. J. Tilstone* 925

'CURATIVE' SURGERY IN CARCINOMA OF THE COLON INVOLVING DUODENUM *Harold Ellis, M. Naunton Morgan, and Christopher Wastell* 932

OESOPHAGEAL PERFORATION DURING ABDOMINAL TRUNCAL VAGOTOMY FOR DUODENAL ULCER *J. J. Price, S. J. A. Powis, and D. M. Morrissey* 936

CIRCUMFERENTIAL OESOPHAGEAL MYOTOMY - - - - - - - *James S. Davidson* 938

GLOMUS JUGULARE TUMOURS—RADIOTHERAPY OR SURGERY? - - - *G. W. Glover and J. Block* 947

ARTERIOVENOUS FISTULAE FOR CHRONIC INTERMITTENT HAEMODIALYSIS: A MODIFIED SURGICAL TECHNIQUE *M. Hashmonai, A. Schramek, C. Chaimovitz, and D. Erlik* 953

ERYTHROCYTE AND PLASMA CIRCULATION TIMES IN HAEMORRHAGIC SHOCK *D. F. L. Watkin and Jennifer Hudson* 957

THORACIC ENTERIC CYSTS AND DIVERTICULAE - - *Saeed Ahmed, Ambrose Jolleys, and John F. Dark* 963

MULTIPLE ORGAN GRAFTS IN THE PIG - *R. Y. Calne, R. A. Sells, V. C. Marshall, P. R. Millard, B. M. Herbertson, E. J. Hadjiyannakis, D. C. Dunn, A. J. Robson, and D. R. Davis* 969

PREDICTION OF 1-YEAR SURVIVAL AFTER RESECTION OF LUNG TUMOURS FROM THE PREOPERATIVE STERIOD EXCRETION PATTERN - - - - - - - - - - *L. G. S. Rao* 977

INVESTIGATION OF OEDEMA OF THE LOWER LIMB FOLLOWING SUCCESSFUL FEMOROPOPLITEAL BY-PASS SURGERY: THE ROLE OF PHLEBOGRAPHY IN DEMONSTRATING VENOUS THROMBOSIS - - - *J. D. Hamer* 979

SHORT NOTES OF RARE OR OBSCURE CASES

RECURRENT SPONTANEOUS RUPTURE OF THE URINARY BLADDER - - - - - *M. H. Wheeler* 983

MASSIVE HAEMORRHAGE IN ELEPHANTIASIS NEUROFIBROMA - - - - - - *P. McMaster* 984

REVIEWS AND NOTICES OF BOOKS

The Laboratory Animal—Principles and Practice—*W. Lane-Petter and A. E. G. Pearson.* Radiation Effect and Tolerance, Normal Tissue. Basic Concepts in Radiation Pathology—ed. *J. M. Vaeth.* Essentials of Artificial Ventilation of the Lungs—*A. R. Hunter.* Orthopaedic Surgery in Spasticity—*Harold M. Frost.* Urologische Operationslehre, Vol. 8—*G. W. Müller, W. Welrheim, and G. W. Heise* 986

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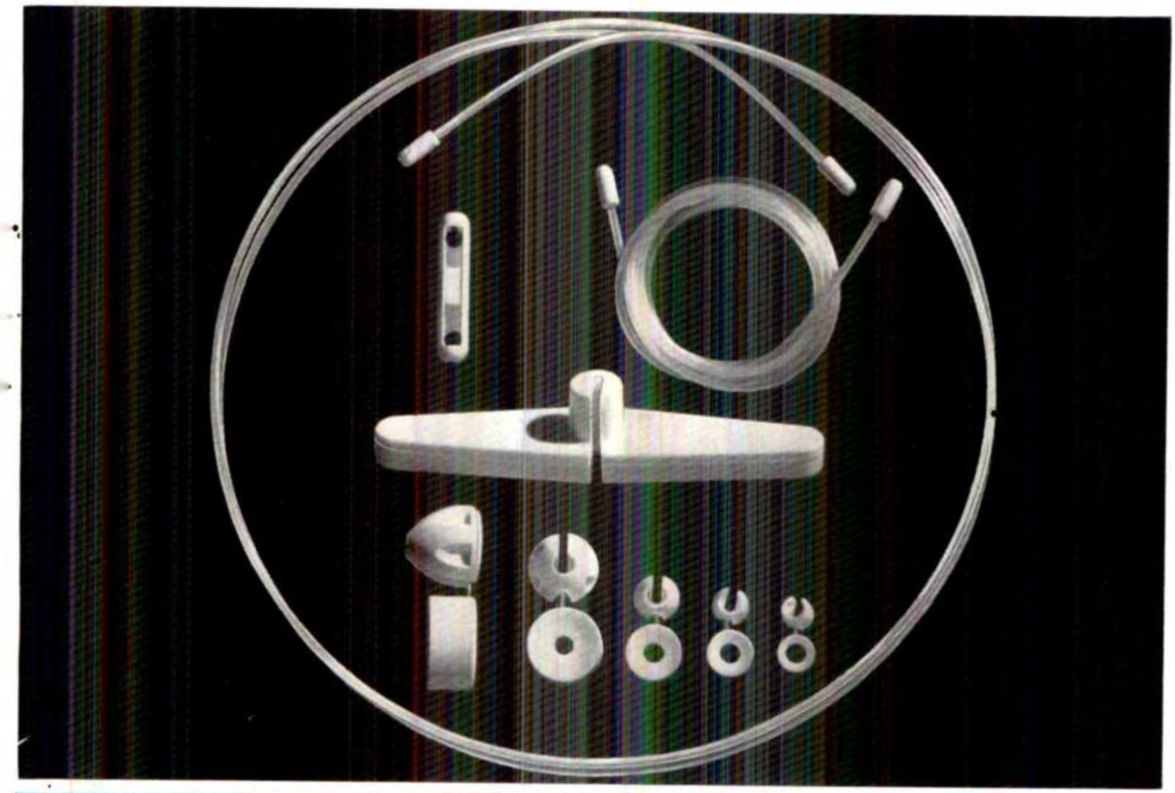

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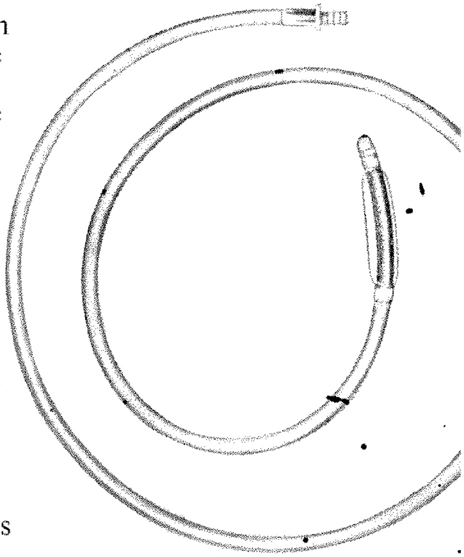

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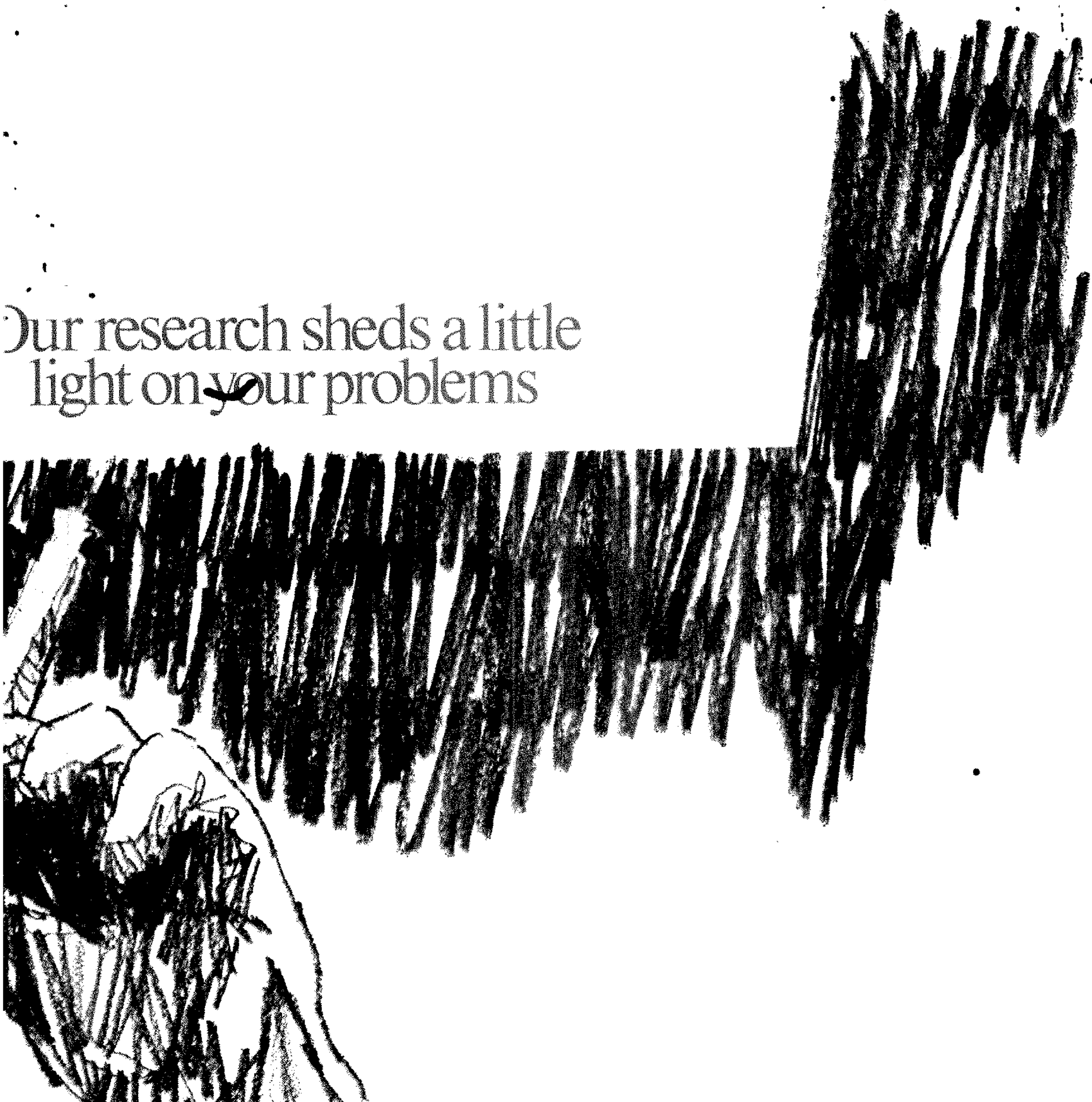

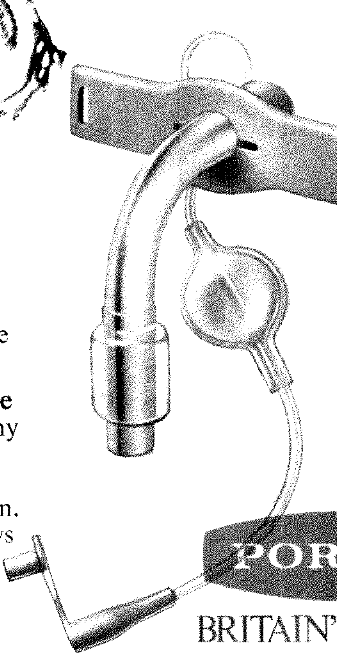

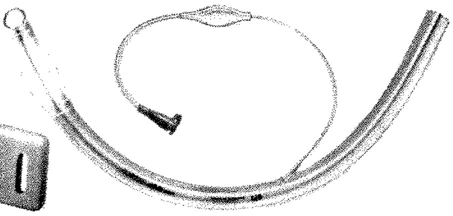

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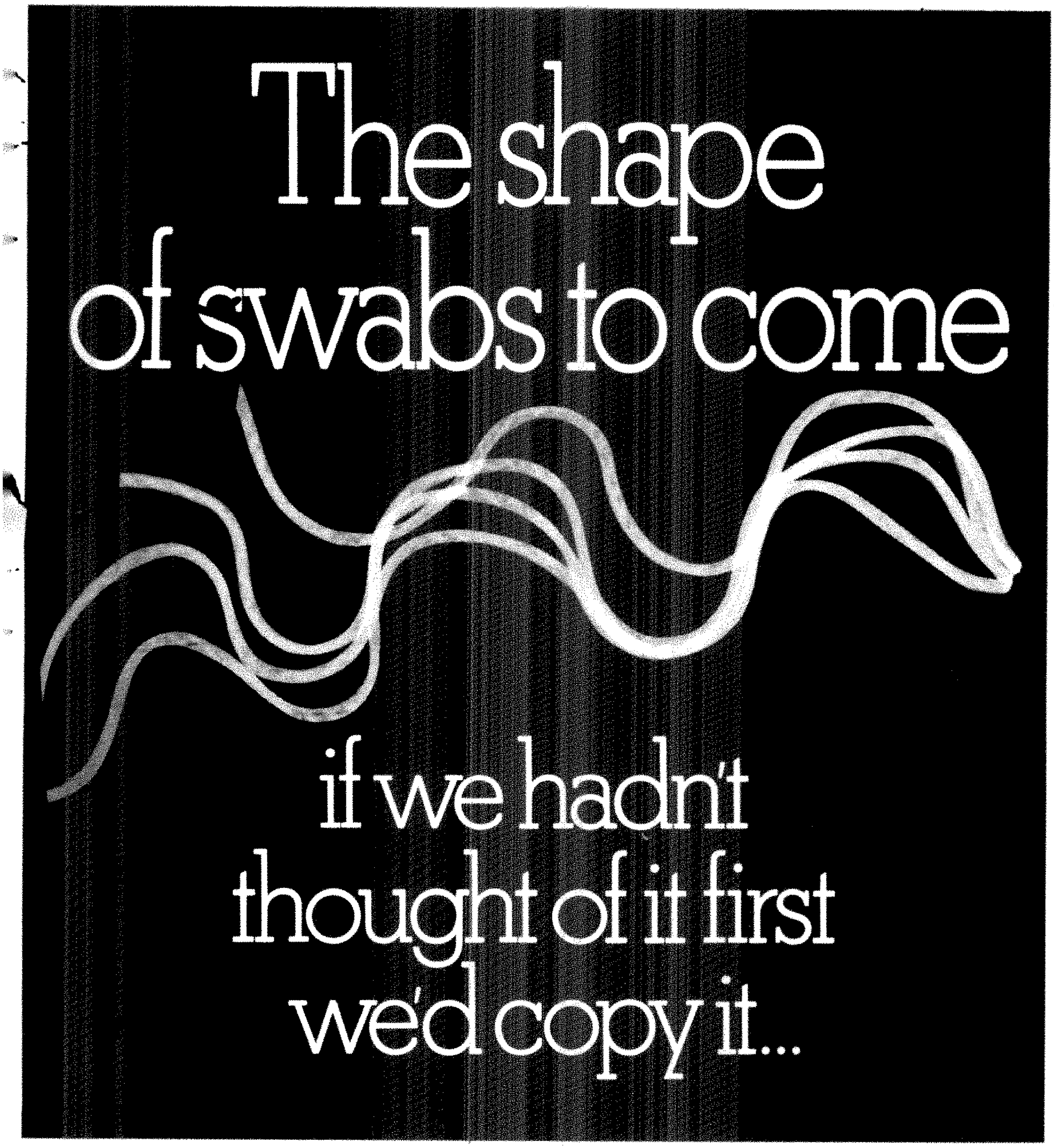

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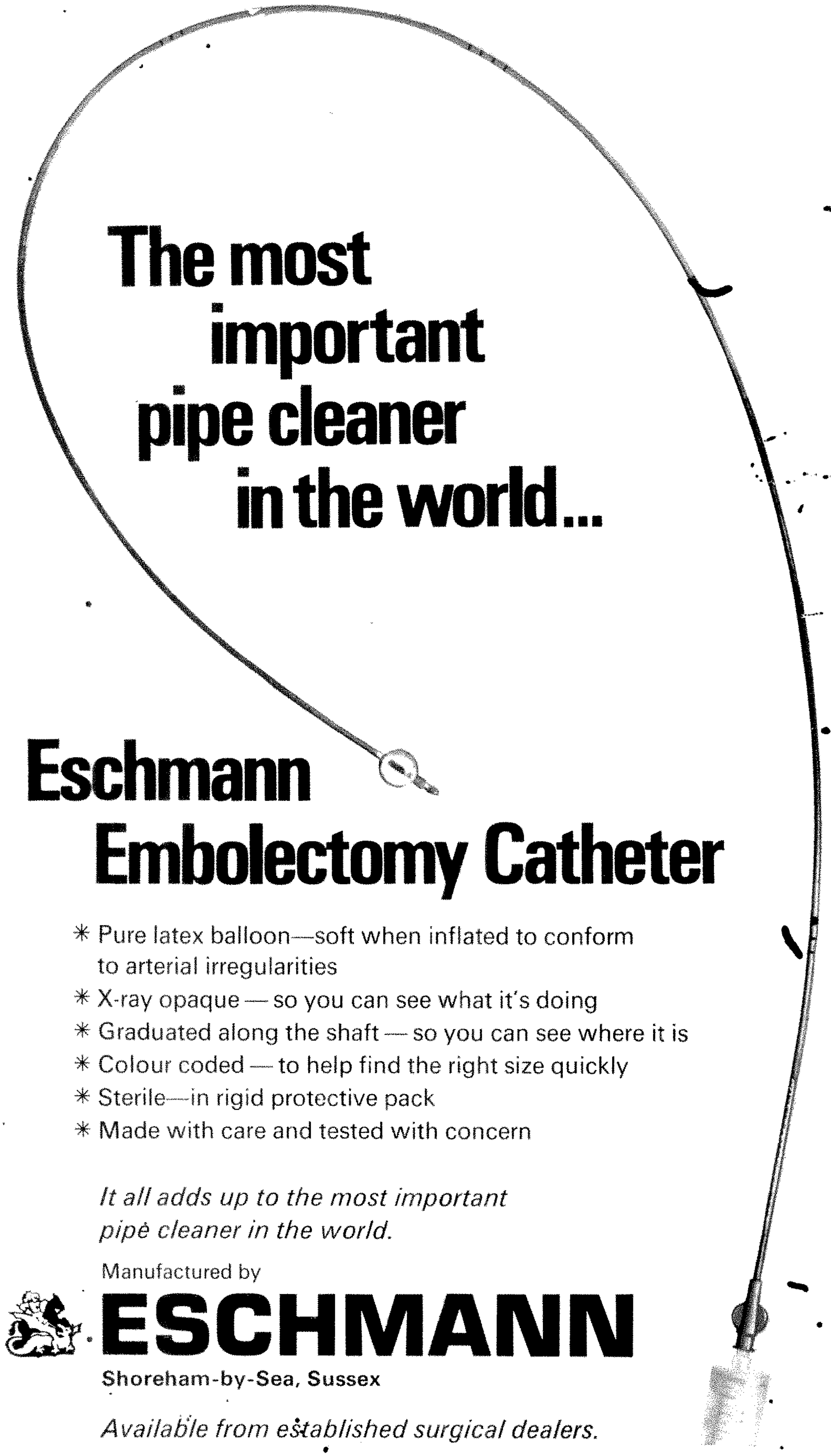

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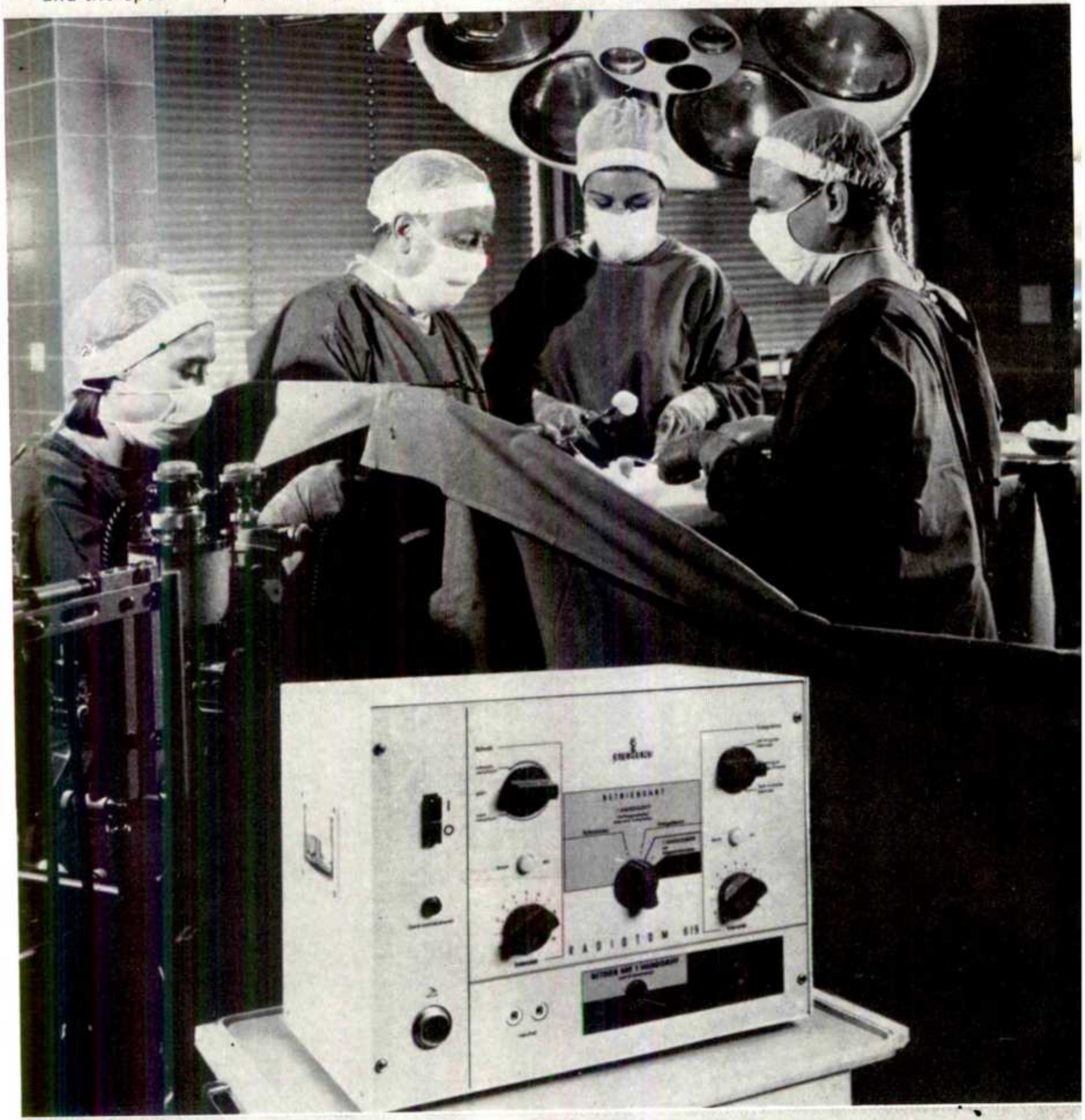

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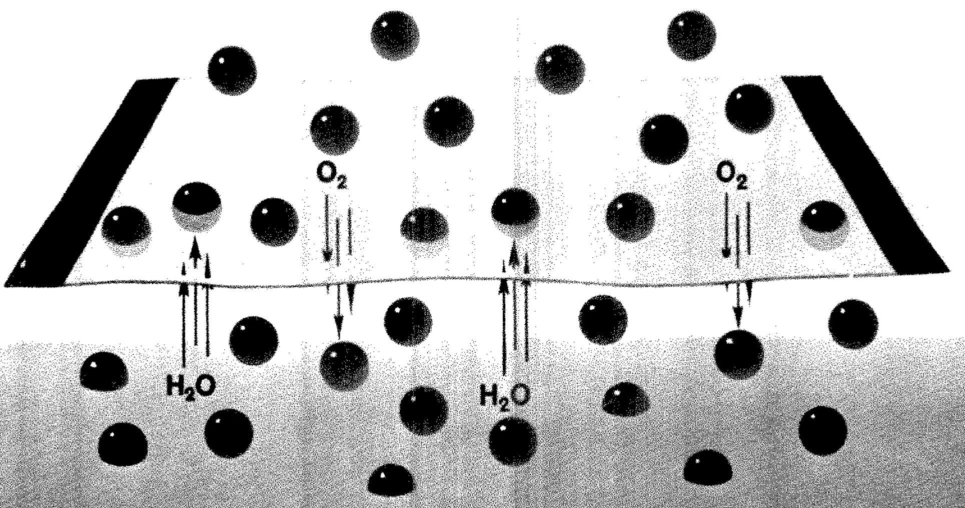

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METABOLISM AFTER INJURY. 1: EFFECTS OF SEVERITY, NUTRITION, AND ENVIRONMENTAL TEMPERATURE ON PROTEIN POTASSIUM, ZINC, AND CREATINE

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SUMMARY

The effect of an environmental temperature of 28–30° C. and a relative humidity of 35–45 per cent on the protein metabolic response to injury of one or more major long bones of the lower limbs has been studied in 29 male patients and 28 similar controls housed at 20–22° C. The metabolic response was reduced at the higher temperature compared with the controls, the more severely injured showed a greater metabolic response than the less severely injured, and the ameliorating influence of environmental temperature was more noticeable in the former. The metabolic response seems to be principally one of catabolism of muscle, with increased urinary excretions of potassium, creatine, and zinc in the urine correlating well with those of nitrogen at 20° C. but not at 30° C. The response (i.e., catabolism of muscle) was not affected by post-injury diet at 20° C. ambient temperature. There was a reduction in the disturbance of the plasma proteins.

In general, the patients tolerated the warm drier conditions. Owing to the intrinsic difficulty in assessing minor changes in bone healing it was not possible to assess what, if any, beneficial change occurred in the fracture site. From our experimental observations on the rat and the work of others on burned patients the reduction in heat production at the higher ambient temperature is accompanied by an enhanced rate of healing of surface wounds.

THE metabolic response to injury is both local and general. It is with the latter in its post-shock manifestations following moderate to severe physical injury to the limbs of man that this report is concerned, and, in particular, with the effect on this response of raising the environmental temperature to the zone of thermoneutrality for clothed man (28–30° C.). This topic has been of considerable interest to those working in the field of metabolic response to trauma (Campbell and Cuthbertson, 1967; Miksche and Caldwell, 1967; Barr, Birke, Liljedahl, and Plantin, 1968; Cuthbertson, Smith, and Tilstone, 1968; Caldwell, 1970; Davies and Liljedahl, 1970; Tilstone and Cuthbertson, 1970; Spivey and Johnston, 1972).

The essential elements in the generalized response to injury were described by one of us (Cuthbertson, 1930, 1932, 1936, 1942) and extended by Wilkinson, Billing, Nagy, and Stewart (1949, 1950) and Moore and Ball (1952) among others. The complex series of reactions to various forms of injury has as its main components over the first 10–14 days after injury increased net protein catabolism and parallel increases in heat loss and oxygen consumption. There are also characteristic changes in plasma-protein levels (Owen, 1967; Cuthbertson and Tilstone, 1969).

The extent of the metabolic response seems to depend on the nature and severity of the injury, being slight for uncomplicated surgery, greater for major skeletal injuries, and considerable in sepsis and major burns (Kinney, Long, and Duke, 1970).

The present report is concerned with our observations on the effect of severity of injury and environmental temperature on the magnitude of the metabolic response and with observations on the major source of the nitrogen which is lost in urine.

MATERIALS AND METHODS

Patients.—Patients were all males ranging in age from adolescence to 70 years. They were either victims of accidentally sustained injuries of moderate to severe extent involving one or more long bones of the lower limbs or were patients undergoing elective arthroplasties of the hip or arthrodeses of the knee- or ankle-joint.

Environmental Control.—The patients were housed in single-bed cubicles which had partition walls of double-sheet aluminium and double glazing. A two-way cupboard allowed urine collections and food residues to be removed without opening the door of the room. Each cubicle had a Rootes Tempair 1½ h.p. water-cooled air-conditioning unit (W. Kemp, Glasgow) with a cooling capacity of 15,000 B.Th.U. per hour, and a 3-kV.A. heating unit with an air flow of 400 c. ft. per minute. Air passing through the unit was filtered in a washable polyurethane filter. Normally the dehumidification unit was not used since this cooled the air and produced rapid temperature drops if the thermostat was 'off' while the humidostat was 'on'. A 1-kV.A. convector heater was also used in winter. This apparatus could maintain a temperature of 29–30° C. and relative humidity of 35–45 per cent in all normal external environmental conditions. Opening the door for access did not cause a major temperature fall (*Fig.* 1).

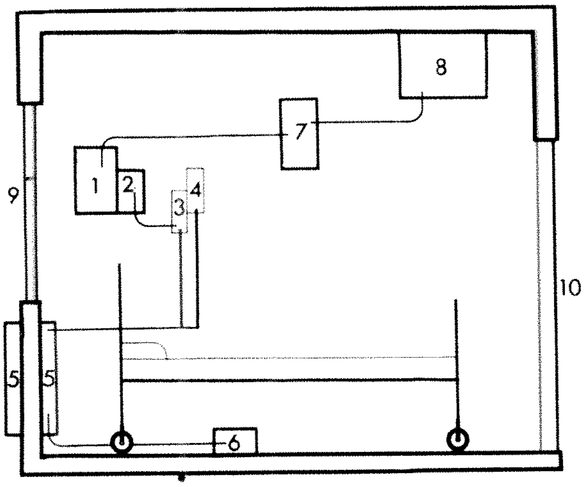

FIG. 1.—Linked thermal and humidity control of air changes in single-bed cubicle. 1–2, Mains junction box and on/off switches. 3, Thermostat. 4, Humidistat. 5, Rootes Tempair 1½ h.p. unit. 6, Water pump. 7, Thermostat and fan. 8, 1-kV.A. convector heater. 9, Cubicle window. 10, Cubicle door.

Experimental Protocol.—Twenty-nine patients were studied with the cubicles maintained at 28–30° C. and 28 with the cubicles maintained at 20–22° C.—the normal range of ward temperature. Subsequently only the figures 30 and 20° C. will be used as most of the cases fell into these temperature levels. The metabolic investigations began as soon as the initial shock phase was over and usually was within 24 hours of injury. Informed consent was obtained from all the patients. A few cases could not tolerate the warmer conditions and were removed from further study. The pattern of the diets presented was based on the patients' normal home intake which had been elicited by questioning, except that a protein intake (76 per cent of animal origin) which contributed not less than 13 per cent of the total calorie intake was always attempted.

Observations were made daily on various parameters of protein and tissue catabolism. Results for all of these are not available for all the patients. In general, results have been averaged for the following four periods: the first 4 days after injury (and we usually did not have results for the first day) and the three subsequent 3-day periods (but some patients were discharged before the end of the last of these 3-day periods).

Excess urine nitrogen was calculated by subtracting each day's food nitrogen intake from the total urinary nitrogen excretion from 08.00 on that day to 07.55 on the next morning. Faecal nitrogen was not measured since it is not indicative of endogenous protein metabolism and Cuthbertson (1936) has shown it to be a fairly constant 6 per cent of intake at all stages after injury in man, and Campbell and Cuthbertson (1967) also found it to be unaffected by trauma in the rat.

Food Intake.—Net food intake was obtained by weighing food presented to the patient and subtracting all the residues. Intake of nitrogen and energy was calculated from the tables of McCance and Widdowson (1960), with occasional checks of nitrogen by analysing one-quarter of total homogenized diets.

Chemical Methods.—Nitrogen was estimated by a semi-mechanized Kjeldahl technique based on that described by Fleck (1967). Zinc was estimated by atomic absorption spectrophotometry using a Pye Unicam SP90, potassium by flame photometry, and creatine by a fluorescent technique using the Auto Analyzer (Tilstone and Fell, 1971). The urine was preserved by providing 5 ml. of 10 per cent thymol in isopropanol.

Statistical Analysis.—Statistical analysis of results was performed on an IBM 1130 computer using standard programmes for analysis of variance, Student's t-test, correlation coefficients, and linear regressions with one or more independent variables.

RESULTS

1. Patients.—Retrospective analysis shows that the two groups of patients, that is those at 20° C. and those at 30° C., were not significantly different in age (t-test, $P > 0{\cdot}05$), extent of traumatic fever (t-test, $P > 0{\cdot}05$), and perhaps also degree of trauma. The extent of traumatic fever was measured by scoring the number of days within the 13-day period on which oral temperature was 37·2–37·7° C., 37·8–38·2° C., or over 38·3° C. at least once a day, the scoring being 1, 2, and 3 points respectively for these zones. The severity of trauma was assessed in two ways: the first was dependent upon the amount of blood replacement which was necessary and the other on the extent of the trauma as defined on an arbitrary scale ranging from 1 to 7, for example, fracture of both femora and both tibiae and fibulae, 7; fracture of one femur and the tibia and fibula of the other leg with deep lacerations including severed tendons of the arm, 5; fracture of both tibiae and fibulae with lacerations and contusions, 4; comminuted fracture of the femur, 3; fracture of the neck of the femur, 2·5; fracture of the tibia and fibula, 2; Pott's fracture, 1; Charnley arthroplasty of one hip-joint, 5; triple arthrodesis of the ankle-joint, 2. On these two bases of assessment the two groups did not appear to be significantly different (t-test, $P > 0{\cdot}05$). The results are shown in *Table I*. A subsequent division in each group into moderate to severe injury on the one hand (+), and less severe on the other (−), was made on the basis of 2·5 and above for the former and below 2·5 for the latter. Only in 3 cases of the latter group was some blood necessary.

Table I.—Comparison of Age, Extent of Traumatic Fever, and Severity of Injury in the Two Groups of Patients

Ambient Temperature (° C.)		Age	Fever Rating	Trauma Rating	
				Score	Pints of Blood
20	Mean (*N*) S.E.M.	41 (28) 3·0	3·0 (21) 1·0	2·7 (28) 0·3	1·5 (12) 0·5
30	Mean (*N*) S.E.M.	37 (29) 3·0	3·0 (26) 0·4	2·6 (29) 0·2	1·0 (9) 0·3

2. Intake of Energy and Nitrogen in Food.—Taking all the patients at 20° C. as one group and all those at 30° C. as the other, their food energy and food nitrogen were compared on the basis of the means for each successive period of study, that is, over the first 4 days, then the subsequent three 3-day periods. A comparison was also made on the basis of the means of all periods taken together. As can be seen from *Table II* there was no significant difference between the two groups at any time in respect of energy or protein intake. It is of interest that intake was not reduced by the warmer atmosphere.

Table II.—Intake of Energy and Nitrogen

Ambient Temperature (° C.)	Intake		Period				
			Overall	1	2	3	4
20	Energy (MJ. per day)	Mean (*N*) S.E.M.	9·5 (97) 0·3	8·0 (23) 0·5	9·5 (25) 0·5	10·0 (25) 0·5	10·2 (24) 0·6
30		Mean (*N*) S.E.M.	10·1 (110) 0·3	9·1 (27) 0·6	10·0 (29) 0·5	10·5 (27) 0·5	10·8 (27) 0·6
20	Nitrogen (g. per day)	Mean (*N*) S.E.M.	12·2 (93) 0·3	10·5 (23) 0·7	12·3 (25) 0·6	12·5 (25) 0·6	12·8 (20) 0·7
30		Mean (*N*) S.E.M.	12·4 (106) 0·3	12·0 (27) 0·8	12·7 (29) 0·6	12·7 (27) 0·6	13·2 (20) 0·7

Table III.—Mean Excess Nitrogen Excretion for Greater (+) or Less (−) Severely Injured Patients

Ambient Temperature (° C.)	Severity	Excess Nitrogen (g. per day ± S.E.M.)			
		Period			
		1	2	3	4
20	+	6·6 ± 1·5	7·3 ± 1·2	6·6 ± 0·9	5·2 ± 1·2
	−	3·2 ± 1·4	4·0 ± 1·6	2·6 ± 1·2*	0·5 ± 1·5*
30	+	3·2 ± 1·8	4·1 ± 1·2	4·1 ± 1·4	2·4 ± 1·1
	−	0·6 ± 1·2	2·9 ± 1·6	1·5 ± 1·5	1·0 ± 1·6
20	All	4·9 ± 1·1	5·6 ± 1·0	4·6 ± 0·9	2·6 ± 1·1
30	All	2·2 ± 1·0†	3·5 ± 1·0	2·7 ± 1·1	1·8 ± 0·9
20	All	All periods: 4·4 ± 0·5			
30	All	All periods: 2·5 ± 0·5‡			

* Differs significantly from severe injury group, $P < 0{\cdot}05$.
† Differs significantly from 20° C. group, $P < 0{\cdot}05$.
‡ Differs significantly from 20° C. group, $P < 0{\cdot}01$.

3. Excess Urine Nitrogen Excretion.—Trauma has been shown not to affect appreciably the digestibility of protein and thus the extent of catabolism of endogenous protein can be measured by following excess nitrogen excreted in urine, that is, the difference between urine nitrogen and food nitrogen. As well as by analysis in temperature groups as described above, the results for excess nitrogen were also subdivided according to the severity of trauma, as scored on the arbitrary scale. Within this subdivision the excess urine nitrogen excretion for the patients at each temperature was compared in each period, that is, those more severely injured and housed at 20° C. were compared with those less severely injured and kept at the same temperature, the comparison being made separately for periods 1, 2, 3, and 4; and similarly for the patients housed at 30° C. Comparisons were also made on the basis of equivalent injury but different temperature, that is, more severely injured at 20° C. against more severely injured at 30° C., and similarly for the less severely injured. These comparisons were made both for the means of the individual periods and for all the periods taken together.

The results (*Table III*) show that at 20° C. the more severely injured patients had a significantly higher excretion of excess nitrogen in the third and fourth periods ($P < 0{\cdot}01$) than did the less severely injured, but at 30° C. the more severely injured did not have such a significantly increased nitrogen excretion at any time. The less severely injured at 20° C. did not have a significantly greater excess nitrogen excretion than those at 30° C., the average being 1·04 g. per day higher at 20° C. but with $t = 0·62$. Taking the more severely injured there was a marginally significant difference in period 2 ($P = 0·05$) and overall the average difference was 3·01 g. per day. When all the degrees of injury are taken together then the difference between the two temperatures is more statistically significant, probably due to the greater number of degrees of freedom. Analysis shows that, taking all the periods together, the patients at 30° C. have a very significant reduction in their nitrogen excretion ($P < 0·01$), which is probably mainly in the early stages of the response, with the first period being significantly reduced at $P < 0·05$.

Table IV.—URINARY EXCRETION OF NITROGEN, ZINC, AND CREATINE

AMBIENT TEMPERATURE (°C.)	METABOLITE		PERIOD				
			Overall	1	2	3	4
20	Nitrogen (g. per day)	Mean (N) S.E.M.	16·5 (98) 0·4	15·6 (24) 0·9	17·9 (25) 0·9	17·7 (25) 0·8	15·2 (23) 0·9
30		Mean (N) S.E.M.	15·1 (109) 0·5	13·9 (29) 0·9	16·3 (29) 1·0	15·6 (27) 0·9	14·8 (24) 0·9
20	Zinc (μg. per day)	Mean (N) S.E.M.	1132 (24) 104	887 (7) 103	1176 (7) 255	1254 (7) 218	1316 (3) 168
30		Mean (N) S.E.M.	1113 (34) 93	732 (9) 120	1095 (9) 115	1286 (9) 211	1404 (7) 238
20	Creatine (mg. per day)	Mean (N) S.E.M.	450 (57) 47	407 (13) 91	526 (13) 140	497 (12) 126	341 (9) 55
30		Mean (N) S.E.M.	391 (54) 542	182 (14) 42*	420 (14) 98	471 (14) 113	509 (12) 154

* Significantly different from 20° C. result, $P < 0·05$.

4. Excretion of Products of Tissue Protein Catabolism.—Excretion of total urinary nitrogen was never significantly different between the two groups no matter how the comparison was made (*Table IV*). It may be felt that if the excess nitrogen is significantly different between the two groups, then food nitrogen and/or urine nitrogen should differ significantly also. Food nitrogen did not differ (*see above*), and the large variance of urine nitrogen excretion, being the sum of the variance due to intake-associated factors and the variance due to endogenous protein catabolism, placed the average difference found in urine nitrogen excretion well below the level required for a statistically significant difference.

We wished to test the extent to which tissue catabolism, particularly muscle, might be responsible for the response of increased net nitrogen as had been shown in the rat (Cuthbertson, McGirr, and Robertson, 1939). To this end the urinary excretions of potassium, creatine, and zinc were examined.

Potassium is primarily an intracellular ion and it is well established that total-body potassium correlates well with the lean body mass.

Cell potassium may at times be quickly depleted following trauma (Moore and Ball, 1952). In the fractured rat an increased urinary excretion of potassium was found, reaching a peak some 3 days after injury, and the loss of potassium from muscle may be greater than for nitrogen over the first few days (Cuthbertson and others, 1939). Wilkinson and others (1950) and Le Quesne (1967) have described the increased excretion of potassium after abdominal injuries and the former showed that it is greater than that attributable to reduced food intake after partial gastrectomy. Moore and Ball (1952) have further delineated the situation, showing that in burns the potassium loss may last for only 2–4 days. They have also drawn attention to the normal early postoperative response whereby there is a greater potassium excretion than would be predicted from nitrogen loss.

In the present paper we further report highly significant correlations between urinary nitrogen and potassium both at 20 and 30° C. ($P < 0·001$) and also a significant correlation between creatine and potassium at 20° C. but not at 30° C. These correlations were for all degrees of severity of injury and at all intervals during the first 2 weeks following the injury. Thus, the effect of the higher ambient temperature is to reduce the overall excess urinary excretion of potassium as well as that of nitrogen.

Creatine is the most abundant extractive of muscle, and more than 95 per cent of the total body content of creatine is found in muscle as creatine phosphate. It is normally excreted in urine after conversion to creatinine, only small amounts of creatine itself being detected. In 14 normal subjects we found a daily urine output of 85 ± 11 mg. (mean ± s.d.).

Creatinuria is commonly observed in muscle diseases (Pennington, 1971). In diverse conditions involving acute wasting of muscle, such as when carbohydrate is absent from food, in diabetes, in hyperthyroidism, and during involution of the uterus following parturition, large increases in urine creatine are reported (Allison and Bird, 1964). After injury a marked rise in plasma creatine was observed in severely injured goats, treated or untreated with penicillin (Gillette, Oppenheimer, Mansberger, Johnson, and Kookootsedes, 1958). The rise in plasma creatine was much greater than that of the other nitrogenous constituents examined, suggesting a rapid release of creatine from muscle cells at a rate faster than the conversion process to creatinine can effect, or a failure of uptake by an effectively reduced muscle cell mass of the creatine synthesized in the liver, leading to incomplete renal tubular reabsorption and creatinuria. The results of our studies are shown in *Table IV*, where they are analysed period by period. The most striking feature is the up to fivefold increase above the normal excretion which was observed, and also that the creatine excretion was less in the first period for the 30° C. group (*t*-test, $P < 0·05$). This finding has subsequently been repeated in a further series after injury (Cuthbertson, Fell, Fleck, and Queen, 1972), and confirms the diminution in the response at the higher environmental temperature.

Table V.—RESULTS OF MULTIPLE REGRESSION $Y = aX_1 + bX_2 + c$, WHERE Y IS URINE NITROGEN (g. per day), X_1 IS FOOD NITROGEN (g. per day), AND X_2 IS FOOD ENERGY (MJ. per day)

AMBIENT TEMPERATURE (°C.)	PERIOD	*a*	*b*	*c*	*P*
20	1	−0·67	+0·87	+16·3	N.S.
	2	−0·30	+0·40	+4·4	N.S.
	3	−0·37	+0·95	+12·5	N.S.
	4	−0·40	+0·90	+11·5	N.S.
30	1	+0·45	−1·24	+7·8	<0·05
	2	+0·88	−0·59	+10·7	N.S.
	3	+0·48	−0·40	+13·8	N.S.
	4	+0·80	−0·81	+13·5	<0·1

Results are average values for each period, with all severities of injury taken together.

N.S., Not significant.

The urinary excretion of zinc is low. For 16 normal subjects we found a daily excretion of 496 ± 197 μg. (mean ± s.d.). It is not affected by urinary volume or dietary intake (Spencer, Osis, Kramer, and Samachson, 1971). More than 60 per cent of the total body zinc is in skeletal muscle and the urinary excretion is known to rise after injury (Henzel, De Weese, and Lichti, 1970). The results shown in *Table IV* demonstrate the two- to threefold increases found after injury, although there was no significant difference in the amount excreted by the two groups of patients.

The evidence of increased potassium, creatine, and zinc excretion in urine after injury clearly demonstrates the quantitative importance of muscle in the protein metabolic response to trauma.

5. Relation between Dietary Nitrogen and Energy and Urine Nitrogen Excretion after Trauma.—Normally one would expect urine nitrogen to be a variable dependent linearly on food nitrogen and food energy, the regression coefficient being positive for food nitrogen and negative for food energy. We tested this relationship in the injured subjects. The multiple linear regression of urine nitrogen on food nitrogen and food energy was computed for the mean intake and excretion values for each patient in each of the four time periods. The results from patients at 20° C. were analysed separately from those at 30° C. Statistically significant linearity was tested by analysis of variance. The results are shown in *Table V*. It is clear that there is never a significant linear relationship at 20° C. and indeed the regression coefficients do not even have the expected signs. At 30° C., however, the regression coefficients all have the expected sign and a statistically linear relationship is achieved in period 1 ($P < 0·05$) and nearly so in period 4 ($P < 0·1$).

6. Correlation between Urine Nitrogen and other Excretory Products of Tissue Catabolism.—Single correlation coefficients were computed for urine nitrogen on urine zinc, urine nitrogen on urine creatine, and urine nitrogen on urine potassium. Urine nitrogen always correlated significantly with urine zinc ($P < 0·005$), with urine creatine ($P < 0·001$), and with urine potassium ($P < 0·001$). Creatine correlated significantly with zinc ($P < 0·001$) and with potassium ($P < 0·01$) at 20° C. but not at 30° C. This further suggests that muscle catabolism is a major factor in the metabolic response and that this is somewhat reduced at ambient temperatures of about 30° C. The results are shown in *Table VI*.

Table VI.—CORRELATIONS BETWEEN URINE NITROGEN AND PRODUCTS OF MUSCLE-TISSUE CATABOLISM (CREATINE, ZINC, AND POTASSIUM) AND BETWEEN URINE CREATINE AND OTHER PRODUCTS OF MUSCLE-TISSUE CATABOLISM (ZINC AND POTASSIUM) FOR PATIENTS WITH ALL SEVERITIES OF TRAUMA AT ALL INTERVALS AFTER INJURY

AMBIENT TEMPERATURE (°C.)	CORRELATION	*r*	*P*
20	Nitrogen and zinc	0·5233	<0·005
	Nitrogen and creatine	0·5337	<0·001
	Nitrogen and potassium	0·6592	<0·001
30	Nitrogen and zinc	0·5167	<0·005
	Nitrogen and creatine	0·4565	<0·005
	Nitrogen and potassium	0·5964	<0·001
20	Creatine and zinc	0·5910	<0·001
	Creatine and potassium	0·3200	<0·05
30	Creatine and zinc	0·2970	N.S.
	Creatine and potassium	0·2219	N.S.

DISCUSSION

The results reported in the present paper allow two important conclusions to be drawn. First, the metabolic response to bony injury (mainly fractures) involves net catabolism of muscle tissue to a quantitatively important extent, and secondly, this response is significantly reduced in the severely injured patient if he is housed at 30° C. ambient temperature.

It has long been inferred that muscle breakdown is involved in the metabolic response to injury. Indeed, the early observations of Cuthbertson (1930) arose from an investigation of the calcium and phosphorus balance in patients with fracture of the long bones of the lower limbs, where there was found to be an unexpected considerable negative phosphorus balance but not a corresponding calcium deficit. Soft tissue seemed to be implicated and further investigations showed a marked loss of nitrogen and sulphur as well as of phosphorus in the first 10–12 days following fracture of a major long bone. These three elements were excreted in proportions which suggested that muscle might be the source of the loss. A few years later Cuthbertson and others (1939) observed similar responses in the rat given experimentally a fracture of femur, and they also reported a creatinuria which paralleled the increased urine-nitrogen loss. This work was not taken much further at the time owing to war-time conditions, but the importance of a dietary-dependent endogenous protein pool was demonstrated by Munro and Cuthbertson (1943) and Munro and Chalmers (1945), who found no increased urine nitrogen following fracture of the femur in the rat if the animals had been fed a protein-free, but calorie-sufficient, diet for some time before injury. They also showed that the proportion of protein in the pre-injury, but not post-injury, diet quantitatively affected the response to trauma. However, in spite of the well-accepted clinical observation of muscle wasting in severe injury and the above observations of Munro and his colleagues, some workers claim that the observed metabolic response to injury is simply that of the reduced voluntary food intake which usually follows major trauma (Abbott and Albertsen, 1963).

The results which we report quite clearly demonstrate the involvement of muscle catabolism in the presence of undiminished food intake, and that this response, entirely separate from dietary conditions, is diminished at the higher ambient temperature. The results of the regression analysis both confirm the effect of the 30° C. environment in reducing the metabolic response and also cast doubt on the value of intensive nutrition, in which high-calorie, high-nitrogen diets are given by intubation or intravenously in the early stages post trauma. Our results indicate that such measures in no way diminish the catabolic response of muscle tissue. It is true that, faced with a long-term apparently hypercatabolic state or with a patient who will be unable to feed normally for some time, intensive nutrition with high-energy regimens will be of value since nitrogen balance should be improved (Peaston, 1968).

The effect of environmental temperature on the metabolic response to trauma is a relatively recent finding. The first observation of a reduction in what Cuthbertson has defined as the 'flow' phase (Cuthbertson, 1942) was made by Caldwell in 1962. This report showed that an ambient temperature of 30° C. reduced negative nitrogen balance and mortality in rats with severe scalding injury. These observations have been confirmed by Barr and others (1968) and Davies and Liljedahl (1970) for man with severe burn injury.

The initial suggestion of Caldwell (1962) was that the warmer environment provided the heat required to evaporate the water that is continuously lost from burned skin and thus relieved the body of a heat burden which can easily exceed 3000 Cal. (12·5 MJ.) per day (Moyer and Butcher, 1967). This may be part of the value of the warmer environment to patients with burns, but it in no way accounts for the similar effect of temperature on the metabolic response to long bone injury in the rat (Campbell and Cuthbertson, 1967) or the results for man reported in the present paper. Unfortunately our experiments do not allow us to draw conclusions about the mechanisms involved. We do know that the corticosteroid response is not affected by the higher temperature, at least in the rat (Tilstone and Roach, 1969) and we feel that more evidence is needed before Caldwell's more recent suggestion (Caldwell, 1970) that the thyroid is definitely concerned can be accepted.

Johnston and others have been studying the effect of exposure to 30° C. on the metabolic response to trauma in patients undergoing elective abdominal surgery. They have recently reported their conclusions (Spivey and Johnston, 1972) and state that temperature does not affect the metabolic response in these patients but point out that the catabolic response to such trauma is usually minor. This agrees with our results from the less severely injured subgroup, but our overall results and those mentioned above from workers dealing with burn injuries quite clearly show that a reduced metabolic response can be achieved by increasing the ambient temperature to 30° C. A beneficial clinical response also seems clear in the burns cases, although we can put forward no conclusions at all about the progress of the long bone injuries other than that it is not impaired. Improved superficial wound healing in rats has already been reported by us (Cuthbertson and Tilstone, 1967). The parallel observations on some of our cases made by Fleck and Ballantyne (1971) in respect of the behaviour of the plasma proteins following injury indicate that at 28–30° C. there is much less disturbance with a diminished rise in acute phase reactants and a diminished fall in plasma-albumin concentration.

Davies (1970), following up the close correlation between the increased rate of nitrogen excretion and the increase in resting metabolic rate both in fractures and burns, has, with his Swedish collaborators (Barr and others, 1968), further demonstrated the beneficial effect of a warm environment (32° C.) on protein metabolism. They have shown that the catabolism of plasma albumin and IgG was increased as the severity of the burns increased and with burns the catabolic rate of these two proteins was reduced by nursing the patients at 32° C.

Campbell and Cuthbertson (1967) and Cuthbertson and others (1968) observed a 15–30 per cent fall in voluntary food intake in the rat at an environmental temperature of 30° C., but we have not found a significant fall in intake in our human patients. However, in an earlier report (Tilstone and Cuthbertson, 1970) we did consider the possible combined effects of the slight increase in intake of energy together with possibly reduced heat loss at 30° C. on urine nitrogen at 30° C., and concluded this to be still insignificant. Similarly skin losses of nitrogen, which amount to about 0·55 g. per day for a sedentary man in a comfortable environment (Calloway, Odell, and Margen, 1971), would not be expected to differ at 30° C. to an extent which would compensate for the reduced excess nitrogen excretion.

Patients vary in the intensity and duration of their response to injury, particularly in terms of heat production (Kinney, Long, and Duke, 1970). Involved in this is the effective circulating blood-volume, the integrity of the particular reaction of the neuro-endocrine system, the nutritional state in respect of its energy reserves, and the effect of environmental temperature.

Following moderate to severe injury there is first the 'ebb phase' of diminished heat production corresponding with the 'shock' period. This depression, as Threfall (1970) has pointed out, is not due to lack of oxygen supply but possibly is effected through changes in the thermoregulatory mechanism. The changes characteristic of tissue hypoxia in experimental animals do not tend to occur until the point when death seems certain. When the metabolic tide 'turns' the increased heat production of the 'flow phase' is apparently brought about through changes in the sites of thermogenesis. The application of heat during this stage in experimental animals has an adverse effect on survival, possibly due to their low thermal capacity. Man has a much greater thermal capacity and heat may be advantageous at an earlier stage than we have applied it, once appropriate blood transfusions have been effected. Cases involving brain damage, however, are an exception.

During the 'flow phase' when heat production and oxygen consumption are increased the hyperglycaemia and glycosuria usually disappear. When the environmental temperature is brought up to thermoneutrality for man, i.e., 28–30° C., the need for increased oxidation of protein and for carbohydrate intermediates and the products of their oxidation is also reduced (Kinney and others, 1970). The increased body temperature associated with moderate to severe injury—traumatic fever—does not appear to be affected by the thermal environment.

The increases in urinary potassium, zinc, and creatine as well as nitrogen at normal ward temperature lend further emphasis to the view that following trauma the major change in metabolism in the 'flow phase' is increased catabolism rather than diminished anabolism.

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'CURATIVE' SURGERY IN CARCINOMA OF THE COLON INVOLVING DUODENUM

A REPORT OF 6 CASES

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SUMMARY

Six examples of duodenal involvement by colonic cancer are reported. Two had an associated duodenal fistula. Radical surgery was carried out in all 6 cases, 3 of whom remain alive and free from recurrence up to 6 years later.

INVASION of adjacent structures by a neoplasm is frequently synonymous with inoperability. The common situation where this general rule meets with its greatest exception is in cancer of the large bowel; here every experienced abdominal surgeon will have encountered examples where radical excision of the growth, together with adjacent adherent or invaded viscera, has been followed by relief of often intolerable symptoms and in a number of cases by long-term survival.

In this paper 6 examples of duodenal involvement by right-sided colonic carcinoma in which radical monobloc resection was possible are reported; in 2 cases there was an established duodenocolic fistula. Two tumours were also adherent to the right kidney, and another had invaded both the anterior abdominal wall and a loop of small intestine.

Brief reports of these 6 cases are as follows. The main features are summarized in *Table I*.

Table I.—DETAILS OF THE CASES IN THE PRESENT SERIES

CASE	AGE AND SEX		SITE	OTHER VISCERA INVOLVED AND RESECTED	RESULT
1. I. H.	45	M.	Transverse colon	1. Third part of duodenum 2. Anterior abdominal wall 3. Loop of jejunum	Alive and well 6 yr. later
2. H. A.	66	M.	Hepatic flexure	1. Second part of duodenum (fistula) 2. Perinephric fat 3. Posterior abdominal wall	Died 1 yr. 4 mth. postoperatively (carcinomatosis)
3. I. H.	70	M.	Ascending colon	1. Second part of duodenum	Alive and well 3 yr. 7 mth. later
4. C. M.	74	F.	Ascending colon	1. Second part of duodenum (fistula) 2. Posterior abdominal wall 3. Perinephric fat (necessitating right nephrectomy)	Died 10 mth. postoperatively (carcinomatosis)
5. J. McK.	45	M.	Ascending colon	1. Second part of duodenum	Alive and well 2 yr. later
6. J. D.	44	M.	Ascending colon	1. Second part of duodenum 2. Right kidney	Died 1 yr. 4 mth. postoperatively (carcinomatosis)

CASE REPORTS

Case 1.—Mr. I. H., aged 45 years, was admitted to another hospital in October, 1966, with a mass in the right iliac fossa. Laparotomy revealed a carcinoma of the transverse colon with a pericolic abscess. A caecostomy was performed. In November, 1966, a further laparotomy was carried out with drainage of an abdominal wall abscess. Biopsy showed an adenocarcinoma and the lesion was considered inoperable.

The patient was transferred to the Westminster Hospital for consideration of radiotherapy or cytotoxic therapy. On admission he was thin and anaemic (haemoglobin 12·7 g.). Faeces were discharging through the caecostomy and there was a palpable mass in the right iliac fossa. This mass was adherent to the laparotomy scar, opening on to which were several purulent sinuses. It was decided first to defunction the tumour region and then, if possible, to carry out a resection.

The first operation was performed on 23 Dec., 1966 (H. E.). A long, oblique, left iliac fossa incision revealed a tumour of the transverse colon which was adherent to the abdominal wall, to a loop of small intestine about 1·5 m. from the duodenojejunal junction, and to the third part of the duodenum. The terminal ileum was divided, the splenic flexure was mobilized and divided, and their distal and proximal ends respectively were closed. An ileosplenic flexure end-to-end anastomosis was then performed (*Fig.* 1). The large bowel was thus defunctioned, as a result of which the infection rapidly subsided and the patient's general condition improved.

The second operation was performed on 10 Jan., 1967 (H. E.). As a preliminary the caecostomy was mobilized and closed. Wide excision of the anterior abdominal wall was performed to include the original scar and the discharging sinuses leading down to the tumour mass. The whole of the defunctioned large bowel was resected *en bloc*, together with the anterior abdominal wall, a portion of the third part of the duodenum which was adherent to the tumour, the loop of involved jejunum, and the spleen. The duodenal defect was closed with two layers of catgut transversely and continuity of the small intestine was restored by end-to-end-anastomosis (*Fig.* 2).

Pathological examination revealed a moderately differentiated adenocarcinoma of the transverse colon infiltrating the pericolic fat and the anterior abdominal wall. It was involving the adherent duodenum and small intestine superficially but had not infiltrated into their muscle walls.

The patient made a satisfactory recovery and remains alive and well 6 years later (*Fig.* 3).

Case 2.—Mr. H. A., aged 66 years, was admitted in March, 1969, with a 12-month history of diarrhoea and colicky abdominal pain. There was a palpable mass in the right hypochondrium and a barium-enema examination revealed a carcinoma of the hepatic flexure with a fistula between the colon and duodenum (*Fig.* 4).

Operation was carried out on 11 March (H. E.). There was an extensive carcinoma of the hepatic flexure with a fistula into the second part of the duodenum. The adjacent posterior abdominal wall and perinephric fat were invaded. A right hemicolectomy was performed with excision of the involved duodenum, the resultant large defect being closed with two layers of catgut.

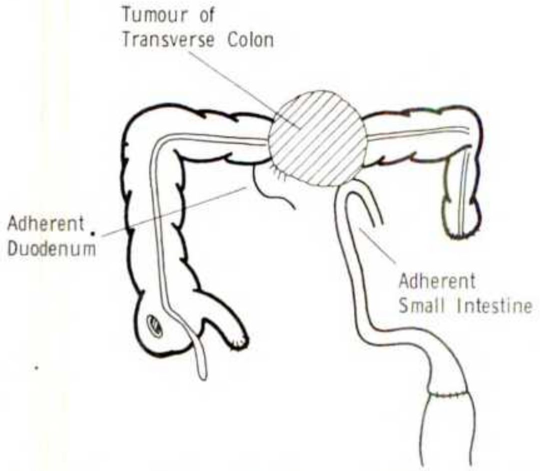

FIG. 1.—*Case* 1. Findings at laparotomy and the short circuit of the tumour of the transverse colon.

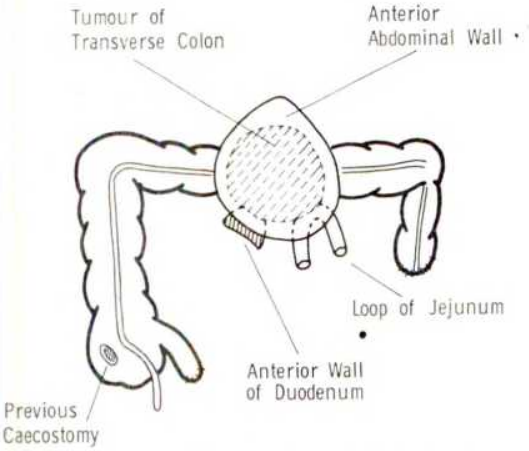

FIG. 2.—*Case* 1. Diagram of the resected specimen.

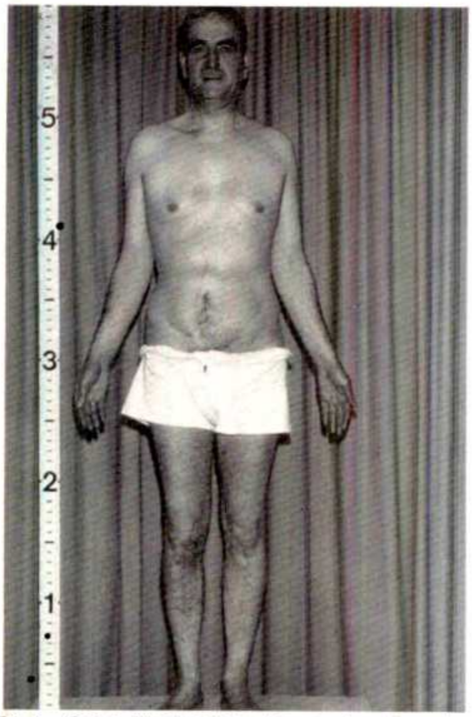

FIG. 3.—*Case* 1. Patient 5 years after resection of a carcinoma of the transverse colon invading the anterior abdominal wall, jejunum, and duodenum.

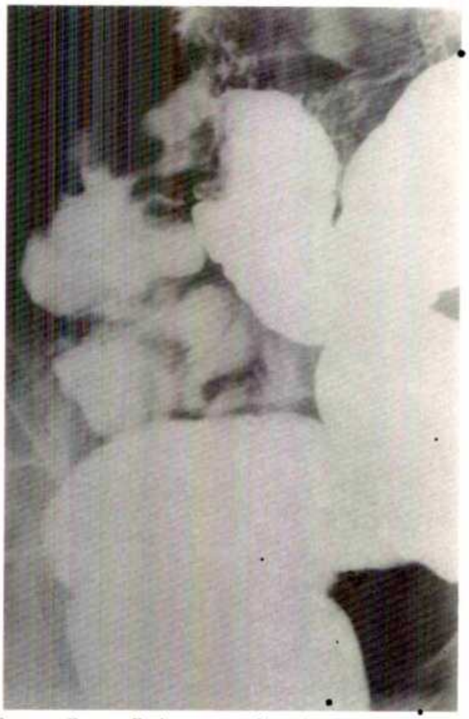

FIG. 4.—*Case* 2. Barium-enema film, showing a carcinomatous stricture of the ascending colon fistulating into the duodenum. Note the reflux of barium into the duodenum and upper jejunum.

Pathological examination of the specimen revealed a well-differentiated adenocarcinoma with fistulation into the adjacent duodenum. The lymph-nodes were not invaded.

The patient made an uneventful recovery but was admitted to Maidenhead Hospital in July, 1970, with carcinomatosis where he died 1 year and 4 months after the operation.

Case 3.—Sir I. H., aged 70 years, was admitted in March, 1969, complaining of diarrhoea, right-sided abdominal pain, loss of appetite, and anaemia over a 9-month period. Examination revealed a mass over the right upper quadrant of the abdomen. The haemoglobin was 7·1 g.

After a blood transfusion laparotomy was carried out on 18 April (C. W.). There was a large mobile carcinoma of the ascending colon which was invading the second part of the duodenum. Right hemicolectomy was performed with resection of a 3-cm. diameter circle of duodenum. The duodenal defect was closed transversely with inner catgut and outer interrupted thread.

Pathological examination revealed an adenocarcinoma invading the serosal surface of the duodenum. The lymph-nodes were not involved.

Recovery was uneventful and the patient is alive and well, at the time of this report, 3 years and 7 months later.

Case 4.—Mrs. C. M., aged 74 years, was admitted in November, 1969, with a 4-year history of anaemia and loss of weight. Examination revealed a mass in the right upper abdomen. The haemoglobin was 7·1 g.

Laparotomy was carried out on 2 Dec. (H. E.) after a preliminary blood transfusion. There was a carcinoma of the ascending colon which had infiltrated the posterior abdominal wall and the perinephric fat of the right kidney and also had fistulated into the second part of the duodenum. A monobloc excision taking the ascending colon, right kidney, and a segment 7·5 cm. long and 4 cm. wide on the anterior duodenal wall was performed. The duodenum was closed transversely with one layer of catgut. Recovery was uneventful.

Pathological examination revealed an annular carcinoma fistulating into the duodenum and invading extensively into the perinephric fat, although the kidney itself was not invaded. Adjacent lymph-nodes were not involved.

The patient developed recurrence of the tumour and died in Westminster Hospital on 12 Sept., 1970.

Case 5.—Mr. J. McK., aged 45 years, was admitted in September, 1970, with a 1-year history of upper abdominal pain and diarrhoea. The haemoglobin was 10·4 g. A barium-enema examination revealed a filling defect just proximal to the hepatic flexure.

An operation on 13 Oct. (M. N. M.) a large tumour of the ascending colon was resected together with the adjacent second part of the duodenum, which was closed transversely in two layers.

Pathological examination showed an annular carcinoma of the colon which was poorly differentiated. The wall of the duodenum was invaded, but the mucosa had not been breached. The lymph-nodes were not involved.

The patient is alive and well over 2 years following operation.

Case 6.—Mr. J. D., aged 44 years, was admitted in April, 1971, with a 6-month history of right-sided abdominal pain and weight-loss. There was a tender mass in the right side of the abdomen and a barium-enema examination showed a filling defect in the ascending colon. Operation on 15 April (M. N. M.) revealed a carcinoma of the ascending colon which had invaded the second part of the duodenum and the right kidney. Right hemicolectomy, right nephrectomy, and excision of the segment of the anterior wall of the duodenum, measuring 2·5 cm. by 7·5 cm., was performed in one procedure. The duodenum was closed transversely in two layers and as there was some narrowing of the lumen an anterior gastro-enterostomy was performed. There was postoperative delay in function of the gastro-enterostomy which was re-explored on 11 May. The stoma appeared widely open and no further procedure was necessary. Following this second laparotomy the patient made a satisfactory recovery. A subsequent barium-meal examination showed free flow of barium through the duodenum.

Pathological examination revealed a poorly differentiated adenocarcinoma of the ascending colon invading both the right kidney and the duodenum although it had not penetrated the muscularis of the duodenum. The lymph-nodes were free from tumour.

The patient died from recurrent disease 16 months after operation.

DISCUSSION

The surgeon setting out to explore a patient with a carcinoma of the colon hopes to find a localized tumour which is amenable to a standard resection procedure. When he encounters disseminated disease or adherence to adjacent structures, considerable judgement is required in order to decide on the correct treatment.

Deposits in the liver, provided that gross hepatic destruction has not taken place, should not deter him from resecting the primary growth and thus relieving or preventing intestinal obstruction, fistulation, etc. Our figures from Westminster Hospital show that one-third of patients submitted to such palliative resection will live for more than 1 year (Oxley and Ellis, 1969).

Adjacent structures which may be found adherent to the growth include the anterior or posterior abdominal wall, small intestine, the greater curvature of the stomach, spleen, duodenum, pancreas, kidney, ureter, bladder, uterus, and Fallopian tubes. This adherence may be entirely inflammatory (Cooke, 1956), but it is wise to assume that tumour invasion has occurred in planning resection. A trial resection is often necessary to assess whether or not *en bloc* removal is a reasonable proposition, and here the patient's general condition and the presence or absence of dissemination of tumour elsewhere should be taken into consideration. Distant peritoneal nodules, the presence of gross ascites, and heavy liver involvement contra-indicate radical surgery.

The results of radical surgery for advanced local disease are, under the circumstances, surprisingly good. Van Prohaska, Govostis, and Lasick (1953) reviewed 225 patients undergoing resection for carcinoma of the colon and rectum; 21 of these (9 per cent) required resection of adjacent structures, which included spleen, abdominal wall, bladder, etc. There was only 1 operative death and 14 of these patients (67 per cent) were alive 2–13 years later. Of particular interest in the present context were 2 patients who underwent right hemicolectomy together with pancreaticoduodenectomy; these survived operation but died 2½ years and 11 months after surgery respectively from metastatic disease. Jensen, Balslev, and Nielsen (1970) reported experience of 554 patients with carcinoma of the colon; 406 underwent resection and 60 of these cases required resection of the abdominal wall or other organs. Of these 60 patients, 23 were found to have only inflammatory adhesions and 13 of these were alive after 5 years. The remaining 37 cases had malignant invasion of adjacent structures and 5 of these were alive 5 years later. Again of particular relevence were 3 patients who had a resection of adjacent duodenum; 2 of these proved to have malignant adherence but both died in the postoperative period. El-Domeiri and Whiteley (1970) noted 10 examples of invasion of the anterior abdominal wall in a series of 327 patients with carcinoma of the caecum undergoing resection; there was 1 postoperative death and 7 of the 9 survivors were still alive at the time of the review, 5 already having survived for 5 years.

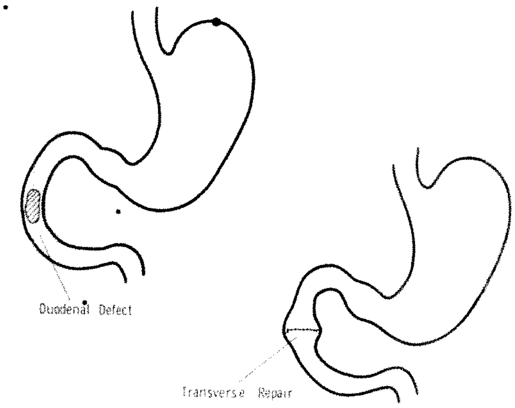

FIG. 5.—Technique of repair of a duodenal defect adopted in this series of patients.

Very few reports deal specifically with the problem presented by adherence or fistulation of cancers in the region of the hepatic flexure and the duodenum. Juvara and Radulescu (1969) encountered 4 such cases in the course of 124 right hemicolectomies. Two of these had a coloduodenal fistula and 2 had malignant involvement of the duodenal wall without fistula formation. In our own experience in the Surgical Unit at the Westminster Hospital 6 cases of duodenal involvement, 2 with a fistula, have been encountered in the course of the past 5 years.

CLOSURE OF THE DUODENAL DEFECT

Having carried out adequate excision of the affected duodenum with a healthy cuff of adjacent bowel, there is the problem of adequate closure of the resultant duodenal defect. In our own cases this has been achieved without difficulty by simple one- or two-layer transverse closure (*Fig.* 5) and we have not encountered problems of either leakage or stenosis, although in 1 instance it was considered prudent to perform a gastrojejunostomy. Fortunately in none of these cases was the pancreatic duct involved since, under such circumstances, it would be necessary to consider a formal pancreaticoduodenectomy.

Juvara and Radulescu (1969) found in their cases that simple repair of the duodenal defect was not possible; they described an ingenious technique in which, following the right hemicolectomy, a loop of the intact terminal ileum just proximal to the ileocolic anastomosis was sutured as a patch over the duodenal defect, stitching the serous surface of the ileum around the edges of the duodenal defect by a series of interrupted seromuscular sutures (*Fig.* 6). This technique of closure of wounds of the duodenum by sewing the intact serosa of a jejunal loop over the defect was described in an experimental animal by Kobold and Thal (1963), and was used for closure of experimentally produced grossly infected perforated duodenal stumps by Jones, Gregory, Smith, Saito, and Joergenson (1964). The technique has been used clinically to patch difficult intestinal perforations (McKittrick, 1965; Ballinger, McLaughlin, and Baranski, 1966; Jones and Steedman, 1969). In our own laboratory we have confirmed the efficacy of this method in the closure of large duodenal defects in the dog. Subsequent histological studies showed that the duodenal mucous membrane grew from the cut edge of the defect over the serosal surface of the jejunal patch so that eventually the lumen of the duodenum became relined with mucous membrane. In 1 animal a fistula between the duodenum and the jejunum used for the patch developed. In view of this it is advisable to use as proximal a piece of bowel as possible. There is no doubt that in any case which we might encounter where duodenal closure is impossible by direct suture, whether such a defect resulted from surgical excision, trauma, or chronic perforation, we would not hesitate to employ this technique.

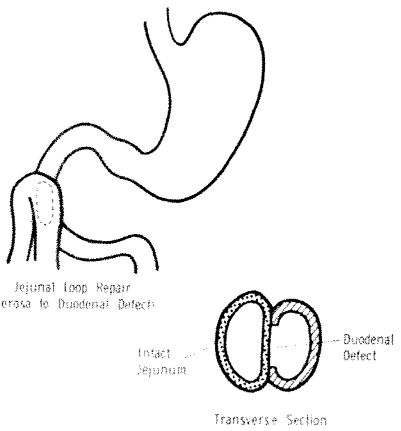

FIG. 6.—Use of intact jejunal loop advocated for the repair of difficult duodenal defects and used in our experimental studies.

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OESOPHAGEAL PERFORATION DURING ABDOMINAL TRUNCAL VAGOTOMY FOR DUODENAL ULCER

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SUMMARY

A retrospective survey of patients having truncal vagotomy for duodenal ulceration has been carried out. In this series 41 cases of oesophageal perforation occurred; 29 were recognized at the time of operation, 6 were diagnosed postoperatively, and in the remaining 6 the time of diagnosis was not specified. Two of the 29 patients in whom the oesophageal perforation was recognized at the time of operation died, as did 2 of the 6 cases diagnosed postoperatively. An increase of mortality and morbidity occurred in those diagnosed postoperatively. The importance of confirming oesophageal integrity at the conclusion of vagotomy is stressed.

DURING the past decade vagotomy and gastric drainage has gained acceptance as a treatment of chronic duodenal ulceration (Goligher, Pulvertaft, de Dombal, and others, 1968a, b; Small and Jahadi, 1970). The mortality of this prodecure is reported to vary between 0 and 3·3 per cent (Holt and Lythgoe, 1961; Mead, 1967). Oesophageal rupture is rarely mentioned as being responsible for mortality or morbidity following vagotomy, only approximately 30 cases appearing in the literature (McBurney, 1969; Postlethwait and Dillon, 1969; Wichern, 1970).

In the present series 35 cases are discussed in detail; the remaining 6 are known to have occurred but full clinical data are not available. The importance of operative diagnosis has already been alluded to (Postlethwait and Dillon, 1969) although the necessity for early diagnosis has not been stressed.

MATERIALS AND METHODS

One hundred and twenty-five surgeons in the Midland Region were requested to provide information regarding their experience of oesophageal injury during vagotomy for duodenal ulceration in the 5-year period 1965–9.

Initial inquiry involved a request for knowledge of the injury; subsequently all those who met with this complication were asked to complete a simple questionnaire (*Table I*).

Computer data are available for all admissions to selected hospitals in the Birmingham Region Hospital Board area. From this information the incidence of perforation and the contribution of this injury to the mortality of vagotomy can be deduced.

RESULTS

Of the 35 patients with full clinical details, all had a perforation of the oesophagus during the course of an elective abdominal truncal vagotomy for duodenal ulcer. Thirty-three of the 35 patients were male and 2 were female, with an average age of 54·7 years (range 36–74 years). The sex and age distribution is in accordance with that for surgical treatment of duodenal ulcer in this region. Twenty-two operations in which perforation of the oesophagus occurred were performed by a surgeon of registrar status and 13 by a surgeon of consultant status. In 7 cases after recognition of a breach of the oesophagus the assistance of a consultant was sought by the junior surgeon performing the operation.

Table I.—THE QUESTIONNAIRE USED IN THE PRESENT SERIES

Name ....

Age................ Sex................ Hospital No.........

Status of surgeon (registrar/consultant).........................

Date of operation.................................

	Incision used for vagotomy:—
	Presence of hiatus hernia on preoperative barium meal—YES/NO
	Presence of hiatus hernia at laparotomy—YES/NO
	Operation findings:—
	Method of dissection of vagus nerve:—
Ryle's tube	in oesophagus at time of vagotomy:—
Diagnosis of perforation of oesophagus	at operation:—
	postoperatively:—
	OUTCOME:—

Thirty-one of the 41 oesophageal perforations in this series occurred in 4026 patients for whom computer data are available, giving an incidence for this injury of 0·8 per cent. The other 10 perforations occurred in hospitals without computer facilities.

Of the 35 cases of oesophageal perforation, 14 occurred when the vagotomy was performed through a midline incision and 16 through a paramedian one. In 5 cases the incision used was other than these or unspecified.

The presence of a hiatus hernia was diagnosed radiologically preoperatively in 16 patients and was confirmed at operation in all of these. Several methods of dissection of the vagus nerves were used including blunt dissection by finger or gauze and in some instances by cholecystectomy forceps or scissors. No method was especially liable to result in oesophageal damage. Several surgeons used a nerve hook to identify the vagus nerves or branches thereof, but in on case was it considered that an oesophageal perforation was attributable to this instrument. A nasogastric tube was invariably in place in the oesophagus (26 cases). In 29 cases the oesophageal damage was diagnosed at the time of operation and in 6 postoperatively. Modes of postoperative presentation included pneumoperitoneum with collapse of the lower lobes with or without empyema, pleural effusion, or pneumothorax. The mortality-rate of those with perforation diagnosed at the time of operation was 2 out of 29 cases, death being due to intraperitoneal sepsis in both. Death in both the patients whose diagnosis was delayed was also due to intraperitoneal sepsis.

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All the patients in whom the leak was diagnosed postoperatively had either a laparotomy or thoracotomy for suture of the perforated oesophagus or drainage of the associated sepsis. All the patients in this group had a protracted postoperative course, in 2 extending to 9 weeks' stay in hospital, and in both of whom a third operation was necessary.

DISCUSSION

The age and sex distribution in this series is similar to that in other published work (Mead, 1967; Small and Jahadi, 1970) and therefore the damage was neither age- nor sex-related. It was not the experience of the surgeons whose cases are recorded here that dissection of the vagus nerves was arduous on account of the patient's body configuration or weight, but in 7 cases vagal dissection was complicated by peri-oesophagitis and in 16 instances was associated with a hiatus hernia. This incidence of hiatus hernia (46 per cent) is even greater than may be expected in a series of patients with or without upper gastro-intestinal tract symptoms (Pridie, 1966; Dyer and Pridie, 1968).

The frequency of oesophageal rupture as a complication of truncal vagotomy in this series is 0·8 per cent. This is much higher than would be expected from other published work, but must represent a more realistic incidence in view of the number of patients and hospitals concerned.

Diagnosis is made at the time of operation, when either the nasogastric tube is seen within the oesophageal lumen or the emergence of gastric contents from the site of perforation is noted. In 2 cases there were two perforations of the oesophagus where the oesophagus hung transfixed with a tape across its lumen. It is, therefore, important to examine carefully the remaining oesophagus within the operative field if one leak is detected. Early diagnosis has a profound effect on the prognosis of the patient, for if the leak is closed, either with absorbable or non-absorbable sutures in one or two layers, postoperative morbidity or mortality attributable to the damage is rarely seen. If the diagnosis is delayed the postoperative period may be complicated by chronic intraperitoneal and intrapleural sepsis. If these conditions are present in the post-vagotomy period the possibility of oesophageal perforation must be considered and investigated. Confirmation of the diagnosis radiologically makes early surgery mandatory to drain any collection there may be and to repair the perforation, for the greater the delay the worse the prognosis is. The mortality-rate in those patients in the present series with an operative diagnosis is 7·2 per cent (2 deaths in 29 patients), which compares favourably with the mortality of those patients in whom diagnosis of the perforation is delayed (2 deaths in 6 patients).

As oesophageal damage is likely to continue to occur in a few cases a method of early diagnosis must be considered, as the sequelae of delay may be very severe.

Diagnosis must be made at the time of laparotomy and, to this end, either the nasogastric tube should be withdrawn into the oesophagus and a dye injected or a double-lumen nasogastric tube should be used with one orifice opening into the oesophagus down which the dye may be injected. If these methods seem unreasonable then at least at the completion of the vagotomy the oesophagus should be very carefully inspected, not forgetting that perforation may occur in the posterior and posterolateral wall of the oesophagus, as it did in one-third of the cases in this series.

An appeal is made by the authors for reports from readers of their experience of this injury to the oesophagus during abdominal truncal vagotomy for duodenal ulcer. Could any such reports please be sent to Mr. D. M. Morrissey.

Acknowledgements.—We wish to thank all members and guests of the West Midlands Surgical Society who replied to the questionnaire and allowed us access to the notes of their patients.

We also wish to thank Miss Wall of the Regional Statistics Department, Birmingham Regional Hospital Board, for providing the computer information.

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CIRCUMFERENTIAL OESOPHAGEAL MYOTOMY

By JAMES S. DAVIDSON

BRADFORD ROYAL INFIRMARY

SUMMARY

Circumferential division of the oesophageal muscle combined with hiatal hernia repair has been carried out in 26 patients, 19 of whom had a peptic stricture. The object of the procedure is to achieve slight elongation and relaxation of the oesophagus so as to make reduction of the hernia easier in the presence of slight degrees of oesophageal shortening and to reduce the likelihood of recurrence. The rationale and technique are described and details of illustrative cases are given. The postoperative radiological appearances, which are somewhat unusual, are illustrated. The indications and contra-indications are discussed. It is claimed that while circumferential myotomy is useless in the presence of gross shortening of the oesophagus it is of value in borderline cases where reduction of the hernia can be effected only by exerting slight tension on the oesophagus.

IN the presence of a peptic stricture with acquired shortening of the oesophagus, reduction of the hernia may be difficult or impossible and recurrence is likely. In 1963 d'Abreu, discussing this problem, said: 'Unfortunately, and I think this is becoming more apparent, adequate hernia operation is often impossible once stricture formation has developed. At thoracotomy in some patients, the oesophagus can be returned to its normal site and with its true length; if, however, the shortening of the oesophagus is material, an ominous sight for the surgeon is the cone-like appearance of the diaphragm round the elevated cardio-oesophageal junction. I now believe that, if the oesophagus has to be dragged down below the diaphragm under tension, the results will be disappointing.' If by some means even a small amount of lengthening and relaxation of the oesophagus could be produced this would increase the number of cases of peptic stricture suitable for treatment by hernial repair, which, in properly selected patients, has advantages over other forms of treatment such as dilatation or resection.

The author's interest in this problem was stimulated by experience with local resection of small carcinomas of the oesophagus and direct oesophageal anastomosis (Davidson, 1967a). In order to do this operation successfully it is necessary to cut close to the growth. It was found best to begin by dividing the muscle coats transversely above and below the tumour. The muscle then retracts upwards and downwards leaving bare mucosa and making it easier to see the mucosal extent of the carcinoma. It was found also that in some instances when the oesophagus is completely divided, contraction of the longitudinal muscle distracts the cut ends to such an extent that it is difficult to reapproximate them. From such observations it was felt that circumferential division of the longitudinal muscle might be of help in cases of peptic stricture where there was a degree of shortening of the oesophagus sufficient to make reduction of the hernia a little difficult. Initially, therefore, the object of such a myotomy was to gain additional length of oesophagus and to relieve the tension in it. As time has passed it has been realized that the procedure may have other advantages and it has been used in some patients with hiatal hernia uncomplicated by stricture.

ANATOMY AND PHYSIOLOGY

There are a number of relevant anatomical and physiological points.

The oesophageal muscle is a well-developed structure. It is relatively a good deal thicker than that of the stomach or small or large intestine. The longitudinal muscle is particularly well developed and unlike the condition usually found in the digestive tube it is as stout as, or in places stouter than, the the circular layer.

The mucous membrane is only loosely attached to the muscle coat by the submucosa. Considerable sliding movement is possible between them. This loose attachment allows the muscle coat to retract when divided transversely and is an important factor in the release of axial tension and the slight elongation of the oesophagus produced by transverse myotomy.

The mucosa is relatively inextensile, having no transverse folds. It is the main obstacle to extending the length of the oesophagus. However, it is not altogether inelastic and when there is a sliding hernia with elevation of the squamocolumnar mucosal junction there may be some redundancy of the mucosa. Stiennon (1968), discussing tertiary contractions in the oesophagus, maintains that transverse mucosal folds may be present when factors maintaining oesophageal length in spite of longitudinal muscle contractions are negated. He refers to hiatal hernia where the inferior attachments of the oesophagus are stretched.

Circumferential myotomy has not been found to cause dysphagia. The passage of peristaltic waves along the oesophagus depends on the continuity of the preganglionic vagal nerve-supply but not on the integrity of the muscle coat. If the oesophageal wall is divided and the superficial nerve plexus left intact the peristaltic wave can still pass normally over the oesophagus (Wright, 1965).

During deglutition and eructation there is an upward movement of the oesophagogastric junction. This is due both to traction by laryngeal elevation and to shortening of the oesophagus as a result of contraction of its longitudinal muscle (Inglefinger, 1958; Code, Kelley, Schlegel, and Olsen, 1962). Johnson (1966) placed markers on the mucosa and muscle of the oesophagus and on the margin of the hiatus in dogs. He showed that immediately after deglutition the markers on the mucosa and the muscle began to rise. This movement was still more marked on eructation. He mentions contraction of the longitudinal muscle and of the muscularis mucosae as causing this upward movement. Dey, Gilbert, Roskelley, and Trump (1945, 1946) claimed that in the dog electrical stimulation of the vagi produced shortening of the oesophagus sufficient, in some instances, to produce a hiatal hernia. The cardia resumes its normal position after swallowing by the elastic recoil of its inferior fascial attachments (Allison, 1970). When there is a sliding hernia this elastic recoil no longer takes place. As the upper part of the oesophagus retains its normal fixation in the crico-pharyngeal region, to the posterior wall of the trachea, and to the left main bronchus while the fixation of its lower end is deficient, the longitudinal muscle acts on the region of the cardia in a relatively unopposed manner tending to elevate it further. Whether contraction of the longitudinal muscle can ever be a primary cause of hiatal hernia or whether weakening of the inferior attachments of the oesophagus must occur first is not known, but it is of interest that there is a relatively high incidence of hiatal hernia in association with diffuse muscle spasm of the oesophagus (Creamer, 1962).

RATIONALE OF CIRCUMFERENTIAL OESOPHAGEAL MYOTOMY

This procedure was first used in the treatment of peptic stricture and it is in this connexion that its rationale is mainly considered. As will be discussed later, it may also have a place in the treatment of some cases of hiatal hernia uncomplicated by stricture.

In the presence of a stricture with shortening of the oesophagus there are at least three forces tending to result in inadequate reduction and recurrence of the hernia. Circumferential myotomy is an attempt to counteract them.

1. When reduction of the hernia is achieved by pulling the oesophagogastric junction down under tension there is an immediate upward pull tending to make repair ineffective and to cause recurrence. Transverse myotomy, by giving a little added length to the oesophagus, reduces this immediate upward traction. It is difficult to measure accurately the amount of lengthening of the oesophagus produced. It certainly varies from case to case. One way of taking this measurement is to determine the distance from the inferior margin of the aortic arch to the oesophagogastric junction with the latter held down under slight tension before and after myotomy. We make the measurement using a length of silk thread. The amount of elongation which can be obtained is small, being in the region of 2–3 cm. However, even this small amount may mean the difference between success and failure in achieving satisfactory repair and competence of the cardia. On occasion where myotomy has not been done and repair of the hernia resulted in a palpably taut oesophagus, myotomy done at this stage has produced obvious relaxation of the oesophagus.

2. As has already been described, the longitudinal muscle exerts an upward pull on the cardia. It is reasonable to assume that when it is divided transversely its action on the cardia will be reduced and that it will dissipate its efforts in causing distraction at the site of myotomy (*Fig.* 1).

3. If there are chronic inflammatory changes in the oesophageal muscle, fibrous contraction may continue postoperatively, causing recurrence of the hernia in much the same way as it produces herniation by traction following corrosive stricture of the oesophagus (Imre and Wooler, 1969). If the muscle layers are divided transversely any further shortening they may undergo should, in theory, result in further separation of their cut ends rather than a direct elevation of the oesophagogastric junction.

If the myotomy is to achieve the objectives for which it was designed, the oesophagogastric junction must be firmly fixed at the time of hernial repair. In the presence of shortening of the oesophagus it is doubtful if any method relying on the diaphragm for fixation is adequate. Possibly the best method of repair in such circumstances is that described by Hill (1967), where the upper part of the lesser curvature is firmly anchored to the median arcuate ligament.

This myotomy has been used to relax and extend the oesophagus in a few patients with sliding hiatal hernia uncomplicated by stricture. Sometimes, when there is a hernia of long standing and with a large amount of slide, it has been found difficult to restore the oesophagogastric junction to its normal position even though there were no obvious chronic inflammatory changes in the deeper layers of the oesophageal wall. In such patients the findings suggest that the oesophageal muscle has become adapted over a long period to its shortened state and will not immediately resume its normal length. It is tentatively suggested that this type of shortening is a true entity differing from the classic acquired shortening due to chronic inflammatory changes in the oesophageal wall.

TECHNIQUE

During the induction of anaesthesia the anaesthetist passes a large stomach tube into the oesophagus. This is more easily and more safety done at this stage than later on during the operation. A left thoracotomy or thoraco-abdominal incision is made. The oesophagus is mobilized up to the aortic arch. The stomach tube is advanced down the oesophagus until held up by the stricture. This is a good way of determining the exact level of the stricture. Account is then taken of the pathological changes in the oesophageal wall and a decision is made as to whether or not it is reasonable to attempt reduction of the hernia. In many instances it will be obvious that reduction is impossible. Where reduction seems feasible attention is turned to the vagi. If they are embedded in an inflamed, swollen, oesophageal wall and are acting as taut cords they are divided. Otherwise, they are isolated and held away from the oesophagus on threads. Myotomy is then done 2–3 cm. above the stricture using blunt-pointed scissors. This site is chosen as there is no risk of encountering the base of an unsuspected ulcer at this level and also because more movement is possible between the mucosa and the muscle coat at some distance from the inflamed stricture. The operative procedure is illustrated in *Fig.* 2.

At the original operations which were done in 1967 efforts were made to confine the myotomy to the longitudinal muscle as it was feared that diverticulum or rupture of the oesophagus might occur if both muscle layers were divided. It was found that by the time it was possible to be certain that the longitudinal muscle layer had been completely divided the mucosa was often visible. During the past 3 years both muscle coats have been divided as not only does this not appear to give rise to complications but also it allows better retraction of the cut ends. As the muscle retracts a tube of bare mucosa about 1·5–2 cm. in length is left exposed.

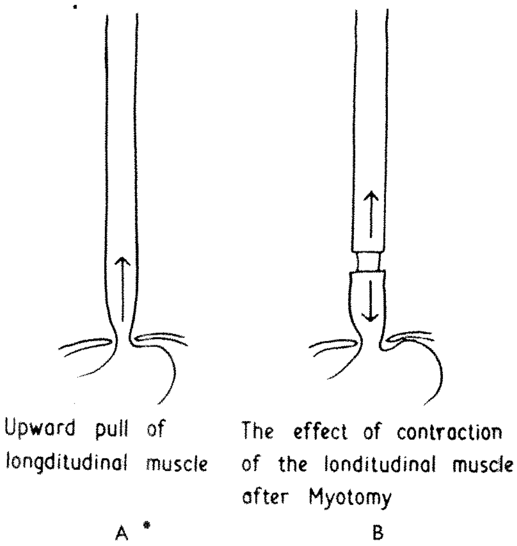

Upward pull of longditudinal muscle
The effect of contraction of the londitudinal muscle after Myotomy
A
B

FIG. 1.—A, The normal action of the longitudinal muscle on the oesophagogastric junction. B, The manner in which it is suggested that the longitudinal muscle acts after it has been divided transversely.

After myotomy the hernia is repaired by Hill's (1967) method.

On two occasions a double myotomy was done with division of the muscle layers just above the stricture and again just below the aortic arch. This is not our normal practice. It is of interest that although in both patients the oesophagus was mobilized up to the aortic arch the blood-supply to the portion of oesophagus between the myotomies remained adequate.

ANALYSIS OF CASE RECORDS

Circumferential myotomy has been combined with hernial repair in 26 patients during a period of 4 years. The sex incidence of the patients was equal. Their average age was 58 years.

In 7 of the earlier patients Allison's method of repair was used (Allison, 1951). In all but 1 of the patients operated on in the past 2½ years the method of repair described by Hill (1967) has been employed.

Vagotomy and a gastric drainage operation were added in 10 patients. The commonest reason for vagotomy was to allow easier reduction of the hernia (5 patients). In 2 patients it was done because of a pathologic condition of the pylorus and in 3 patients both of these indications for vagotomy were present.

Nineteen patients had a peptic stricture. There must be differences of opinion on occasion as to whether or not the lesion is a true stricture. The diagnosis was made on the radiological appearances, the oesophagoscopic findings with obstruction to the passage of bougies, and, at operation, the arrest of a stomach tube passed down the oesophagus.

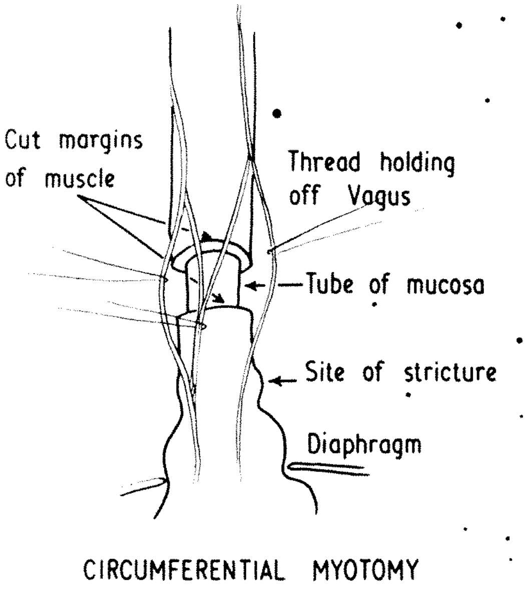


FIG. 2.—A diagrammatic representation of the operative procedure.

In 14 patients the stricture was described at oesophagoscopy as being soft and inflamed. More often than not there was acute oesophagitis above it. Oesophageal biopsies showed chronic inflammatory infiltration or evidence of mucosal ulceration. In 2 patients the stricture felt hard and became increasingly difficult to dilate. One such stricture had developed after an operation for diverticulitis. In 3 patients the stricture was associated with a penetrating ulcer and biopsies showed either granulation tissue or part of an ulcer base.

The common findings at thoracotomy were those of a thickened area in the oesophageal wall either extending from the oesophagogastric junction for a varying distance upwards or with its lower limit just above the junction. In most of the patients with a stricture there was peri-oesophagitis with enlarged mediastinal glands. In 8 patients the degree of peri-oesophagitis was such as to make mobilization of the oesophagus tedious.

The average distance of the stricture from the upper incisor teeth as measured at oesophagoscopy was 34 cm. At thoracotomy the stomach tube was commonly held up a short distance above the apparent oesophagogastric junction.

It was usually impossible to decide preoperatively from the radiological and oesophagoscopic findings if the hernia was reducible. The decision had to be made at operation.

In 5 patients there was no stricture but the hernia was difficult to reduce, and in 1 female patient myotomy was added to hernial repair as she had severe aerophagy. On radiographic screening frequent upward jerking movements of the cardia were seen with each eructation. The aerophagy was so bad that, according to her husband, she kept swallowing flies if he took her for a walk on a summer's evening.

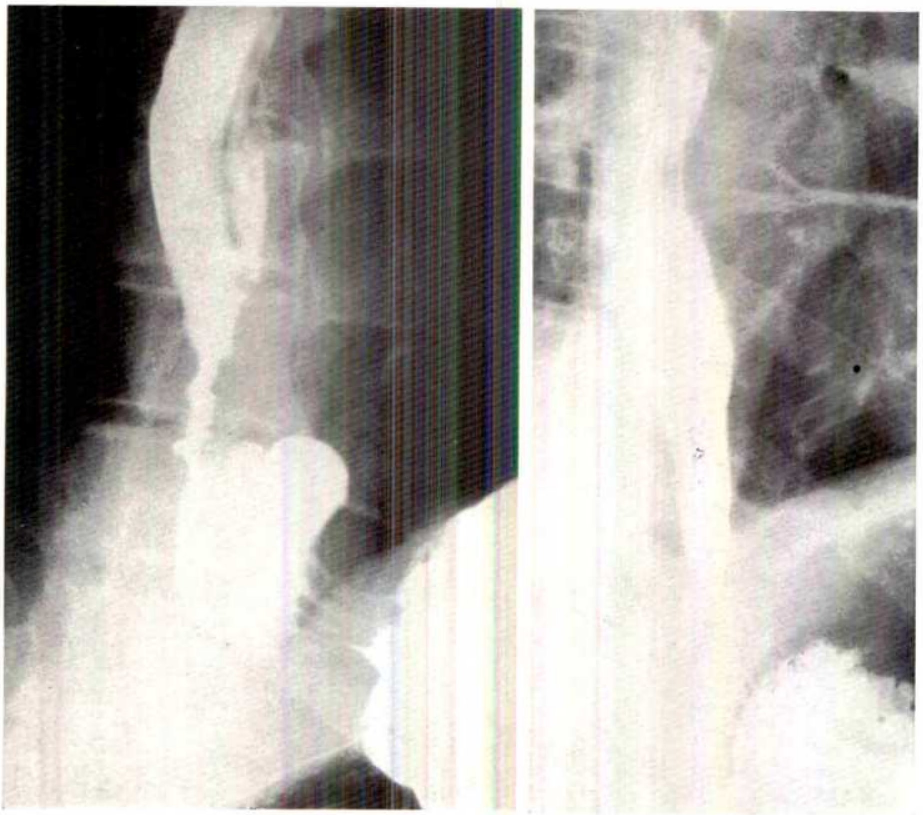

A B

FIG. 3.—*Case* 1. A, Preoperative barium-swallow film, showing a hiatal hernia and stricture. B, Postoperative barium-swallow film.

The following representative case records are illustrative of various types of lesion dealt with, namely, strictures at or near the cardia, postoperative stricture, stenosis with a penetrating ulcer, and sliding hernia uncomplicated by stricture.

1. Strictures at or near the Cardia.—

Case 1.—J. H., a man aged 55 years. This patient who was first seen in 1967 gave a 3-year history of intermittent dysphagia and episodes of food impaction. The dysphagia had become worse in the previous 6 months. The barium-swallow film is shown in *Fig.* 3 A. At oesophagoscopy there was a soft, irregular stricture at 36 cm. A biopsy from it showed granulation tissue. Towards the end of 1969 the patient began to have pain in addition to dysphagia and an operation was performed on 4 March, 1970. There was a thickened, rather firm segment of oesophagus about 3 cm. in length with its lower limit 2 cm. above the cardia. Peri-oesophagitis was present. The oesophagus was mobilized up to the aortic arch. The vagi, which were embedded in the thickened oesophageal wall, were divided and pyloromyotomy was done. The muscle coats were divided above the stricture. The hernia was repaired by Hill's method. *Fig.* 3 B shows the postoperative barium-swallow film. The cardia appeared to be competent. At postoperative oesophagoscopy there was no stricture to be seen. During the follow-up of 17 months the patient has remained free from symptoms.

Case 2.—M. C., a woman aged 57 years. This patient had a 14-month history of dysphagia. The barium-swallow film is shown in *Fig.* 4 A. At oesophagoscopy there was a soft, inflamed, bleeding stricture at 34 cm. A biopsy showed patchy ulceration of the mucosa with mixed inflammatory infiltrate at the squamocolumnar junction. At operation on 28 April, 1970, there was a sliding hiatal hernia and about 2·5 cm. above the cardia there was a thickened segment of oesophagus 2·5 cm. in length. A moderate amount of peri-oesophagitis with enlarged mediastinal glands was noticed. The hernia was difficult to reduce. Myotomy of both muscle layers was done above the stricture. The vagi were preserved and pyloromyotomy was carried out. The hernia was repaired by Hill's method. *Fig.* 4 B shows the postoperative barium-swallow film. Reflux could not be produced. At oesophagoscopy there was no evidence of stricture or of oesophagitis. During a follow-up of 16 months the patient has remained free from symptoms.

2. Postoperative Peptic Stricture.—

Case 3.—A. C., a man of 60 years. This patient had been known to have a hiatal hernia for 10 years. He developed dysphagia 2 weeks after an operation for diverticulitis. *Fig.* 5 A shows the barium-swallow film. In 1967

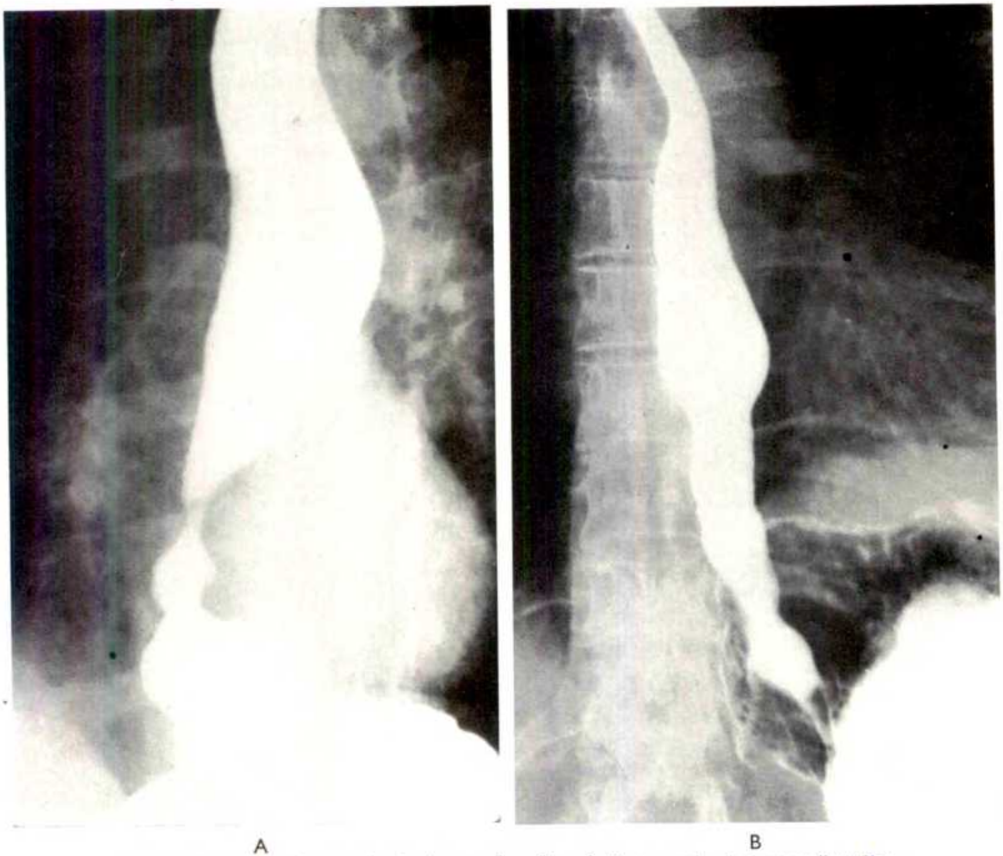


FIG. 4.—*Case* 2. A, Preoperative barium-swallow film. B, Postoperative barium-swallow film.

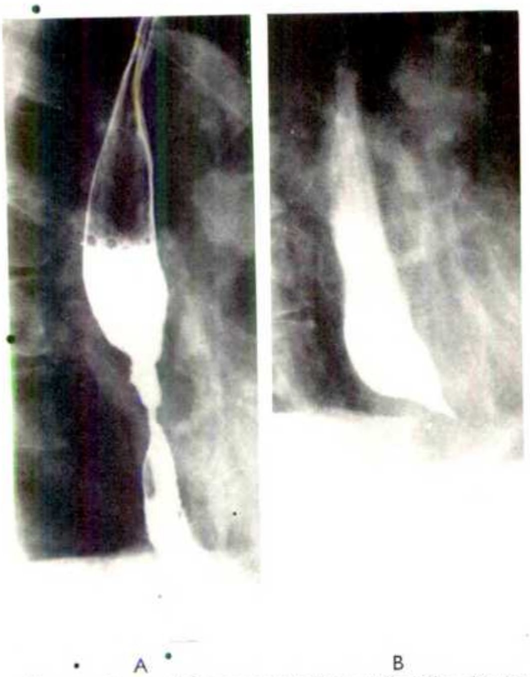


FIG. 5.—*Case* 3. A, Preoperative barium-swallow film, showing a stricture which developed after an operation for diverticulitis. B, Postoperative barium-swallow film.

an inflamed stricture at 38 cm. was noted. Oesophagoscopy was carried out twice during the next 3 months and the stricture became harder and more difficult to dilate. At operation in February, 1968, a sliding hernia was found. The oesophagus was thickened and hard at and above the cardia. It was mobilized with a good deal of difficulty. Myotomy was done just above the stricture and again just below the aortic arch together with vagotomy and pyloromyotomy. *Fig.* 5 B shows the postoperative barium-swallow film. At oesophagoscopy there is now a smooth narrowing at the lower end of the oesophagus. During the past 3½ years the patient has put on weight and has kept well apart from occasional slight dysphagia.

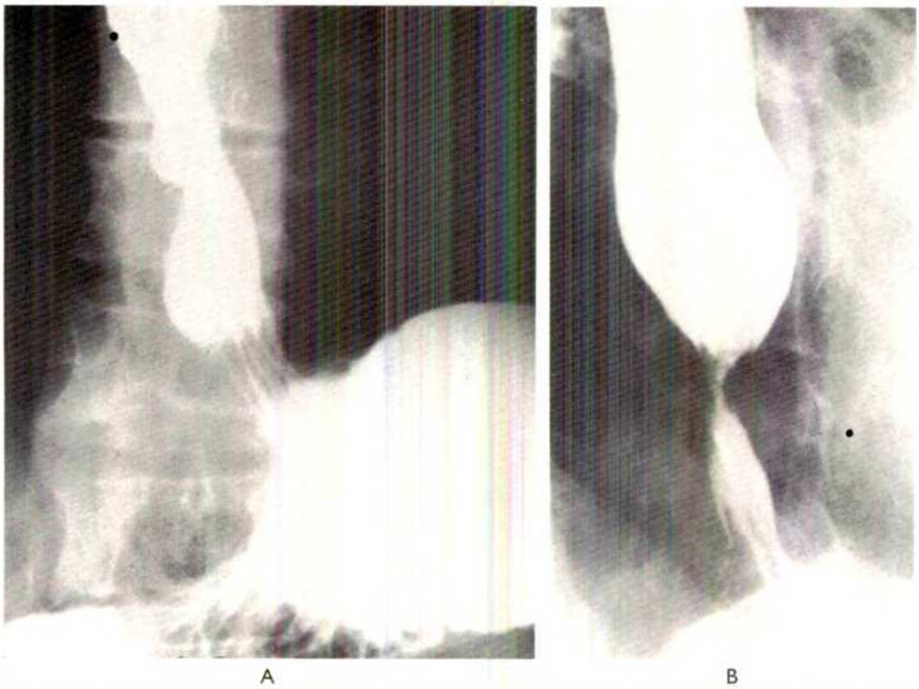
3. Penetrating Ulcer.—

Case 4.—F. P., a man of 57 years with a history of varying degrees of dysphagia for 7 years. *Fig.* 6 A shows the barium-swallow film denoting a penetrating ulcer at the stricture. There was also cicatricial contracture of the duodenum. At oesophagoscopy in 1967 an inflamed, ulcerated stricture at 35 cm. was found. Endoscopy was repeated in 1968 and 1969 with the same findings. Operation was carried out in March, 1969. The oesophagus was difficult to mobilize. It felt thickened up to the aortic arch with a hard area a short distance above the cardia. There was a small sliding hernia. The vagi, which were embedded in the oesophageal wall, were divided and a gastrojejunostomy was performed. The oesophageal muscle was divided transversely just above the hard area and again just below the aortic arch. The hernia was repaired by Hill's method.

Temporary improvement followed but severe dysphagia recurred owing to a tight, hard, fibrous stricture which is shown in *Fig.* 6 B. At a second operation 5 months later no hernia could be seen. A stomach tube was held up 3 cm. above the hiatus. The lower part of the oesophagus was resected with interposition of a jejunal segment between the oesophagus and the stomach. Histological examination showed a healed ulcer deep to which there was dense fibrosis extending through all coats of the oesophagus. Healing was by squamous epithelium.

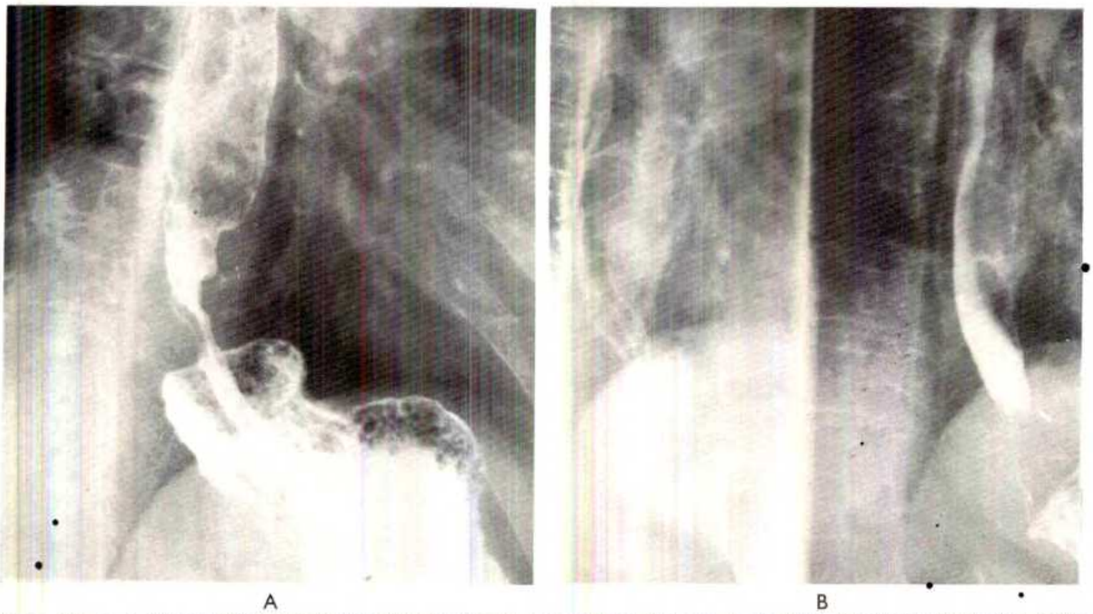
The patient has remained well for 2 years.

Case 5.—N. W., a woman aged 67 years, had been known to have a hiatal hernia for 6 years. When seen in 1970 her symptoms had become worse and she had a great deal of pain and dysphagia. The barium-swallow film is shown in *Fig.* 7 A. Oesophagoscopy showed a stricture with a hard ulcer on the posterior wall lying at 36 cm. A biopsy from the region of the ulcer contained columnar epithelium. At operation on 28 July, 1970, a sliding hernia was found and the oesophagus felt hard,



A B

FIG. 6.—*Case* 4. A, Preoperative barium-swallow film, showing a penetrating ulcer at the site of the stricture. B, Postoperative barium-swallow film, showing the presence of a tight fibrous stricture following healing of the penetrating ulcer.



A B

FIG. 7.—*Case* 5. A, Preoperative barium-swallow film, showing a peptic stricture with a penetrating ulcer. B, Postoperative barium-swallow films, showing healing of the ulcer and disappearance of the stricture. Some reflux persists.

above the cardia. There was a palpable ulcer with a dimple on the external surface of the oesophagus at the ulcer base. Enlarged glands were noted in the adjacent mediastinum. Thickening of the oesophagus extended upwards to just above the level of the inferior pulmonary vein. The hernia was difficult to reduce. Myotomy was done above the stricture together with vagotomy, pyloromyotomy, and hernial repair by Hill's method.

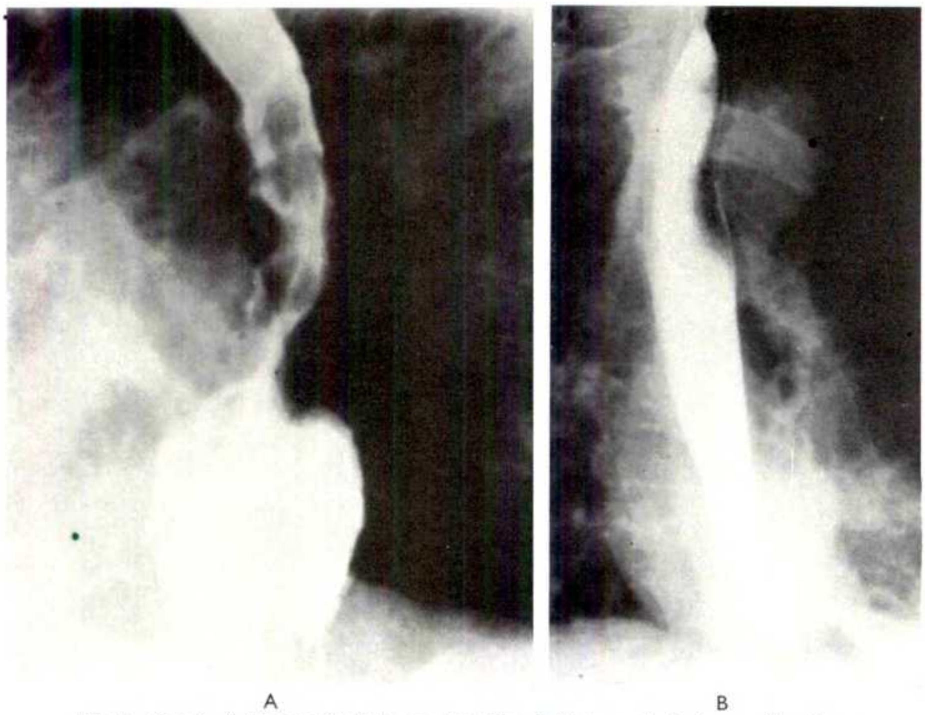


FIG. 8.—*Case* 6. A, Preoperative barium-swallow film. B, Postoperative barium-swallow film.

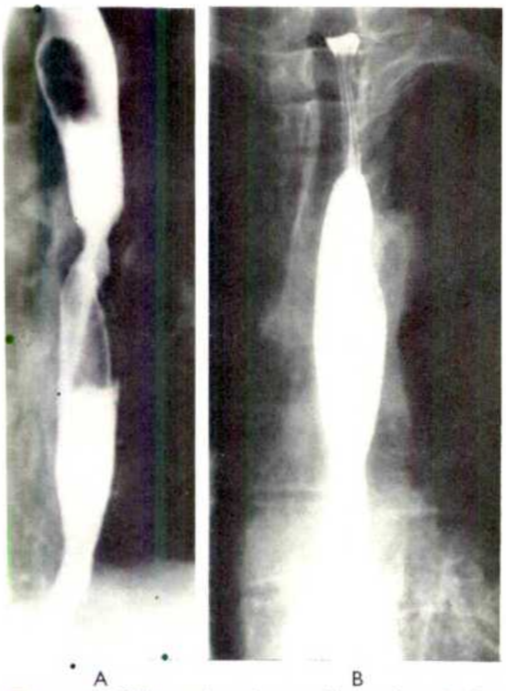


FIG. 9.—A, High peptic stricture with an ulcer. B, Postoperative barium-swallow film, showing a slight residual stenosis.

Fig. 7 B shows postoperative barium-swallow films. It is still possible to produce some reflux of barium. At oesophagoscopy the ulcer is no longer visible and there is no sign of stricture.

During follow-up of 1 year the patient has remained free from symptoms.

4. Sliding Hernia uncomplicated by Stricture but difficult to reduce.—

Case 6.—W. S., a man of 62 years with a long history of heartburn and regurgitation, repeated laryngitis, pneumonitis, pleurisy, and chronic bronchitis. The barium-swallow film is shown in *Fig.* 8 A. The distance to the cardia measured 38 cm. at oesophagoscopy. It appeared to be incompetent and there were superficial mucosal erosions above it. At operation the lower part of the oesophagus felt soft and there was no peri-oesophagitis but the hernia was difficult to reduce. The vagi were preserved. Myotomy was done and the hernia was repaired by Allison's method. *Fig.* 8 B shows the postoperative barium-swallow film. During a brief follow-up of 8 months the patient has been free from his previous symptoms but has suffered from post-thoracotomy wound pain.

RESULTS

As the first myotomy in the present series was done in 1967 the follow-up is limited. In some of the earlier patients postoperative oesophagoscopy was not done.

In 14 patients with soft, inflamed strictures the symptomatic results were good. In 2 of them some reflux could still be produced by the radiologist.

Where postoperative oesophagoscopy was done (7 patients) a smooth, soft, residual narrowing insufficient to cause dysphagia was seen in 1 patient. In the others no stenosis was visible.

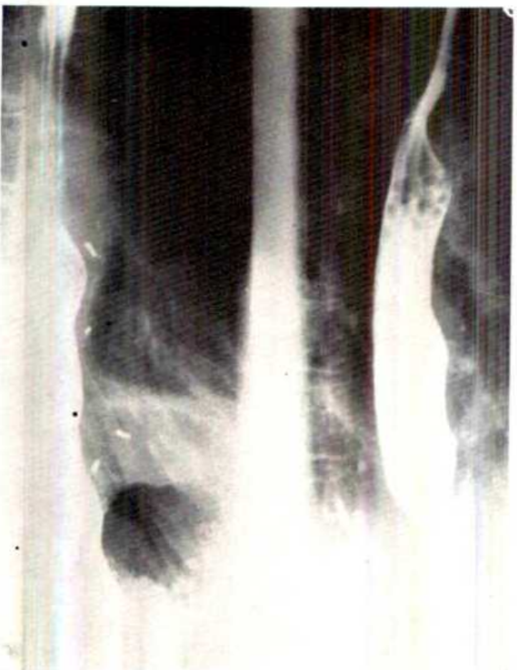


FIG. 10.—The left-hand barium-swallow film shows four markers. The upper two are on the cut ends of muscle, the lowest one is on the oesophagogastric junction, and the one immediately above it is on the hiatal margin. This film shows the characteristic 'wiped-joint' appearance caused by mucosal bulging at the myotomy. The bulging, which is present in certain phases of swallowing only, is less marked on the right-hand film.

In 1 patient with a postoperative stricture the symptomatic result was good but a moderate smooth stenosis is still to be seen at endoscopy.

Of 3 patients with a penetrating ulcer, 2 were complete failures. In both of the failures the ulcer healed with squamous epithelium, leaving a tight fibrous stricture. The other patient has a good symptomatic result but reflux is still seen on screening. In spite of this the ulcer and stricture are no longer visible.

In 1 patient with a high ulcerated stricture (*Fig.* 9 A) where myotomy was done below the lesion the ulcer healed leaving a very slight soft stenosis which was visible both radiologically (*Fig.* 9 B) and at oesophagoscopy but which was insufficient to cause dysphagia.

The patients with uncomplicated hernia which were difficult to reduce all had good symptomatic and radiological results.

The patient with severe aerophagy lost her previous heartburn and now swallows air only very occasionally.

Postoperative Radiological Appearances.—After circumferential myotomy the radiological appearances are both novel and interesting. In order to make it easier to identify the landmarks Cushing clips were placed on the cut ends of muscle, on the margin of the hiatus, and on the oesophagogastric junction.

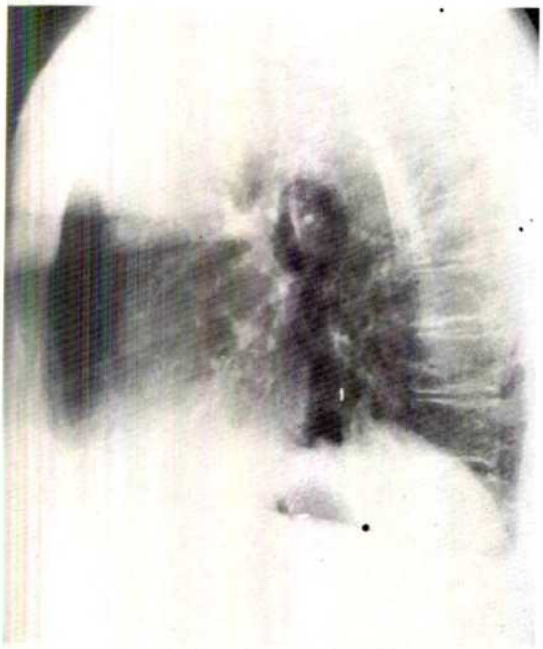


FIG. 11.—This film shows three markers. The upper two are on the cut ends of muscle and the lowest one is on the hiatal margin. The myotomy markers are 3 cm. apart in this patient.

The characteristic appearance is that of a smooth bulging which the markers show to be at the site of myotomy (*Fig.* 10). It has the appearance of a plumber's 'wiped joint', it is present in certain phases of swallowing only, and it has not been observed to increase in size with the passage of time.

The cut ends of muscle separate for a distance of 2–3 cm. (*Fig.* 11). In 1 patient the myotomy markers remained closer together (*Fig.* 12). This is unusual. If there is any subsequent change in the relative positions of the myotomy markers it is in the direction of further slight separation.

No hold up of barium can be detected as a result of the myotomy, which is in accord with the fact that where the stricture has been cured the patient has no dysphagia.

It has been possible to perform cineradiography in only 2 patients. It was observed that during swallowing there was an upward movement of the upper myotomy marker increasing its distance from the lower myotomy marker while the latter maintained a constant relation to the marker on the hiatal margin. The relative position of the markers in two phases of swallow is shown in *Fig.* 13. These findings suggest that contraction of the longitudinal muscle is causing distraction at the myotomy rather than an upward pull on the cardia.

The postoperative films in the successful cases show disappearance of the stricture with satisfactory reduction of the hernia and with a good angle between the fundus and the oesophagus.

Indications.—The successful treatment of peptic stricture by hernial repair depends on the possibility of adequate reduction of the hernia with a low recurrence rate and also on the pathological changes in the oesophagus being reversible. A decision on both of these aspects must be a matter of experience and judgement.

Circumferential myotomy makes reduction of the hernia possible in some patients where there would otherwise be undue tension on the oesophagus. It must be emphasized that it is effective only in borderline cases and that its indications are strictly limited.

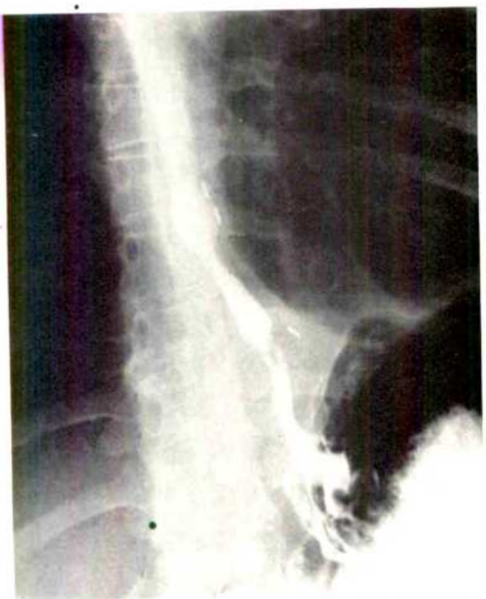


FIG. 12.—A film showing a less common situation where the myotomy markers have remained relatively close together. The position of the lower two markers shows that the oesophagogastric junction is lying well below hiatal level.

It is not indicated in the following circumstances:

1. Where there is a long area of total mucosal loss with gross changes in the oesophageal wall and peri-oesophageal tissues, the hernia is obviously irreducible and the limited effect of myotomy will not alter the situation.

2. Penetrating ulcer. Although 1 patient with a penetrating ulcer did well, 2 were total failures. A penetrating ulcer is considered to be a contra-indication to myotomy and hernial repair.

3. Postoperative peptic stricture. Although the 1 patient with a postoperative stricture did well it is probable that this type of lesion is often irreversible. Postoperative strictures are usually associated with changes involving all the coats of the oesophageal wall (Davidson, 1967b).

DISCUSSION

After Heller's longitudinal myotomy, diverticulum formation or oesophageal rupture is not a hazard. So far it would seem that a transverse myotomy is also a safe procedure. Unlike Heller's operation or the more extended longitudinal myotomy used in the treatment of diffuse muscle spasm of the oesophagus, after circumferential myotomy there is an obvious bulging of the mucosa, as seen in certain phases of swallowing on the barium-swallow film. This weakened area has not given rise to complications. On two occasions where a second thoracotomy was done there was nothing to suggest the presence of a weak area likely to give rise to a diverticulum or to rupture.

Manometric and motility studies have not been done. They may prove interesting both in connexion with the effect of the myotomy on the distal part of the oesophagus and the mechanism of the passage of food along the oesophagus after interruption of the muscle coat.

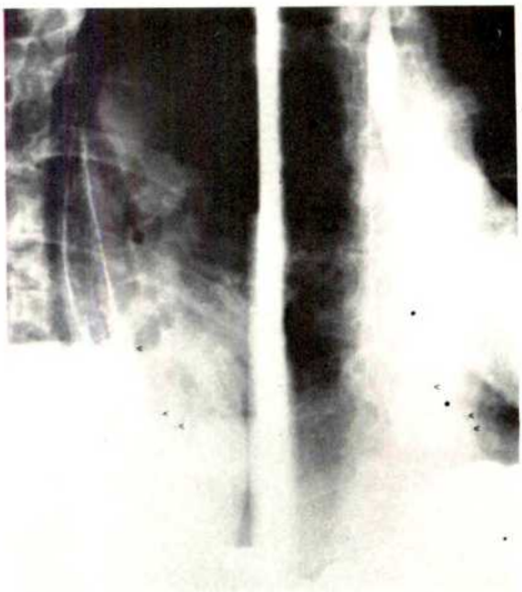


FIG. 13.—Two films in different phases of swallowing. During swallowing the upper myotomy marker has moved upwards on the left-hand film while the lower myotomy marker remains in the same relative position to the hiatal margin in both films. This suggests that contraction of the longitudinal muscle is causing distraction of the cut ends of muscle rather than exerting a direct upward pull on the cardia.

Does myotomy serve any useful function? It may be that all our patients with or without a peptic stricture who were successfully treated by myotomy and hernial repair could have been dealt with just as well by hernial repair alone. This is difficult to prove or disprove. The problem is further complicated by the fact that in a number of cases vagotomy and a drainage procedure were also done and the improvement could be attributed to such measures. All that can be said at this stage is that the results with the addition of myotomy seem better than those previously obtained by us in similar cases. The fact that myotomy results in a little measurable elongation of the oesophagus, that a taut oesophagus becomes less so after myotomy, and that muscle contraction appears to cause distraction at the site of myotomy rather than an upward pull on the cardia suggests that it is a rational procedure in properly selected cases.

The number of cases of peptic stricture seen by any one surgeon is not large and the number suitable for circumferential myotomy is much smaller still. It is difficult for any individual surgeon to gain adequate experience of the procedure. Although 26 patients have had this operation over a period of 4 years this number includes at least 5 where hernial repair would not now be attempted. It has been necessary to exceed the indications for the operation in order to learn both its virtues and its limitations.

So far transverse myotomy has been used mainly in the treatment of stricture. The importance of contraction of the longitudinal muscle of the oesophagus in relation to hiatal hernia has not yet been assessed. Whether or not there is a place for myotomy, especially of the longitudinal muscle, in the surgery of hiatal hernia uncomplicated by stricture is not known. It is suggested that this is a field for further study.

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GLOMUS JUGULARE TUMOURS—RADIOTHERAPY OR SURGERY?

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SUMMARY

Seven patients with glomus tumours are described. Many authors still advocate surgery for these tumours, despite the excellent results obtained with radiotherapy. The results obtained by irradiation in the present series strongly support the view that it is the treatment of choice in large petrosal tumours and those with intracranial extension.

THE glomus jugulare was first described by Guild (1941) as a tiny structure situated in the adventitia of the dome of the jugular bulb. It is a small ovoid body, measuring approximately 0·5 × 0·25 mm., and several similar structures may be associated with the tympanic branch of the glossopharyngeal nerve and with the auricular branch of the vagus. When present in the middle ear, usually in association with the tympanic plexus, the structure is known as the glomus tympanicum. These glomus bodies are all histologically identical with other chemoreceptor tissues, such as the carotid body and the aortic body.

Rosenwasser (1945), in describing a vascular tumour arising in the hypotympanum and histologically resembling the carotid body, suggested that it had originated in the glomus jugulare. Since this first case many series have been reported and the glomus jugulare tumour is now recognized as the commonest tumour of the middle ear. From a pathological point of view tumours of the chemoreceptor tissues arising at any site appear to be identical. It has become customary to refer to them as chemodectomas or non-chromaffin paragangliomas.

The original concept of treatment of glomus jugulare tumours was conditioned by the fact that the previously well-documented carotid body chemodectoma was considered to be radio-resistant. It is the purpose of this paper to demonstrate the role that radiotherapy can play in the management of these tumours and to confirm its superiority over surgery in the large petrosal and extra-petrosal tumours with intracranial extension.

CASE REPORTS

Case 1.—W. R., male, born in 1921. This patient had a radical mastoidectomy in 1942 for a discharging left ear. Postoperatively he developed a total left-sided facial palsy which recovered gradually over the next 9 months. In 1944 the ear was re-explored because of severe pain and a biopsy was reported then as showing an 'angio-endothelioma'. He again developed a postoperative facial palsy which never recovered completely. Postoperatively he received a course of irradiation to a total of 1250 r.

He remained well until 1953, when he presented to a neurosurgical unit complaining of sudden weakness in all four limbs, unsteadiness, dysphagia, and hoarseness. He was noted to have papilloedema, a gross nystagmus slow to the left, paralysis of the left seventh, eighth, ninth, and tenth cranial nerves, and left-sided ataxia. A pink granulomatous lesion was present in the floor of the left external auditory meatus. His condition suddenly deteriorated with grave respiratory embarrassment, and cerebellar decompression was necessary. At operation (Professor Norman M. Dott) a severe foraminal herniation was found with gross displacement of the contents of the posterior fossa by a large mass situated anteriorly on the left side. The lesion was so vascular and the cerebellum so tight that it was not possible to approach the tumour for a biopsy to be taken without the risk of a catastrophic haemorrhage. A biopsy was finally taken via the external auditory meatus from the middle-ear region, and this time histological examination showed the typical features of a tumour of the glomus jugulare.

Postoperatively, although the patient's foraminal impaction had been relieved his other neurological signs were not significantly changed. Three weeks later he received a radical course of radiotherapy, a maximum skin dose of 4000 r and a minimum tumour dose of 3425 r being delivered over a period of 4 weeks. Thereafter his symptoms gradually improved and his papilloedema resolved. By 1955 he was working full-time without undue difficulty.

At present the patient still has a total left-sided facial palsy and impairment of the eighth, ninth, tenth, and eleventh cranial nerves. There are no granulations in the ear, the mastoid cavity being sealed off by a false membrane. Tomography (*Fig.* 1) shows sclerosis of the partially destroyed petrous bone on the left.

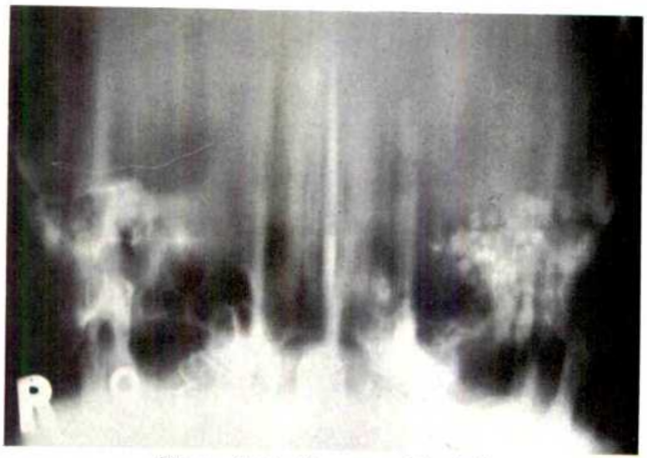

FIG. 1.—*Case* 1. Tomogram of the skull.

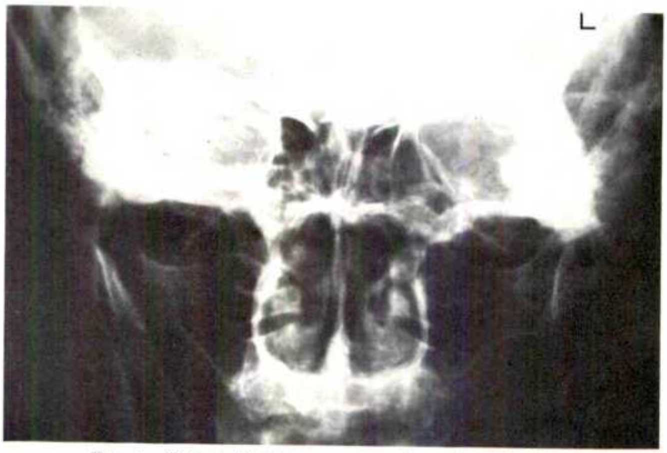

FIG. 2.—*Case* 2. Posterior-anterior radiograph of the skull.

Case 2.—M. C., female, born in 1915. This patient's symptoms began in 1942 with pain in the left side of the face and a feeling of fullness in the left ear. Unilateral deafness was noted in 1947 in association with a large polypus in the meatus and slight weakness of the left side of the face. Radical mastoidectomy in 1948 was accompanied by profuse haemorrhage. Histology of the removed tissue was reported as 'granulations of a chronic inflammatory type'.

By 1955 the pain and weakness of the face had increased and the patient developed dysphagia, hoarseness, persistent tinnitus, and a tendency to fall to the left. There was a large pulsatile mass in the left parapharyngeal space bulging the lateral wall of the pharynx. She now had total impairment of the seventh to twelfth cranial nerves on the left side. Radiographs showed gross enlargement of the foramen lacerum which had enlarged partly at the expense of the tip of the petrous temporal bone and partly at the expense of the greater wing of the sphenoid. The foramen ovale was also enlarged. This is shown on the radiograph published in a previous report on this patient (Stewart, Ogilvie, and Sammon, 1956). The biopsy taken in 1948 was reviewed at this stage and was now reported as showing a glomus jugulare tumour. She was given a radical course of radiotherapy with a tumour dose of 3920 r in 4 weeks and a maximum skin dose of 4750 r. Following therapy the pulsatile mass vanished.

The patient has been in good health since the course of radiotherapy and her only symptoms at present are persistent tinnitus in the left ear, slight pain in the face, and a tendency to fall occasionally to the left. The facial palsy has partly recovered but there is still total impairment of the other cranial nerves affected. There is no evidence of tumour clinically and the mastoid cavity is dry and healthy. Radiographs of the skull show considerable erosion of the petrous temporal and adjacent floor of the middle fossa (*Figs.* 2 and 3) and this is confirmed by tomography.

Case 3.—M. L., female, born in 1921. This patient was first seen in 1955 with left-sided deafness and tinnitus and an episode of hoarseness and dysphagia. At that time she was found to have a paralysed left vocal cord and a non-functioning left ear. She was kept under observation until 1960 when she was referred to a neurosurgical unit. In addition to the above findings she had now developed a horizontal nystagmus, loss of sensation on the left side including the face, and a mild spastic hemiparesis with impaired co-ordination on that side. Tomograms of the internal auditory meati were normal. Myodil ventriculography showed a displacement of the aqueduct and the fourth ventricle to the right. A posterior fossa exploration was carried out and a tumour was found in the left cerebellopontine angle. Only a subtotal removal could be achieved because of the close application of the tumour to the brain-stem and the ninth and tenth cranial nerves. Histological examination proved it to be a tumour of the glomus jugulare.

The patient's subsequent progress was marred by bizarre symptomatology, such as tinnitus with lateral gaze to the left and a gross disturbance of balance which was mostly functional.

In 1966 a red blush was noted behind the postero-inferior quadrant of the left tympanic membrane. A subtraction vertebral angiogram (*Fig.* 4) showed the tumour circulation postero-inferiorly to the petrous apex. A radical course of radiotherapy was given on the linear accelerator: 4940 r in 20 treatments.

The patient remains well despite her continued functional symptoms, with a much smaller blush still present behind the tympanic membrane. The left vocal cord is still paralysed, there is a mild paresis of the left side of her palate, and there is slight atrophy and weakness of the tongue on the left side.

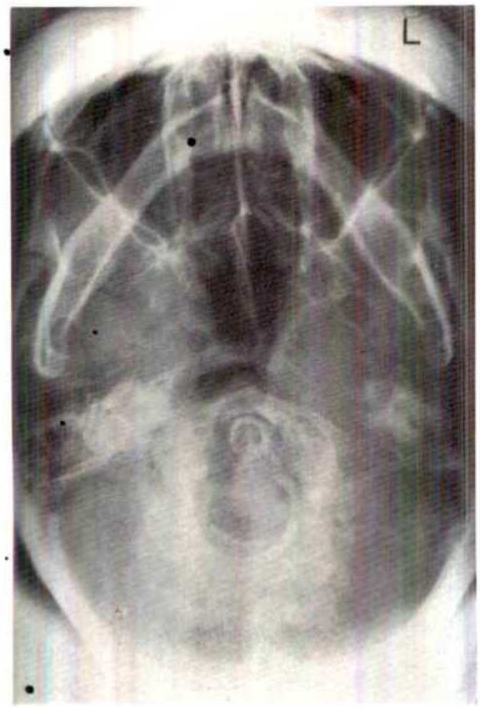

FIG. 3.—*Case* 2. Radiograph of the base of the skull.

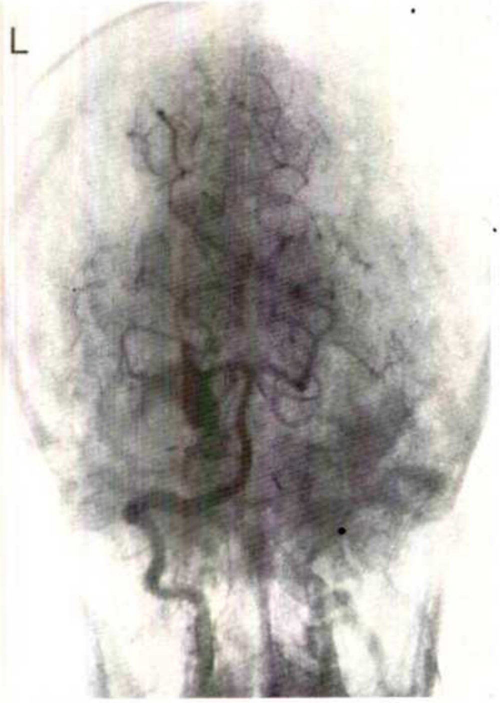

FIG. 4.—*Case* 3. Subtraction vertebral angiogram.

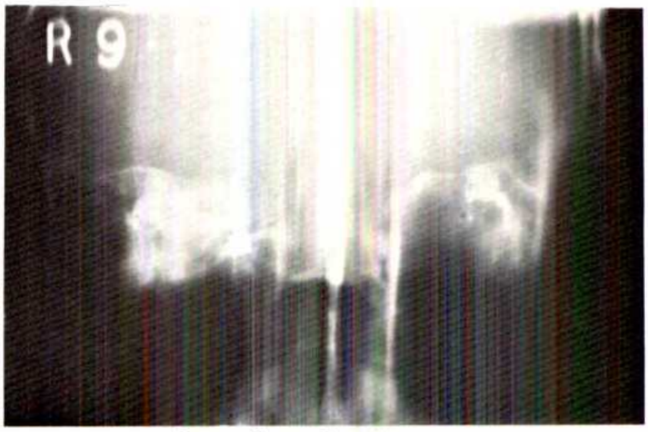

FIG. 5.—*Case* 4. Coronal tomogram.

Case 4.—D. J., female, born in 1947. This patient was admitted in 1961 with acute mastoiditis. Exploration of the mastoid revealed a considerable quantity of pus but excessive haemorrhage requiring transfusion did not permit the operation to be completed. A biopsy of the granulation tissue in the middle ear showed 'the histological appearance of a very vascular fibrous and granular tissue, in part covered by squamous epithelium, and considerable infiltration by chronic inflammatory cells'. Re-exploration 1 week later converted the mastoid and middle ear into a modified radical mastoid cavity and once again profuse haemorrhage was encountered and transfusion was necessary.

In 1963 the patient presented with spontaneous haemorrhage from the left ear, a peripheral facial paresis, and wasting of the left side of the tongue. Coronal tomography (*Fig.* 5) showed an extensive destructive lesion in the left petrous extending to the apex and obliterating the internal auditory meatus. Left carotid and vertebral angiograms showed the bulk of the blood-supply arising from branches of the vertebral axis and virtually no filling from either the internal or the external carotid. A biopsy of the tissue within the mastoid cavity showed the characteristics of a glomus jugulare tumour. A radical course of radiotherapy was given on the linear accelerator, 5500 r being delivered by a combination of wedge fields and a direct lateral field.

At the present time the patient is symptom-free and there is no evidence of the tumour. She has a residual left facial and hypoglossal palsy and total deafness. Surprisingly, the vocal cords and palate move normally.

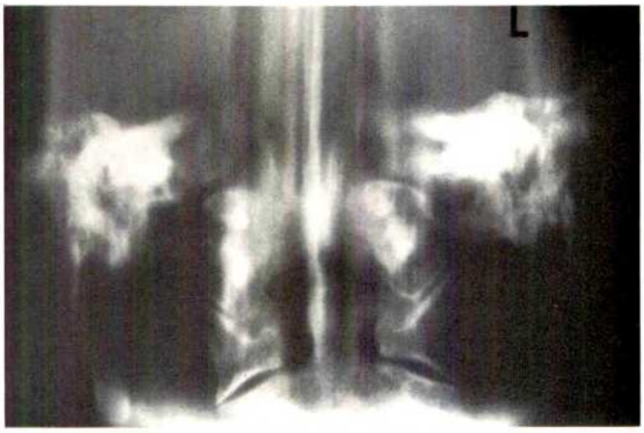

FIG. 6.—*Case* 5. Coronal tomogram.

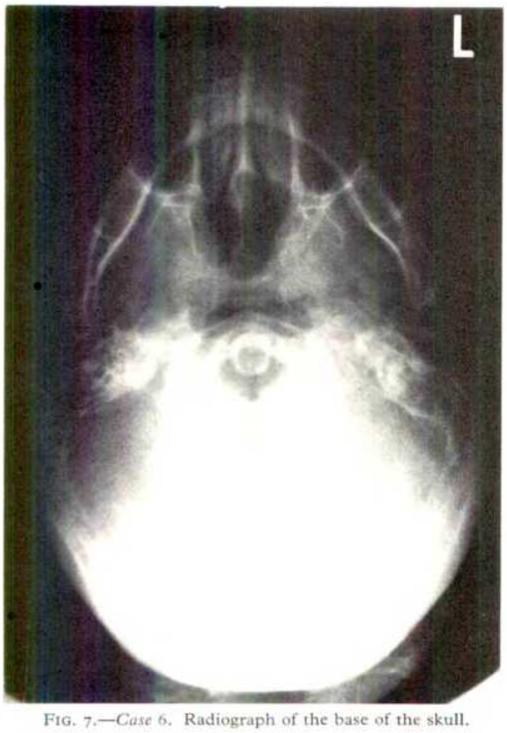

FIG. 7.—*Case* 6. Radiograph of the base of the skull.

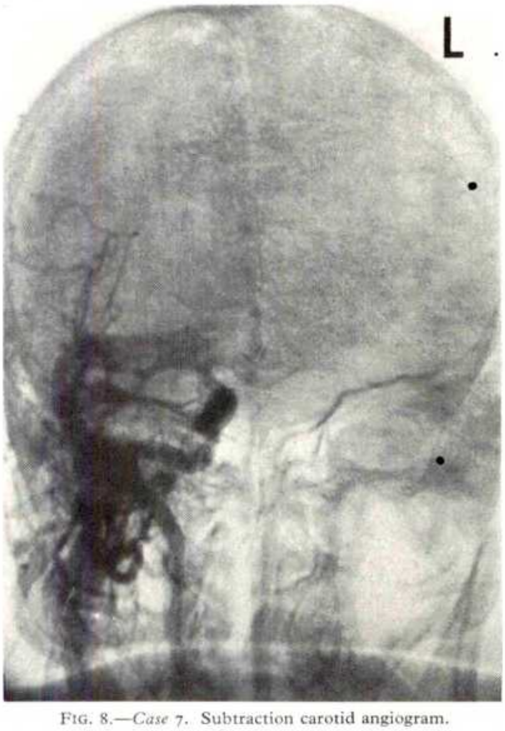

FIG. 8.—*Case* 7. Subtraction carotid angiogram.

Case 5.—I. M., female, born in 1893. This patient presented in 1963 with a short history of right-sided pulsing tinnitus. A red blush was noted behind the tympanic membrane. The cranial nerves were intact. Coronal tomography (*Fig.* 6) showed erosion of the apex of the petrous bone and expansion of the internal auditory meatus.

A biopsy was not taken and although radiotherapy was considered it was held in reserve in view of the known slow growth of these tumours and the patient's poor general condition. She was followed for a period of 7 years with little change in the size of the tumour. Her tinnitus continued unabated without any cranial nerve involvement. She died of unrelated causes in 1970.

Case 6.—C. C., female, born in 1896. This patient attended in 1964 with a 6-week history of hoarseness and left-sided deafness. She had a paralysed left vocal cord and the left tympanic membrane was of a uniform pink colour. A submentovertical radiograph (*Fig.* 7) showed a small defect of the petrous apex and adjacent bone in the region of the jugular foramen.

A tympanotomy was carried out and a biopsy taken. This showed a tumour of the glomus jugulare. A radical course of radiotherapy was then given on the linear accelerator, 5500 r being delivered by wedge fields over 4 weeks. The patient was followed over the next 6 years and showed no progression of the neurological features. The pink colour of the tympanic membrane persisted. The patient died in 1969 of an unrelated complaint. At post-mortem examination a large asymptomatic acoustic neuroma was present on the same side as the glomus jugulare tumour and she was also found to have a small frontal meningioma.

Table I.—ANALYSIS OF THE CASES IN THE PRESENT SERIES

CASE NO.	AGE AT ONSET OF SYMPTOMS (yr.)	SEX	CRANIAL NERVES INVOLVED	TREATMENT	RESULTS OF TREATMENT	PERIOD ELAPSED SINCE ONSET OF SYMPTOMS (yr.)	PERIOD OF FOLLOW-UP AFTER IRRADIATION (yr.)
1	21	M.	VII, VIII, IX, X, XI	Mastoidectomy, craniotomy, irradiation	+ + +	29	18
2	27	F.	VII, VIII, IX, X, XI, XII	Mastoidectomy, irradiation	+ + +	29	16
3	34	F.	VIII, IX, X, XI, XII	Craniotomy, irradiation	+ +	16	5
4	14	F.	VII, VIII, XII	Mastoidectomy, irradiation	+ + +	10	8
5	70	F.	—	Nil	+	6*	—
6	68	F.	IX, X, XI	Tympanotomy, irradiation	+ +	5*	5
7	62	F.	VII, VIII, IX, X, XI, XII	Irradiation	+ + +	1	1

+ + +, No visible sign of tumour; + +, regression in size; +, no change.

* Died of unrelated causes.

Case 7.—A. B., female, born in 1908. This patient presented in 1970 with a 3-month history of progressive right-sided deafness and pain in the right side of the face and right ear. She also complained of unsteadiness. Examination showed papilloedema, a partial right facial palsy, and total impairment of the eighth to twelfth cranial nerves. The tympanic membrane was bright red and there was a loud bruit over the right temporal region. There were, in fact, no cerebellar signs.

Plain radiographs of the skull followed by tomography in the occipito-mental and coronal planes showed extensive destruction of the occipital bone around the jugular foramen, the apex of the petrous in the region of the internal auditory meatus, and the sphenoid near the foramen lacerum and the foramen ovale. Carotid angiography (*Fig.* 8) showed the tumour filling rapidly and acting as an arteriovenous shunt; in the arterial phase there is already filling of the right sigmoid and transverse sinus.

The diagnosis of a glomus jugulare tumour was a clinical one since it was felt that a biopsy would be too hazardous. The patient was therefore referred for radiotherapy and given a radical course of 5500 r in 4 weeks by the linear accelerator. This was delivered as one lateral and two wedge fields at right-angles. The treatment was given to a block of tissue which included the whole of the petrous temporal bone, the greater wing of the sphenoid in front, and part of the occipital bone behind. Following this there was considerable objective improvement in the clinical features. The facial palsy showed almost total recovery, the bruit disappeared, and the papilloedema resolved completely. The functions of the last four cranial nerves show no sign of improvement.

ANALYSIS OF CASES

The series is summarized in *Table I*. Of the 7 patients, 6 had tumours of the glomus jugulare and 1 a tumour of the glomus tympanicum (*Case* 5).

In 5 of these 7 patients surgery was undertaken for various reasons but removal was incomplete and was followed by radiotherapy. Attempted removal by posterior fossa exploration was unsuccessful in 2 of the 5 cases, and removal by mastoidectomy was inadequate in a further 2 patients. One patient received radiotherapy following a positive biopsy at tympanotomy, and 1 patient was irradiated without biopsy, the diagnosis being made on clinical and radiological grounds. The patient with the tumour of the glomus tympanicum had neither surgery nor radiotherapy. Of the 6 patients given radiotherapy, 5 are still alive and well without evidence of progression of the tumour at periods ranging from 1 to 18 years following irradiation; the other died of unrelated causes.

Six of the 7 patients had multiple cranial nerve palsies implying intracranial extension, together with radiographic evidence of bone erosion. Although improvement in the cranial nerve palsies has been minimal, the striking feature has been the improvement in the intracranial hypertension in the 2 cases where this was a feature. In 1 of these (*Case* 1) the patient was *in extremis*; surgical decompression of the posterior fossa provided a respite to allow radiotherapy to take effect. In the second patient (*Case* 7) the condition was not as serious and the papilloedema resolved with radiotherapy alone.

DISCUSSION

It has been claimed that the blood-supply of these tumours arises from the ascending pharyngeal branch of the external carotid artery (Kempe, 1970). However, a supply from the vertebrobasilar system has been reported (Farrell and Hawkins, 1967; Lauren, 1968). In both the patients in our series where vertebral angiography was done (*Cases* 3 and 4) there was a significant supply from the vertebral system. Plain radiography, tomography, and detailed angiographic mapping, including if possible differential carotid angiography, vertebral angiography, and retrograde jugular phlebography, would be invaluable guides in assessing tumour size and planning the best fields for radiotherapy.

The treatment of glomus jugulare tumours will naturally depend on factors such as the patient's symptoms, age, and general condition. Apart from these features, the treatment will be dictated by the size of the tumour at the time of diagnosis, the amount of destruction that it has produced both clinically and radiographically, its accessibility, and its vascularity.

It is possible to watch a small blush behind a tympanic membrane for 15–20 years with virtually no change; *Case* 5 was followed for 6 years without progression of the tumour and ultimately died of unrelated causes. Agreement exists that in elderly patients with this kind of tumour or in patients in poor condition it may be justifiable to keep them under regular observation without specific treatment. Where these considerations do not apply it has generally been accepted that slowly growing tumours of the glomus tympanicum are best handled surgically. This has been challenged: Black (1964) states that many believe that in these cases one should proceed to radiotherapy without even biopsy to confirm the diagnosis.

Even greater argument, however, arises over the management of the large petrosal and extra-petrosal tumours. These tumours often show massive destruction radiographically, are extremely vascular, and produce multiple cranial nerve palsies (*Cases* 1, 2, 3, 4, 6, and 7). In a comprehensive review of the management of glomus jugulare tumours Williams, Childs, Parkhill, and Pugh (1955) traced the evolution of the management from the initial enthusiasm for surgery and disillusion with radiotherapy to a final opinion that radical surgery has no place in the treatment, the situation and vascularity of these tumours making any surgical approach extremely hazardous. Their experience with radiotherapy is very satisfactory. This conclusion has been reached by many others (Capps, 1957, 1958; Foote, 1958; Grubb and Lampe, 1965; McCabe and Fletcher, 1967; Rosenwasser, 1967a; Diepeveen, Hentzer, and Rovsing, 1969; Smith, 1970).

Despite these convincing reviews of the effectiveness of radiotherapy many still remain unconvinced. Meacham and Capps (1960) and Thomas, Shaw, and Trowbridge (1960) believe that many of these lesions are surgically resectable, and even though this may require a staged procedure it is preferable to radiotherapy. Ash, Beck, and Wilkes (1964) state that these tumours appear indifferently sensitive to irradiation therapy. Burman (1955) also declares that chemodectomas are entirely radio-resistant. Conley (1970) agrees with the view that the paraganglionic cell is not radio-sensitive and suggests partial resection for decompression, complemented by electro-desiccation in those tumours with multiple cranial palsies. Kempe (1970) is adamant that surgical excision is the treatment of choice and asserts that irradiation is of absolutely no value in glomus jugulare tumours. Curiously, in a more recent article (Kempe, Vanderark, and Smith, 1971) describing his surgical procedure Kempe fails to provide mortality and morbidity figures in support of his radical views.

The advocates of surgery have used the following arguments:—

1. Glomus jugulare tumours are radio-resistant and recurrences occur following irradiation.
2. Irradiation may cause brain necrosis or delayed amyloid degeneration of nervous tissue.
3. The inherent tendency of these tumours to grow slowly exaggerates the reported effectiveness of radiotherapy.

The original concept of radio-resistance arises from early experience with carotid body tumours. These lesions always present with a much larger mass than the glomus jugulare tumours. (The latter, by virtue of their proximity to the lower cranial nerves, manifest themselves when the tumour volume is much smaller.) Radiotherapy is less likely to be effective with the larger carotid body mass. In addition, because these tumours are so much more easily accessible to the surgeon, they are seldom referred for radiotherapy.

The excellent results obtained by radiotherapy, both in this series and others, entirely vitiate the argument of radio-resistance. The tumour is extremely vascular and a relatively small dose of irradiation can produce an endarteritis with obliteration of vessels and a subsequent decrease in the size of the tumour mass. The natural tendency for these tumours to fibrose over the years is thus enhanced by radiotherapy (Schade, 1953). In addition, there is evidence that the tumour cells themselves are sensitive to radiation (Rosenwasser, 1967b).

Recurrences may follow irradiation but this is equally true of surgical removal. When the hazards of surgical removal are considered it is clear that attempts at total excision must often fail owing to the tremendous vascularity and the anatomical site; only the few successful cases are reported.

In fact, there has been no evidence of tumour progression following irradiation in any case in our series.

The dose of irradiation which is needed does not cause tissue necrosis in the central nervous system as has been suggested. Even our patients (*Cases* 1, 2, and 4) who were treated in the days before modern megavoltage therapy experienced no complications and have been followed for periods up to 18 years. Van Miert (1964), in his excellent report, states: 'Megavoltage X-ray therapy in the 4–6 MV. range offers several advantages over 250 kV. X-rays and should give better results. With megavoltage X-rays, because of the clear-cut definition of the beam with very little shading off of dose at the edge, and because of the improved depth-dose obtained, the treated volume can be kept to a minimum. There is considerably less bone absorption, so that a more uniform dose is given to the treated volume and the risk of bone necrosis is negligible. Finally, there is very much less skin reaction. Because of these various factors treatment can be given safely to a considerably higher tumour dose than by conventional X-rays. Properly applied, the morbidity from treatment with 4 MV. X-rays should be nil.' He also advocates a wedge field method of administration in preference to a single lateral field in order to minimize irradiation of the brain-stem.

The third argument against radiotherapy promoted the idea that the inherent slow growth of these tumours would give a misleading impression of its effectiveness. This theoretical argument is controverted by our experience. There is no doubt that in our patients (*Cases* 1, 2, and 7) radiotherapy produced a visibly dramatic improvement with diminution of the tumour mass and resolution of cerebral oedema and papilloedema. There is no visible sign of the tumour in 4 patients (*Cases* 1, 2, 4, and 7) and this is of interest since it was in these patients that the tumour was the most destructive, as seen both clinically and radiologically.

We would still advocate complete surgical excision in the small middle-ear tumours, but surgery for glomus jugulare tumours with intracranial extension and multiple cranial nerve palsies is not justified. Radiotherapy has evolved from its initial palliative application in failed surgery to that of the treatment of choice.

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ARTERIOVENOUS FISTULAE FOR CHRONIC INTERMITTENT HAEMODIALYSIS: A MODIFIED SURGICAL TECHNIQUE

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SUMMARY

A side-to-end technique for arteriovenous fistulae of the wrist vessels for use in chronic intermittent haemodialysis with venepuncture is proposed. A series of 14 patients in whom this technique has been used is presented. A survey of the different shunting techniques described in the literature is given and their advantages and disadvantages are discussed. The problem of turbulence due to a sharp angulation of the flow through the anastomosis and the possibility of its causing aneurysmata and thrombosis of the fistulae are considered. This problem and its sequelae, together with the problem of the use of the sole remaining artery of the hand when the other has been either occluded or ligated in previous operations, and the possibility of creating an arteriovenous fistula with a vein distant from the artery, are all overcome by this technique.

CHRONIC intermittent haemodialysis is now an established procedure for the treatment of patients in terminal renal failure. This method was introduced in 1960 by Scribner and others (22).* In the same year Quinton and others (20) developed an arteriovenous shunting device by means of prolonged external artery and vein cannulation. Although this technique was adopted in all centres for haemodialysis it presented several problems: clotting of the shunt, infection, haemorrhage, and partial occlusion leading to decreased flow, as well as embolic accidents during declotting procedures. Therefore a new method was sought, and in 1966 Brescia and others (1) introduced the internal arteriovenous fistula which facilitated the venepuncture technique for haemodialysis which had first been proposed by Cimino and Brescia (4) in 1962. However, this technique also has problems. The classic method of Brescia and others (1) for a surgically created arteriovenous fistula is a side-to-side anastomosis between the radial artery and the cephalic vein at the wrist level. This device necessitates a large patent cephalic or other neighbouring vein. However, in many cases such a vein cannot be found, particularly if shunts or fistulae have previously been performed in the same limb.

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* Throughout, figures in parentheses relate to the reference numbers.

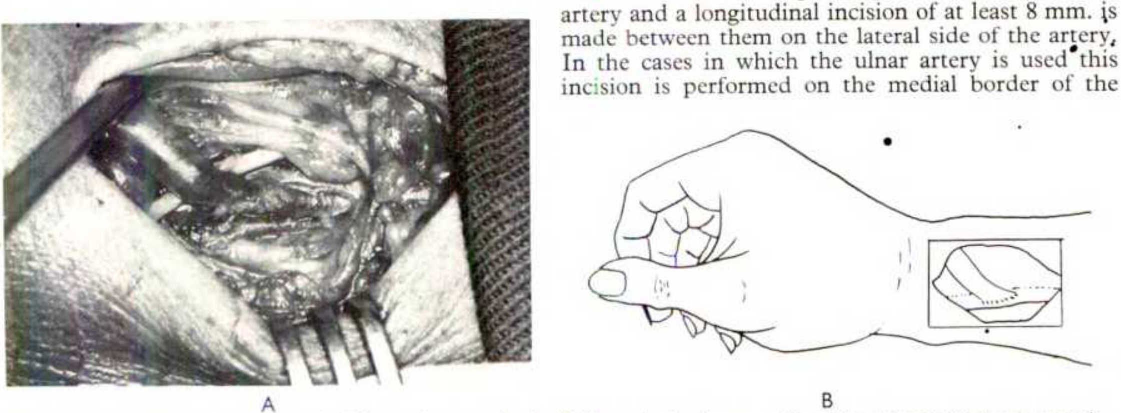

FIG. 1.—*Case* 7. A, Operative photograph of the arteriovenous fistula. B, Frame in the diagram outlines the part shown in the photograph.

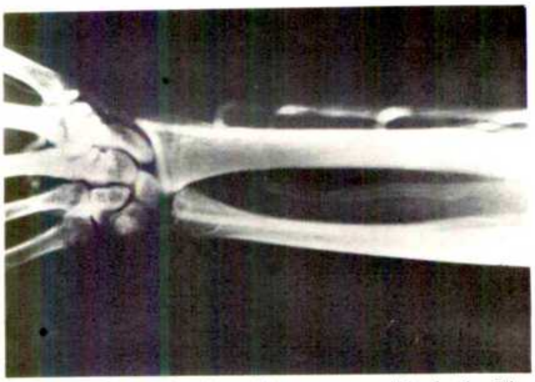

FIG. 2.—*Case* 7. Arteriographic appearance of the fistula. The apparent shortness of the venous arch in the film is due to the position in which the forearm was radiographed.

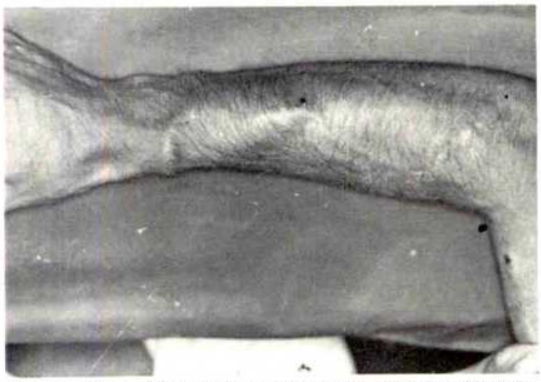

FIG. 3.—*Case* 3. Photograph of the forearm. Note the wide arch.

Several modifications have therefore been developed to overcome this problem (7, 13, 14, 16, 19, 21, 24). An alternative technique with the purpose of solving this and some other problems is presented here.

MATERIALS AND METHODS

An axillary block anaesthesia is used which seldom requires an additional local anaesthetic. One of the dorsal metacarpal veins is chosen, usually the one between the third and fifth metacarpal bones. A small transverse incision is performed on the dorsum of the wrist over the vein, which is then dissected distally to a point near the metacarpophalangeal joints. Occasionally it is necessary to perform a second incision over this point. The vein is transected as distally as possible and its digital end is ligated. The proximal part is pulled through the incision over the wrist. Another longitudinal incision is performed over the radial artery (or the ulnar artery in the cases in which the radial artery has been occluded by previous cannulations or fistulae). The artery is dissected for a distance of about 2 cm. A subcutaneous tunnel is prepared between the two skin incisions and the free part of the vein is arched through this tunnel to the artery. The aperture of the vein is enlarged to a width of 8–10 mm. either by a diagonal incision or, when the vein is very narrow, by longitudinal splitting and trimming of the corners. Two bulldog clamps are applied to the artery and a longitudinal incision of at least 8 mm. is made between them on the lateral side of the artery. In the cases in which the ulnar artery is used this incision is performed on the medial border of the vessel. The end of the vein is then anastomosed to the side of the artery with a 000000 running Tevdek suture so that the vein forms an acute angle with the distal part of the artery (*Fig.* 1). The clamps are removed and a pulse and thrill can immediately be detected over the vein which has become distended. The end-result is a wide arch, the blood flowing from the artery into the vein first in a distal direction, which then progressively becomes proximal. The arteriographic and external appearances of a limb in which a fistula has been performed are presented in *Figs.* 2 and 3.

RESULTS

During the period from November, 1970, to October, 1971, 14 arteriovenous fistulae using this technique were performed in the Department of General and Vascular Surgery, Rambam Government Hospital, on 14 patients on a chronic haemodialysis programme. In 1 additional patient a saphenous vein interposition graft was required as owing to several previous external arteriovenous shunts there were no remaining patent superficial veins at the wrists. The 14 cases are listed in *Table I*. Despite previous shunts and arteriovenous fistulae only in 2 cases was the radial artery obliterated and it was necessary to use the ulnar artery.

One of the patients died a few days after the fistula had been performed. The remaining 13 patients still have a patent fistula. Nine patients perform regular dialysis by means of their fistula in our haemodialysis unit. The remaining 4 patients have been transferred to other dialysis centres. One of these had regular dialysis until a successful kidney transplantation was performed, while the others are still on dialysis. The number of dialyses performed up to October, 1971, in the patients in our unit is given in *Table I*. The output values of the fistulae are also listed in *Table I*. The calibre of the arteries at the level of the anastomoses ranged between 1·5 and 3 mm. The veins were occasionally larger, but in some cases only a very narrow one could be found (less than 1 mm. in diameter in the collapsed state). Despite this a sufficiently large net of veins developed in the dorsum of the forearm and haemodialysis using the arteriovenous fistula could be performed in all the cases 2 days to 4 weeks after the creation of the fistula. No major oedema of the hand was noticed following the operation. No aneurysm of the venous limb occurred. As already stated, no immediate or late thrombosis of the fistulae or insufficient output prevented the regular use of the fistulae for chronic intermittent haemodialysis.

Table I.—Details of the Cases in the Present Series

Case		Age and Sex		Date of Operation	Artery used for the Anastomosis	Output of the Fistula (ml. per min.)	Average No. of Dialyses per Month
1.	H. M.	23	F.	19 Nov., 1970	Radial	—	—
2.	W. M.	23	M.	29 Nov., 1970	Ulnar	350	10
3.	H. U.	23	M.	6 Dec., 1970	Radial	360	12
4.	Z. E.	36	M.	13 Dec., 1970	Radial	320	10
5.	H. P.	43	M.	24 Jan., 1971	Radial	365	8
6.	L. N.	52	M.	8 June, 1971	Radial	340	8
7.	R. A.	19	M.	20 June, 1971	Radial	370	9
8.	G. L.	46	M.	7 July, 1971	Radial	360	9
9.	W. M.	29	F.	15 July, 1971	Radial	—	—
10.	B. E.	27	F.	9 Sept., 1971	Radial	—	—
11.	S. F.	63	F.	12 Sept., 1971	Radial	320	8
12.	O. S.	28	F.	26 Sept., 1971	Radial	—	—
13.	G. S.	22	M.	3 Oct., 1971	Radial	355	9
14.	S. A.	50	M.	5 Oct., 1971	Ulnar	—	—

DISCUSSION

The superiority of internal arteriovenous fistulae over external ones has been well established (1, 3, 5, 8, 10, 15, 17, 18, 21, 25, 26). Not only has the internal fistula a much longer survival time but also complications such as haemorrhage and infection are practically nil. As already mentioned, the first internal arteriovenous fistulae were introduced by Brescia and others in 1966 (1). Today, this method is accepted in most centres (2, 3, 4, 5, 6, 8, 9, 10, 11, 17, 18, 23, 25, 26). However, an analysis of this technique reveals some pitfalls. A side-to-side anastomosis necessitates a neighbouring vein of good calibre. This cannot always be found, particularly when previous shunting operations have been performed at the same site. The blood-flow from the artery into the vein when the anastomosis is opened splits into two. One engages the distal part of the vein, and this reverse flow in the vein either leads to a certain degree of congestion of the hand or sometimes is stopped by valves and ceases completely. This is obvious in some of the arteriographs presented in the literature (10). However, in both cases the main flow through the anastomosis turns sharply in the proximal direction (*Fig.* 4). Such an acute angulation is of poor haemodynamic value, causing turbulence. This may be the reason for both aneurysmal changes in the venous limb and thrombosis of the fistula. While the occasional impossibility of creating a side-to-side arteriovenous fistula has given rise to modified techniques to overcome the problem, no attention has been given to the sharp angulation in the flow through the anastomosis.

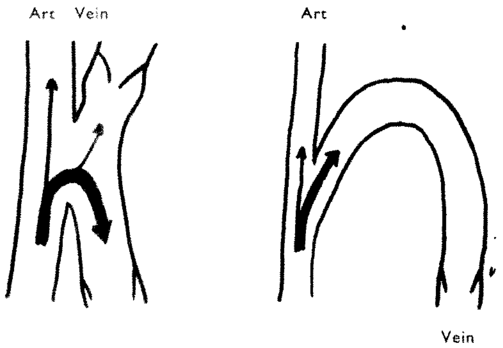

Fig. 4.—Diagrams of (A) side-to-side and (B) side-to-end arteriovenous fistulae, showing the sharp angulation of the blood-flow through the side-to-side anastomosis which is missing in the side-to-end type in which there is a wide arch.

Two main modifications to the Brescia technique have been published. The one advocated by Sperling and others (24) in 1967 and by Salomon and others (21) in 1968 is an end-to-end anastomosis between the radial artery and one of the veins in the forearm or wrist. This method allows the use of a distant vein but it necessitates the ligation of the radial artery. In cases in which one of the two arteries of the forearm is already obliterated or ligated by previous shunting operations the ligation of the second artery may put the blood-flow to the hand in jeopardy. Another method was proposed first by Florez-Izquierdo and others (7) in 1969 for children in whom the vessels in the wrist are very small and later was also advocated by Lazorthes and others (13), May and others (14), and Mozes and others (16).

They also used an interposition saphenous vein-graft. The first three groups of workers anastomosed the graft in the antecubital fossa, positioning the saphenous vein as a U loop in the volar part of the forearm, either side to side or end to end. Mozes and others (16) branched the saphenous vein to the artery at a right-angle in the wrist and brought it to the proximal vein in a Z shape. However, while Mozes and others (16) reported successful shunts in 2 patients, Lacombe and others (12), using the method of Lazorthes and others (13), claimed a 50 per cent failure rate, including thromboses and aneurysmal transformation of the graft, and recommended the discarding of this technique. Another major point in all saphenous graftings is the much longer time necessitated by the operation and the more complicated anaesthesia required (usually a general one) in poor-risk patients who are frequently in a bad general condition and prone to infection.

The technique proposed here is a simple one. It necessitates a minor anaesthetic procedure, it allows the use of a vein distant from the artery, a wide 8–10-mm. anastomosis is easily obtained, and the blood flowing through it causes little turbulence. The length of the operation is about 1 hour. Though the cause of the reported failures in the literature of the side-to-side technique has been attributed to either a small (less than 4 mm.) artery (25), a narrow vein (5, 6, 8, 10, 17, 26), or a narrow anastomosis (26) we have not been impressed by the first two of these factors as a possible cause for occlusion of the fistula. All the arteries in our cases were less than 4 mm. in diameter and we have also successfully used narrow veins. The width of the anastomosis is considered an important factor in the patency of the fistula. Though some authors consider a 3–5-mm. aperture sufficient (1, 8, 10, 17), many others advocate an 8-mm. one (5, 7, 15, 18, 19) and this is also our opinion. However, we consider an anastomosis of 15–35 mm. (26) as unnecessarily large. Compared with a 10–18 per cent failure rate in the side-to-side technique as reported by many authors (1, 5, 8, 10, 25, 26), and bearing in mind the problems which have been overcome by our technique, the result of our series, though a rather small one, is satisfactory.

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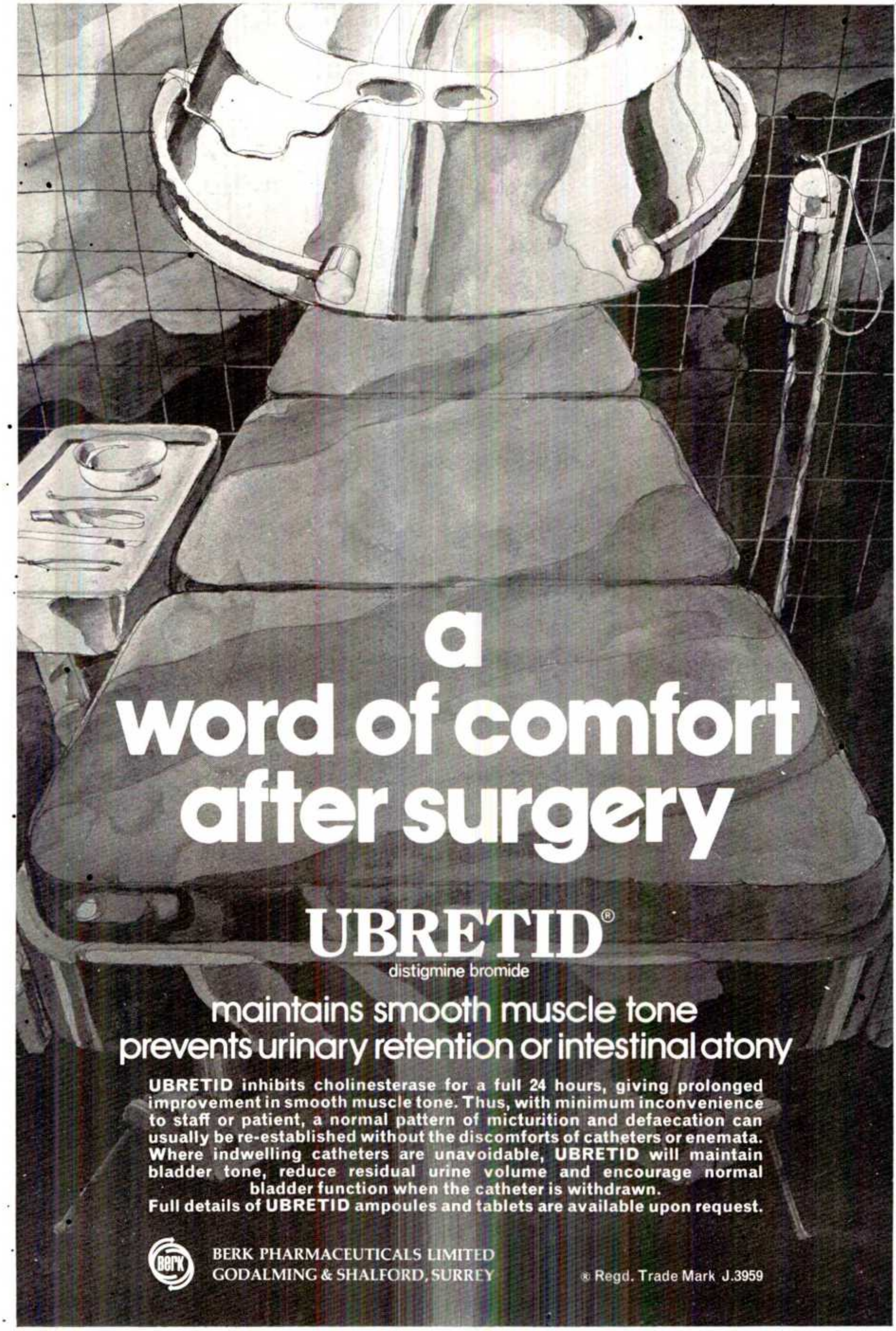

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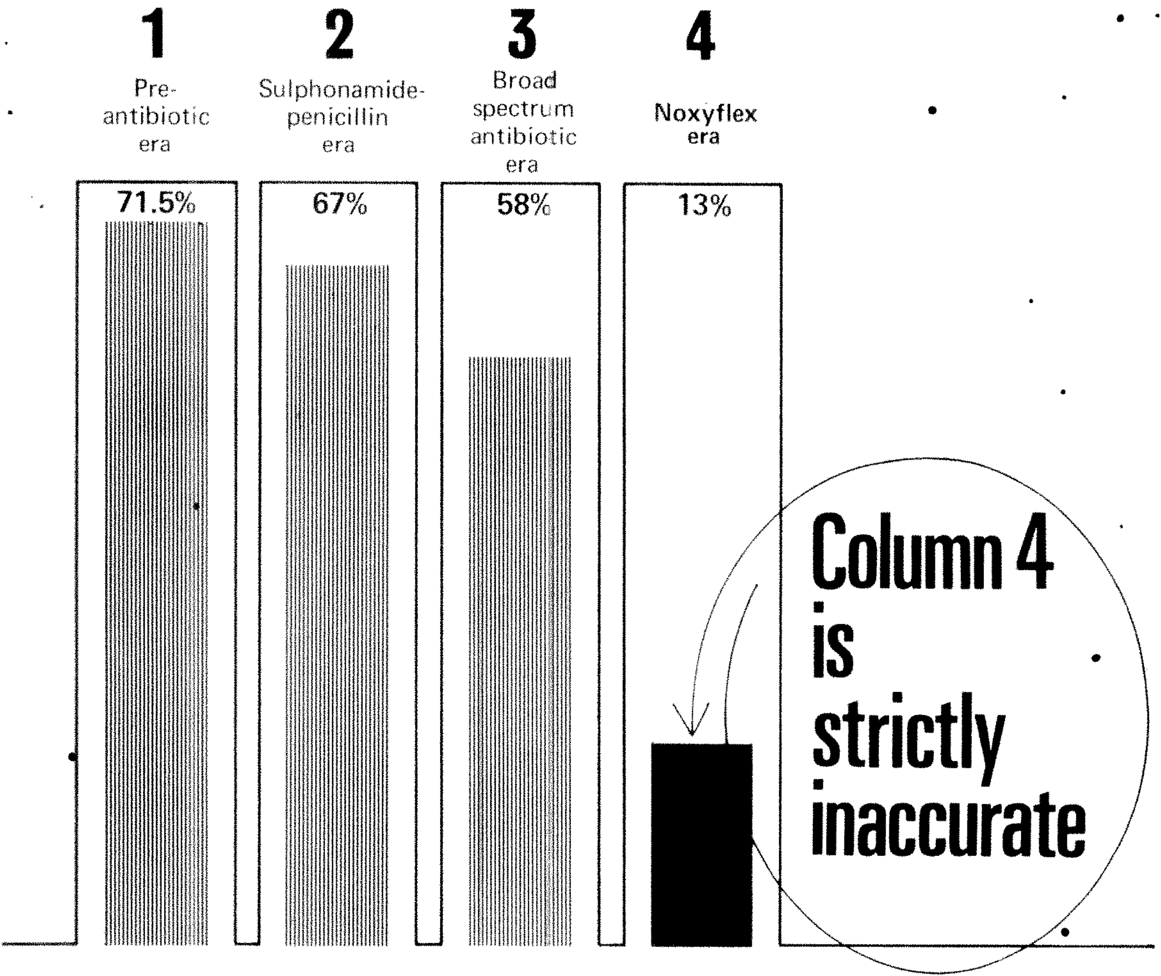
It is not pedantically accurate because its sources differ. But the point is fairly made.



Column 4 is strictly inaccurate

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ERYTHROCYTE AND PLASMA CIRCULATION TIMES IN HAEMORRHAGIC SHOCK

By D. F. L. WATKIN* and JENNIFER HUDSON

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SUMMARY

A method has been developed in which the simultaneous administration of ^{51}Cr-labelled red blood-cells and ^{125}I-labelled albumin in the dog has been used to compare the flow rates and transit times of erythrocytes and of plasma in three circulatory beds —the hindlimb, the kidney, and the small intestine. Blood-flow rates calculated from either isotope agreed well and were significantly greater than simultaneous direct measurements and electromagnetic flowmeter readings. This difference was due to incomplete recovery of the isotope from the venous cannula, recovery ranging from 23 to 96 per cent. When the isotope-flow results were corrected for these losses they did not differ significantly from direct measurements though they were still greater than the electromagnetic flowmeter readings.

The mean transit time for erythrocytes was, on average, 6–8 per cent shorter than that for plasma. There was no significant difference in this percentage for the three vascular beds studied or between a control period and haemorrhagic shock. Thus, in this shock preparation red-cell 'sludging' cannot have been extensive. The rationale for the use of low-molecular-weight dextran as a specific 'anti-sludging' agent in shock is, therefore, not supported.

CIRCULATORY shock is a state in which the circulation fails to meet the nutritional needs of the body at rest (Guyton and Crowell, 1964). The absolute reduction in blood-flow in shock may be accompanied by disruption of the orderly passage of erythrocytes through the capillaries, as seen by direct observation of the microcirculation using the techniques of Chambers and Zweifach (1944). Aggregation and slowing of the red cells, plasma skimming, and arteriovenous shunting have been observed in these circumstances (Gelin, 1961). The present paper is concerned with the first of these microcirculatory effects—the slowing of the flow of erythrocytes relative to plasma which is often described as 'sludging'. Low-molecular-weight dextran (L.M.W.D.) therapy is designed to correct this process (Bergentz, Gelin, Rudenstam, and Zederfeldt, 1961).

The evidence of *in vivo* microscopy is qualitative and is obtained in artificial situations, as with the rat's meso-appendix spread on a microscope stage. To provide a quantitative measure of any relative slowing of the red cells their transit times from artery to vein have been compared with those for plasma. In health the circulation time for erythrocytes is 10–15 per cent shorter than that for plasma (Rowlands, Groom, and Thomas, 1963), the difference being attributed to axial streaming of cells in the smaller blood-vessels. If the changes seen on microscopy are occurring on a physiologically important scale, then in shock the mean transit time should be longer for erythrocytes than for plasma.

METHODS

The measurements were made in 14 anaesthetized mongrel dogs weighing from 15 to 32 kg. (mean, 21·6 kg.). Transit times for red cells and plasma were compared before and after the production of haemorrhagic shock. The experimental method was established in the hindlimb and subsequently was applied to the renal and intestinal vascular beds in separate series of experiments.

For each comparison a bolus containing ^{51}Cr-labelled erythrocytes and ^{125}I-labelled albumin was injected via a small catheter placed in the artery supplying the organ under investigation. The radioactivity in its venous effluent was monitored by a scintillation counter connected to twin-channel ratemeters and recorders. From the indicator-dilution curves mean transit times and flow rates have been calculated. These flow rates were compared with simultaneous measurements by an electromagnetic flowmeter and also, in some experiments, with direct measurements. In 8 experiments the venous effluent was collected and its radioactivity was measured to assess the proportion of the injected bolus returning via the monitor.

Indicators.—The radioactive labels for erythrocytes and plasma were selected for stability and for their suitability for simultaneous monitoring by an external counter. ^{51}Cr has a γ energy of 323 keV. and is readily distinguishable from ^{125}I which has a 35-keV. γ emission and a 27-keV. X emission. A sample of the dog's own red blood-cells (R.B.C.) was labelled with ^{51}Cr by the method of Gray and Sterling (1950). ^{125}I-tagged human serum-albumin (H.S.A.) was obtained commercially (Radiochemical Centre, Amersham). The radioactivity of an accurately diluted 'standard' of each stock preparation was measured using the same counter as was employed for the venous stream. The two indicator preparations were combined in a 2-ml. plastic syringe immediately before injection, the quantities being measured by weighing. Approximately 50 μc. of ^{51}Cr R.B.C.s and 4 μc. of ^{125}I H.S.A. were used for each injection.

Instrumentation.—The radioactivity of the venous blood was monitored as it passed through a thin-walled polythene tube of 7 mm. internal diameter in front of a 2·5-cm.-diameter, 2·5-cm.-thick, sodium-iodide crystal and a photomultiplier. This scintillation counter was connected to twin-channel amplifiers and pulse-height analysers. The ^{51}Cr channel counted only pulses of over 85 keV., while the ^{125}I channel was set to accept those in the range 22–36 keV. The system gave counting efficiencies of 0·65 per cent for ^{51}Cr and 9·7 per cent for ^{125}I. ^{51}Cr was also recorded on the ^{125}I channel with an efficiency of 0·025 per cent. The output from the pulse-height analysers was fed into ratemeters connected to a twin-channel pen-recorder.

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Venous blood-flow was also measured by a cannulated electromagnetic flowmeter recording on a Grass polygraph recorder. At the end of each experiment this instrument was calibrated against a pump.

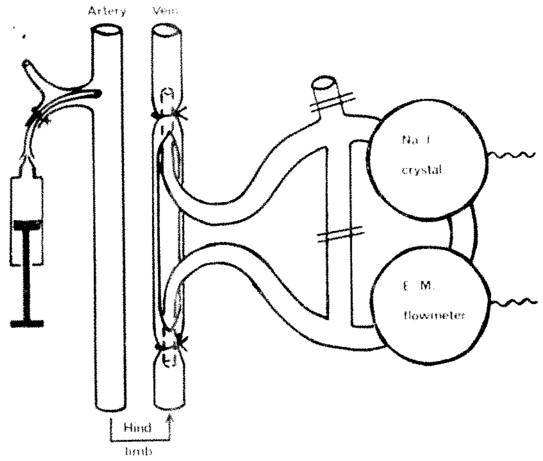

FIG. 1.—Cannulations and venous circuit for the hindlimb experiments.

The radioactivity of samples of the venous blood collected after passage through the monitor was measured in a well counter cross-calibrated with the original isotope 'standards'.

The Animal Preparation.—Anaesthesia was induced with intravenous thiopentone and maintained by intermittent intravenous pentobarbitone. The dog was ventilated with air at 170 ml. per kg. per minute via a cuffed endotracheal tube. A long catheter passed via the right femoral vein into the right side of the heart was used to obtain central venous samples for haematocrit estimations and for the administration of drugs. The right femoral artery was cannulated for continuous recording of the blood-pressure and to permit bleeding into a graduated bottle. A fine plastic catheter (1·6 mm. external diameter) was placed with its tip in the main artery supplying the organ to be studied. The injections of the isotopes were made by needle puncture through a rubber diaphragm covering the hilt. For the femoral and superior mesenteric arteries the catheter was introduced through a small branch. When investigating the renal circulation it was passed into the right renal artery, across the aorta, and manipulated into the left renal artery.

Cannulae placed in the femoral, renal, or portal veins were used to divert the entire venous stream through the circuit, which is shown connected for the hindlimb experiments in *Fig.* 1. The blood was returned to the dog via a proximal cannula in the femoral or portal vein; in the renal experiments the circuit led to a femoral cannula. The circuit consisted of the electromagnetic flowmeter, the scintillation counter, and a side-arm through which the blood could be diverted into a measuring cylinder. A cross-arm controlled with a haemostat served to zero the flowmeter. Heparin (500 U. per kg.) was administered to prevent clotting in the circuit in the limb experiments, but proved unnecessary at the higher flow rates obtained in the renal and intestinal studies.

Experimental Groups.—The hindlimb was studied in 6 dogs, the kidney in 4, and the intestinal circulation in 4. In 4 of the hindlimb experiments the venous blood was collected during the recording of each pair of isotope dilution curves. The larger volumes rapidly removed in this way in the renal and intestinal studies were not well tolerated and therefore 'collections' were restricted to the final 'control' and 'shock' readings in 2 experiments from each of these groups.

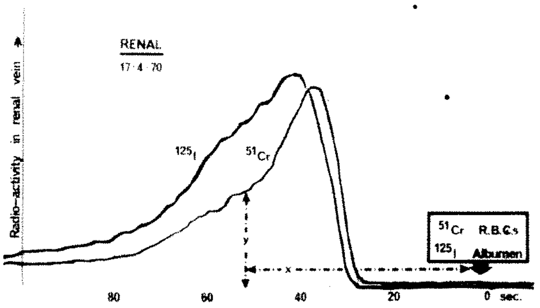

FIG. 2.—Method for analysis of indicator-dilution curves.

Experimental Procedure.—After the cannulations had been carried out the procedure was as follows:—

1. *Control Period* (0–30 minutes).—Three combined injections of ^{125}I H.S.A. and ^{51}Cr R.B.C.s were made at 15-minute intervals.
2. *Controlled Hypotension* (30–75 minutes).—The dog was bled to a systolic blood-pressure of 30–40 mm. Hg for 45 minutes. If the volume bled was less than 25 ml. per kg. in the limb experiments or less than 20 ml. per kg. in the other two groups the animal was excluded from the series.
3. *Shock Period* (75–105 minutes).—Three further dual isotope injections were made at 15-minute intervals.

Analysis of the Indicator-dilution Curves.—A typical pair of curves is shown in *Fig.* 2. Before each injection the recording was adjusted to zero in order to eliminate the background radioactivity due to equilibration of the previous injections. Two calculations were made from each curve: the blood-flow and the mean transit time of the indicator. Each curve was analysed by measuring its height (y) at 2-second intervals. From the sum of these heights was derived the area under the curve for use in the indicator-dilution blood-flow calculation (Powers and Sevelius, 1965). Each value of y was then multiplied by the time which had elapsed since injection (x). The mean transit time (M.T.T.) for an indicator is then given by the equation:—

$$\text{M.T.T.} = \sum xy \Big/ \sum y.$$

As no recirculation point could be identified on the curves they were counted to three times the transit time of the peak. Using this convention, the last point counted was always close to the level of the final equilibrium.

RESULTS

The volume bled averaged 31·9 ml. per kg. in the hindlimb experiments, 25·2 ml. per kg. in the renal experiments, and 25·6 ml. per kg. in the intestinal studies. The mean haematocrit following haemorrhage was 3·9 per cent lower than in the control period, indicating that relatively little haemodilution was occurring during the time span of the experiments. The severe degree of shock produced is demonstrated by the deaths of 3 other dogs before completion of the bleeding phase and of 2 more shortly before the final isotope injection was due.

Flow Measurement.—The flow rates calculated from the ^{125}I H.S.A. and ^{51}Cr R.B.C. dilution curves are compared in *Table I*. The mean values agreed well in both the control and the shock periods in each vascular bed. When the ^{125}I H.S.A. results are expressed as a percentage of the ^{51}Cr R.B.C. results the mean value ranges from 98·8 to 104·4 per cent with a standard deviation of 11·1 per cent or less, showing that the individual pairs of values were in close agreement. However, the flow rates obtained by the isotope method (expressed, for simplicity, as the mean of the ^{125}I H.S.A. and ^{51}Cr R.B.C. figures) were significantly greater than the electromagnetic flowmeter readings (*Table II*). The mean ratio between these two measures of blood-flow varied with the organ being studied, ranging from approximately 3 : 1 in the hindlimb to 4 : 3 in the small intestine. The ratio also tended to be higher during the shock period. The discrepancy between the isotope-flow results and the electromagnetic flowmeter readings varied considerably between experiments, as indicated by the large standard deviation of the ratio seen in *Table II*. A possible explanation for the differences between these two methods of measurement of blood-flow is considered later.

Table I.—BLOOD-FLOW CALCULATED FROM ^{125}I H.S.A. AND ^{51}Cr R.B.C. DILUTION CURVES

VASCULAR BED STUDIED	NO. OF DOGS*	BLOOD-FLOW (ml. per kg. per min.; mean ± S.D.)					
		Control Period			*Shock Period*		
		^{125}I H.S.A. (a)	^{51}Cr R.B.C. (b)	(a) as a Percentage of (b)	^{125}I H.S.A. (c)	^{51}Cr R.B.C. (d)	(c) as a Percentage of (d)
Hindlimb	6	7·1 ± 3·7	7·2 ± 3·7	99 ± 8	2·3 ± 0·6	2·3 ± 0·6	100 ± 7
Kidney	4	10·3 ± 2·1	10·2 ± 2·6	102 ± 8	2·1 ± 0·7	2·0 ± 0·7	104 ± 10
Small intestine	4	14·6 ± 4·8	14·7 ± 4·6	99 ± 6	4·1 ± 0·8	4·1 ± 0·7	99 ± 11

* Three readings in each period in each dog.

Table II.—BLOOD-FLOW MEASURED BY ISOTOPE DILUTION AND THE ELECTROMAGNETIC FLOWMETER

VASCULAR BED STUDIED	NO. OF DOGS*	BLOOD-FLOW (ml. per kg. per min.; mean ± S.D.)†					
		Control Period			*Shock Period*		
		Mean Isotope Result (a)	Electromagnetic Flowmeter (b)	(a) as a Percentage of (b)	Mean Isotope Result (c)	Electromagnetic Flowmeter (d)	(c) as a Percentage of (d)
Hindlimb	6	7·1 ± 3·7	2·7 ± 1·5	272 ± 66	2·3 ± 0·6	0·7 ± 0·3	378 ± 184
Kidney	4	10·3 ± 2·4	7·2 ± 2·2	150 ± 46	2·0 ± 0·7	1·1 ± 0·6	269 ± 208
Small intestine	4	14·7 ± 4·7	11·5 ± 2·3	125 ± 24	4·4 ± 0·7	3·1 ± 0·7	137 ± 30

* Three readings in each period in each dog.

† For each comparison of isotope and electromagnetic flowmeter results $P < 0·01$.

Isotope Recoveries.—The mean percentages of the injected isotopes recovered in the 8 'collection' experiments are shown in *Table III*. There was no significant difference between the recoveries of the two isotopes in either the control period or in shock. The percentage recovery of ^{125}I was significantly greater during the control period than in shock ($P < 0·02$), but the corresponding difference for ^{51}Cr recovery just failed to reach significance at the 5 per cent level. The large standard deviations of the percentage recoveries reflect the wide range of individual values which are given in detail in *Table IV*. Presumably the incomplete recovery of the isotopes was due to some of the injected material spilling over into the aorta or returning by other venous channels.

Table III.—PERCENTAGE RECOVERY OF INJECTED ISOTOPES IN 8 EXPERIMENTS

ISOTOPE	CONTROL PERIOD	SHOCK PERIOD	PAIRED t-TEST
^{125}I	72 ± 23	57 ± 29	$P < 0·02$
^{51}Cr	71 ± 22	59 ± 27	$0·05 < P < 0·06$

Corrected Indicator-dilution Flow Rates.—The indicator-dilution blood-flow calculation,

$$F = \alpha\ (I/A)$$

(where F = flow, I = radioactivity injected, A = area under the dilution curve, and α is a geometric constant), assumes that all the injected material reaches the monitor. Thus, in these experiments, the radioactivity injected must be multipled by the percentage recovery to give a 'corrected' flow rate. *Table IV* shows the uncorrected and corrected isotope-flow results and compares them with direct flow measurement and with the electromagnetic flowmeter readings.

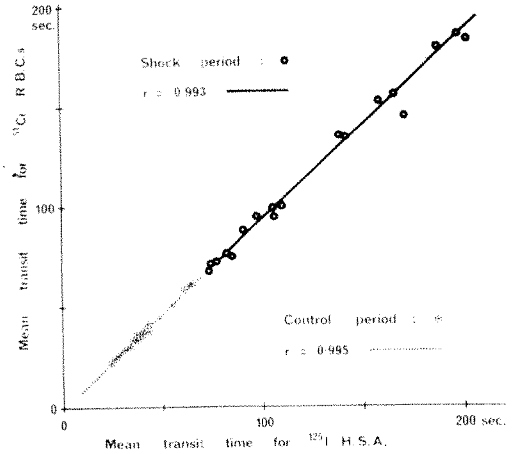

Fig. 3.—Mean transit times for erythrocytes and plasma in the hindlimb.

Table IV.—UNCORRECTED AND CORRECTED ISOTOPE-FLOW RESULTS COMPARED WITH DIRECT MEASUREMENT AND THE ELECTROMAGNETIC FLOWMETER RESULTS* (Flow expressed as ml. per kg. per minute)

VASCULAR BED STUDIED	DOG NO.†	MEAN ISOTOPE FLOW (UNCORRECTED)	MEAN PERCENTAGE ISOTOPE RECOVERY	ISOTOPE FLOW CORRECTED FOR PERCENTAGE RECOVERY	DIRECT FLOW	ELECTROMAGNETIC FLOWMETER
Control period						
Hindlimb	3	7·6	33	2·5	2·9	2·8
	4	2·9	60	1·7	1·8	1·3
	5	11·9	53	6·4	4·5	2·6
	6	3·3	75	2·5	2·4	1·3
Kidney	7	12·3	90	11·1	11·5	10·5
	8	12·7	90	11·4	9·4	6·2
Small intestine	11	16·8	76	13·0	11·8	11·8
	12	10·1	95	9·6	9·2	9·2
Shock period						
Hindlimb	3	2·2	23	0·5	0·5	0·7
	4	1·7	36	0·6	0·7	0·4
	5	2·3	35	0·8	1·0	0·3
	6	1·9	70	1·3	1·3	0·9
Kidney	7	2·2	96	2·1	—	0·7
	8	1·8	72	1·3	1·0	0·6
Small intestine	11	4·2	40	1·7	1·4	2·4
	12	4·5	91	4·1	4·3	3·6

* For hindlimb experiments each line is the mean of three readings but for renal and intestinal studies it represents a single reading.

† Statistical analysis: uncorrected isotope flow was significantly greater than direct measurement or the electromagnetic flowmeter in each period ($P < 0{\cdot}02$). Corrected isotope flow was not significantly different from direct measurement. Corrected isotope flow was significantly greater than the electromagnetic flowmeter result in shock but not in the control period.

The uncorrected isotope-flow result in these 8 experiments was a mean of 165 per cent of the direct flow in the control period and of 232 per cent in shock. The corresponding figures for isotope flow and the electromagnetic flowmeter were 224 per cent and 324 per cent. Each of these differences is statistically significant ($P < 0{\cdot}02$).

After correction for percentage recovery, the isotope results were a mean of 108 per cent of direct-flow measurement in the control period and of 103 per cent in shock, neither difference being statistically significant. The corrected isotope-flow results were still respectively 147 per cent and 167 per cent of the electromagnetic flowmeter readings in the control and shock periods, the former difference being significant at the 5 per cent level. Thus, the incomplete recovery of the isotopes provides a satisfactory explanation for the differences between isotope and direct-flow measurements, and partially explains the discrepancy between the isotope method and the electromagnetic flowmeter.

Mean Transit Time.—The mean transit time for both plasma and erythrocytes varied with the organ studied. During the control period the average for the two isotopes ranged from 14·1 (± 2·2) seconds for the renal circulation to 31·4 (± 5·0) seconds for the intestine, and 40·5 (± 11·8) seconds for the hindlimb. In shock the mean values were 79·7 (± 43·7) seconds for the small intestine, 92·7 (± 42·8) seconds for the kidney, and 121·8 (± 42·0) seconds for the hindlimb.

In every instance the mean transit time was shorter for erythrocytes than for plasma. The excellent correlation between the paired values in the hindlimb is shown in *Fig.* 3, the correlation coefficient being 0·997 for the control period and 0·993 in shock. The regression lines for the control and shock periods are not significantly different. The results for the renal and intestinal circulations showed a very similar pattern.

Comparisons between the relative transit times for erythrocytes and plasma in the three vascular beds and in the control and shock periods have been made by expressing the mean transit time for erythrocytes as a percentage of the concurrent result for plasma. The individual values ranged from 84·1 per cent to 98·9 per cent. The mean values for each vascular bed in the control and shock periods are given in *Table V*. They range from 92·4 (± 3·8) per cent in the renal circulation in the shock period to 94·0 (± 3·5) per cent in the small intestine, also in shock. Student's *t*-test showed no significant difference between any two organs, or between the control period and the shock period in any of the vascular beds studied ($P > 0\cdot 2$ in every case).

Table V.—MEAN TRANSIT TIME FOR ^{51}Cr R.B.C.S AS A PERCENTAGE OF MEAN TRANSIT TIME FOR ^{125}I H.S.A.

VASCULAR BED	NO OF DOGS*	CONTROL PERIOD	SHOCK PERIOD
Hindlimb	6	93·7 ± 2·0	92·8 ± 3·3
Kidney	4	92·5 ± 2·9	92·4 ± 3·8
Small intestine	4	92·6 ± 2·8	94·0 ± 3·5

* Three readings in each period in each dog.

Table VI.—REGIONAL BLOOD-FLOW IN THE DOG AS MEASURED BY AN ELECTROMAGNETIC FLOWMETER

AUTHOR	BLOOD-FLOW (Mean Result in ml. per min. per kg. Body-weight)						SEVERITY OF SHOCK	
	Control Period			*Shock Period*				
	Femoral Artery	Renal Artery	Superior Mesenteric Artery	Femoral Artery	Renal Artery	Superior Mesenteric Artery	Volume bled	Duration (min.)
Smith, Reeves, and Hinshaw (1965)	5·6	10·0	9·2	0·7	3·4	2·7	25 ml. per kg.	150
Brobmann, Underwood, McCoy, Price, and Jacobson (1970)	3·4	10·3	16·0	0·9	6·0	6·2	30 per cent	30
Present series	2·7	7·2	11·5	0·7	1·1	3·1	25–30 ml. per kg.	45

DISCUSSION

A dual-label isotope technique such as this does not appear to have been applied previously to a comparison of erythrocyte and plasma circulation times in shock. The method therefore requires careful appraisal.

Blood-flow.—The good correlation observed between the whole-blood flow rates calculated from the dilution curves for each isotope (*Table I*) indicates that the measurements of radioactivity in both the control and the shock phase were of satisfactory accuracy. Conventional reproducibility studies were impracticable because equilibration of the injected isotopes throughout the animal is required before the next reading; during this 15-minute period the flow rates (as indicated by the electromagnetic flowmeter) often changed. An explanation is required for the difference (up to threefold) between the blood-flow as measured by the isotope-dilution technique either directly or by the electromagnetic flowmeter. Strictly, the indicator-dilution method of blood-flow measurement gives the flow in the artery into which the injection is made and assumes that the whole bolus passes peripherally in that artery and ultimately reaches the venous monitor (Powers and Sevelius, 1965). Our experimental preparations may fail to meet these ideals in two respects: some of the injected material may spill over into arteries upstream of the catheter tip and so perfuse other vascular beds and, in the limb, part of the venous return may by-pass the cannulation site. Even though the kidney appears to have an ideal 'end artery' for these studies, a rapid injection could reflux into the aorta. Experiments have confirmed that soon after injection via the renal or superior mesenteric arterial catheters a brief peak of radioactivity can be detected over the femoral artery. The vascular anatomy of the hindlimb is also compatible with the second explanation, for a large profunda femoris vein joins the common femoral vein just above the level of cannulation and could account for the lower percentage recoveries in this group of experiments. The variation in isotope recovery rates between individual experiments on the same organ may be attributed to differences in the siting of the catheter tip, or in the volume of the bolus (Hobbs, Agrifolio, and Edwards, 1962), or in the relative sizes of main and collateral veins. The lower recoveries in shock may be due to greater arterial overspill occurring at lower flow rates. These suggested explanations for the differences between the uncorrected isotope blood-flow rates and the electromagnetic flowmeter readings are supported by the improved relationships obtained after correction of the former for the percentage recovery of the isotopes (*Table IV*). The residual 25 per cent difference between the corrected isotope results and the electromagnetic flowmeter measurements is similar to the 19 per cent excess of the isotope-dilution flow results over the readings of a mechanical flowmeter reported by Hobbs and others (1962). Both differences are unexplained.

The values obtained for regional blood-flow vary widely between authors. Hobbs and others (1962), in a review of the literature concerning femoral arterial flow in the dog, found results ranging from 1·4 to 41·0 ml. per minute per kg. body-weight. In this context our results, using a cannulated electromagnetic flowmeter, are consistent with recent reports of measurements by a 'wrap-around' instrument (*Table VI*).

The calculation of mean transit times from the indicator-dilution curves, fortunately, is not dependent upon any assumptions concerning isotope-recovery rates. The finding in the control period of erythrocyte transit times 6–8 per cent shorter than those for plasma is in accordance with previous reports. There were no significant differences between the three vascular beds studied (*Table V*). Rowlands and others (1963), using the anaesthetized cat, found that red-cell transit from the femoral artery to the femoral artery was 14 per cent shorter than that for plasma. This effect was considered to be due to axial streaming of erythrocytes in the smaller blood-vessels. A similar mean difference of 14·5 per cent had been found in the renal circulation in dogs by Lilienfield, Rose, and Porfido (1957), though they attributed it to preferential arteriovenous shunting of erythrocytes. In man Larsen and Lassen (1964) reported a mean 12 per cent lead for red cells over plasma between the carotid artery and the jugular bulb.

The more rapid transit time for erythrocytes must, in a steady state, be accompanied by a lower haematocrit in the microvasculature than in large vessels. Williams (1965) has demonstrated such a relationship in dogs. The whole-body haematocrit was measured by a dual-label equilibration method and erythrocyte and plasma transit times were compared using the same indicators. The shorter the transit time of the red cells relative to the plasma, the lower was the ratio of the whole-body haematocrit to the venous haematocrit. Thus, the ratio of erythrocyte to plasma transit times provides an indirect measure of the haematocrit of the blood flowing through the microcirculation.

Haemorrhagic Shock.—The normal relationship between erythrocyte and plasma transit times was not significantly altered in this haemorrhagic shock preparation (*Fig.* 3; *Table V*). There was not a single reading in which the red cells were slower than the plasma. These results do not appear to be compatible with a haemodynamically significant degree of slowing of erythrocytes relative to plasma or with any increase in the microvascular haematocrit. They imply that the normal axial streaming of red cells is maintained.

These findings are in conflict with the evidence of *in vivo* microscopy. Chambers, Zweifach, and Lowenstein (1943) described slowing of erythrocytes relative to plasma in the whole rat following trauma inflicted in a rotating drum, and Knisely, Eliot, and Bloch (1945) noted this change in the vicinity of a localized injury. Subsequently similar observations were made in haemorrhagic shock (Zweifach, Chambers, Lee, and Hyman, 1948). A good correlation between the severity of the microscopic changes in the omentum and the percentage of the original blood-volume shed (Schumer and Durrani, 1963) suggests that the changes are closely related to the severity of shock. There are, however, three dissenting reports: Page and Abell (1943) did not see pooling or slowing of red cells in cats in tourniquet shock, while Bellman, Lambert, and Fine (1962) saw sludging in rabbits in haemorrhagic shock only in the vicinity of local trauma; in dogs in haemorrhagic shock Stallworthy, Ramirez, Barrington, and Bradham (1969) found no slowing or margination of individual R.B.C.s, though they did note the formation of masses of erythrocytes when flow temporarily ceased in a vessel. *In vivo* microscopy has two apparent limitations: although erythrocyte movement is obvious the plasma flow rate can only be inferred from the movement of platelets; also the appearances may be dependent upon local damage resulting from placement upon the microscope stage or insertion of a quartz rod into a solid viscus for illumination.

The discrepancy between the quantitative findings in our experiments and the changes reported on microscopy might be due to an insufficiently severe degree of shock in the present study or to some misinterpretation of the microscopic appearances. The volumes bled and the resulting reductions in blood-flow were similar to those reported by others (*Table VI*). Unfortunately, the descriptions of microcirculatory changes in haemorrhagic shock do not include measurements of regional blood-flow, but Schumer and Durrani (1963) and Matsumoto, Hardaway, and McClain (1967) do state that the 'sludging' of erythrocytes occurred as haemorrhage approached 50 per cent of the initial blood-volume. We have no data for blood-volume, but taking the initial value as 9·25 per cent of body-weight (Sjöstrand, 1962) the volumes bled in the present series would range from 26 to 42 per cent of the total. The deaths of 5 dogs before completion of the experiments likewise argue that our animals were truly shocked. Nevertheless, a more prolonged shock procedure or induction by methods other than haemorrhage might yield different results.

Hardaway and Drake (1963) have offered an alternative interpretation of the microvascular changes in shock. They consider that as shock proceeds an increasing proportion of the small blood-vessels becomes occluded by thrombosis. The present dynamic studies would be unlikely to register immobilization of erythrocytes by this process. The heparin given in the experiments on the hindlimb might prevent such microthrombosis, but as heparin was not used in the renal and intestinal studies it cannot be responsible for our inability to detect 'sludging' of red cells.

CONCLUSIONS

The discrepancy between the lack of slowing of erythrocytes relative to plasma in our quantitative studies and the 'sludging' seen on microscopy seems likely to be the result of a misinterpretation of the latter appearances. These may represent a combination of an effect of local trauma and the development of microvascular thromboses. There is at present no quantitative haemodynamic evidence to provide a rationale for the choice of an 'anti-sludging' agent, such as low-molecular-weight dextran, for intravenous infusion in haemorrhagic shock.

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THORACIC ENTERIC CYSTS AND DIVERTICULAE

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ROYAL MANCHESTER CHILDREN'S HOSPITAL, PENDLEBURY

SUMMARY

Six cases of thoracic enteric cysts and diverticulae are described to illustrate a manifestation of the split notochord syndrome. The varied clinical, radiological, and operative picture in these cases is emphasized, the common triad being respiratory symptoms, a posterior mediastinal mass, and a vertebral anomaly. The symptoms may, however, be entirely gastro-intestinal in the form of abdominal enlargement or gastro-intestinal haemorrhage. Because of the diversity of presentation these patients may come under the domain of the paediatric surgeon, the thoracic surgeon, or the neurosurgeon, and occasionally a combined team approach may be required to obtain satisfactory results in surgical treatment, which is mandatory.

ALIMENTARY tract duplications, to use the term in its broadest sense, may occur anywhere from the mouth to the anal canal. The duplications have a wall in which normal bowel structure is reproduced and a mucosal lining in which one or more types of epithelium are represented. From an aetiological point of view the duplications may be divided into two groups:—

1. Those that result from a localized fault in development and include most intra-abdominal duplications, which are not discussed further in this paper.
2. Those associated with vertebral anomalies and include thoracic enteric cysts and duplications, which, according to the terminology proposed by Bentley and Smith (1960), should be called 'prevertebral enteric cysts' and 'thoracic enteric diverticulae'.

Vertebral anomalies are also seen in association with duplications of the colon and the anal canal (Soper, 1968; Smith, 1969), although not as frequently as in thoracic duplications. Occasionally a thoracic duplication may be seen without a demonstrable vertebral anomaly.

Apart from enteric malformations, developmental anomalies of the skin and the central nervous system are often seen in association with vertebral anomalies. These may be included collectively under the term the 'split notochord syndrome' (Bentley and Smith, 1960). The purpose of this paper is to review the clinical manifestations of this syndrome as applied to thoracic enteric cysts and diverticulae which are illustrated by 6 cases admitted to the Manchester Children's Hospitals during the years 1960 up to 1971. All the cases occurred in male children, all of whom survived.

CASE REPORTS

Case 1.—D. W. has previously been reported by Goldberg and Johnson (1963). He presented at the age of 6 days having had breathlessness and cyanosis since birth. A chest radiograph showed an air-filled cyst in the right lower chest and a spinal anomaly, which consisted of hemivertebrae of the whole cervical and upper dorsal spine.

Barium-meal and follow-through examination showed a normal stomach and malrotation of the midgut. In addition barium was seen to enter a blind loop of jejunum and pass upwards through the diaphragm into the right pleural cavity, where it filled the previously noted air-filled cyst. Through separate abdominal and thoracic incisions, a massive thoracic enteric diverticulum was removed, along with a segment of normal jejunum with which it communicated. The child made an excellent postoperative recovery and is now 10 years old with no disability and no positive neurological signs although a chest radiograph shows a complex anomaly of the cervico-dorsal spine (*Fig.* 1).

The surgical specimen consisted of small intestinal structures only. It was 33 cm. long (9·5 cm. subdiaphragmatic and 23·5 cm. supradiaphragmatic) and joined the resected jejunum obliquely end to side.

Case 2.—I. W. was first admitted to Manchester Children's Hospital at the age of 2 years. At birth he had had severe respiratory depression, which was considered to be due to an intracranial haemorrhage, from which he had recovered satisfactorily. This had been followed by several episodes of respiratory infection and his mother also thought that on one occasion his sputum had been blood-stained.

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At birth he had also been noticed to have a large abdomen which had become bigger (*Fig.* 2). A barium enema had shown no evidence of Hirschsprung's disease. Later he had had abdominal pain and vomiting and he had brought up blood and mucus.

A barium-meal examination showed a normal oesophagus and stomach with no evidence of gastro-oesophageal reflux. A follow-through film showed no change in the bowels except for failure of descent of the caecum. He had some occult blood in the stools and

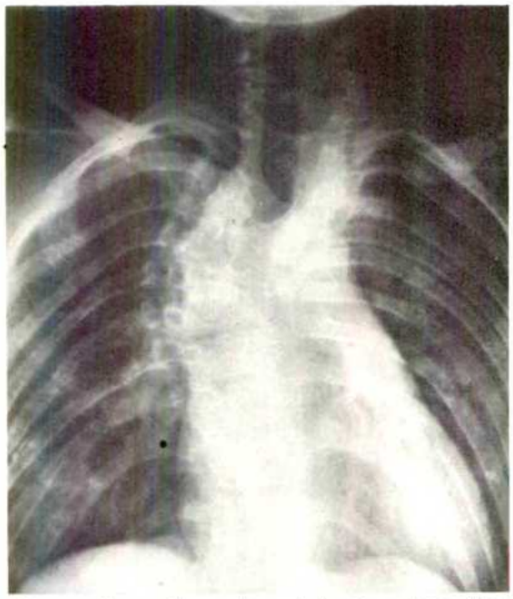


Fig. 1.—*Case* 1. Chest radiograph showing scoliosis. Hemivertebrae in the cervical and dorsal spine up to D.V. 7, and diastematomyelia were noted on tomograms.

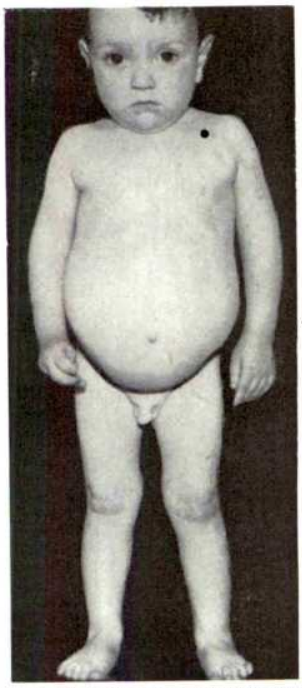
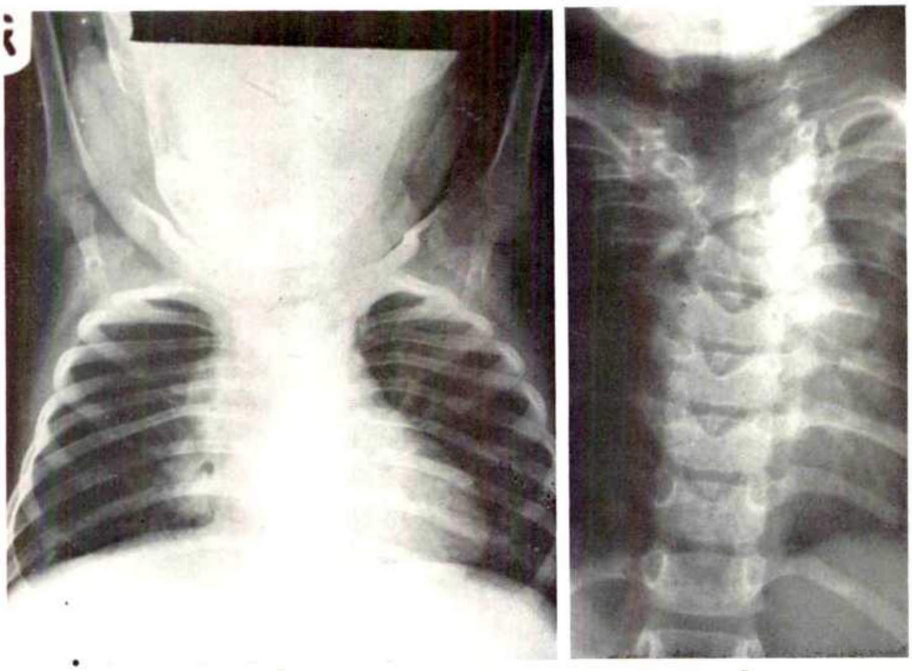


Fig. 2.—*Case* 2. I. W., aged 2 years, showing abdominal enlargement in an otherwise well-nourished child.



A

B

Fig. 3.—*Case* 2. A, Preoperative chest radiograph showing a right hilar shadow. An anomaly of the spine had also been observed preoperatively but a hemivertebra (D.V. 4) is more clearly seen in B, which is a postoperative film.

an iron-deficiency anaemia. Liver-function tests and absorption studies were normal.

Some months later a chest radiograph showed a hilar shadow on the right and an anomaly of the upper dorsal spine (*Fig.* 3). The significance of this was not appreciated at first. Investigation for tuberculosis was negative. After a frank haemoptysis, a tomogram and bronchoscopy were performed.

The radiographs showed compression of the right main bronchus by a mass and enlargement of the perihilar

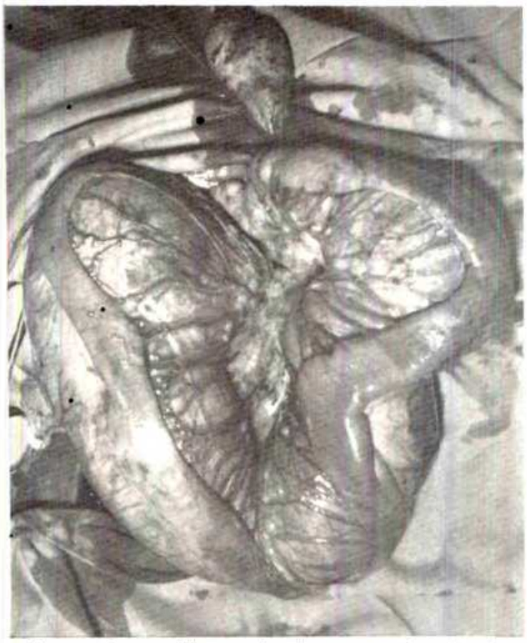


FIG. 4.—*Case* 2. Photograph taken at operation showing a massive jejunal duplication lying in the mesentery with the normal bowel stretched over it. The upper blind end of the duplication is seen at the top of the picture.

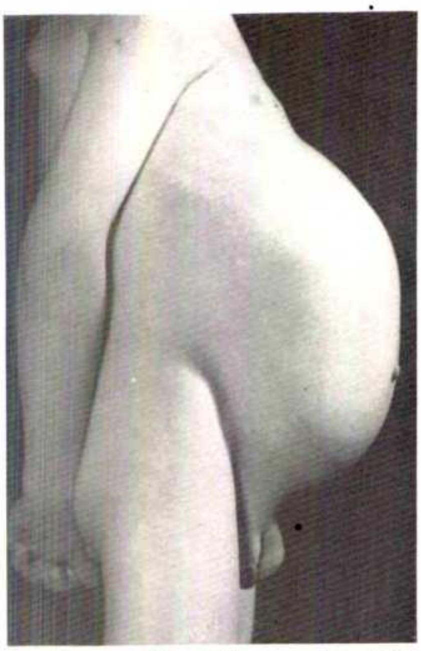


FIG. 5.—*Case* 4. H. B., aged 5 years, with a very large protuberant abdomen.

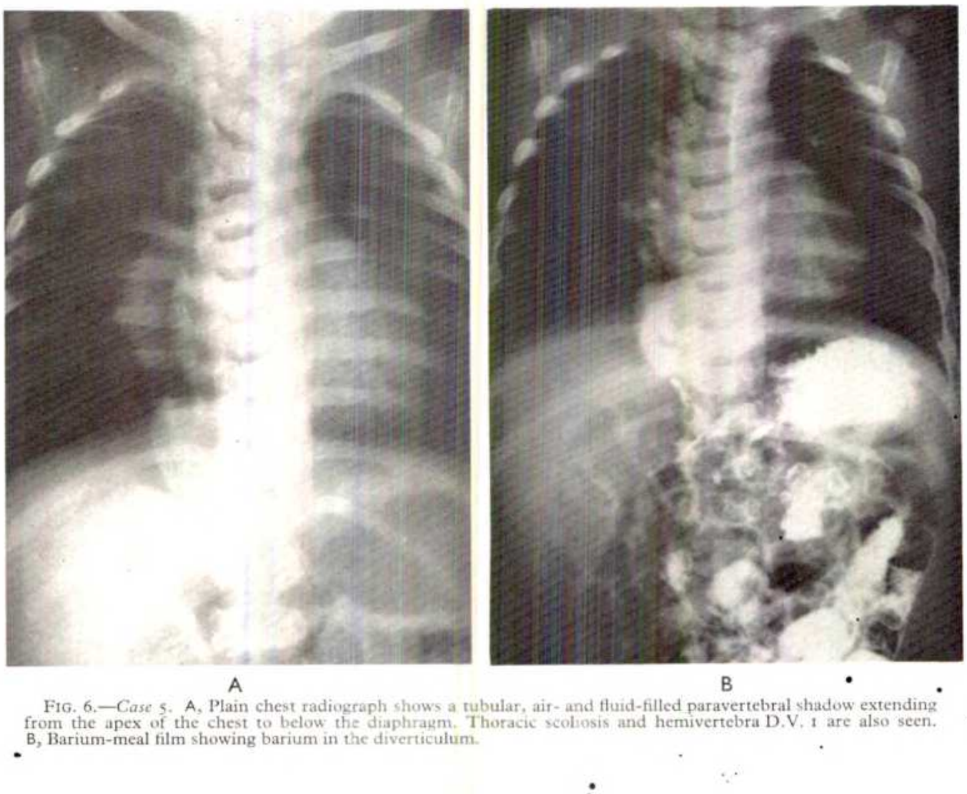


FIG. 6.—*Case* 5. A, Plain chest radiograph shows a tubular, air- and fluid-filled paravertebral shadow extending from the apex of the chest to below the diaphragm. Thoracic scoliosis and hemivertebra D.V. 1 are also seen. B, Barium-meal film showing barium in the diverticulum.

lymph-glands. Bronchoscopy (J. F. D.) confirmed that the right main bronchus was occluded by an ulcerated mass. Biopsy showed some gastric tissue with peptic ulceration. This finding along with the vertebral anomaly eventually indicated the diagnosis of thoracic enteric cyst.

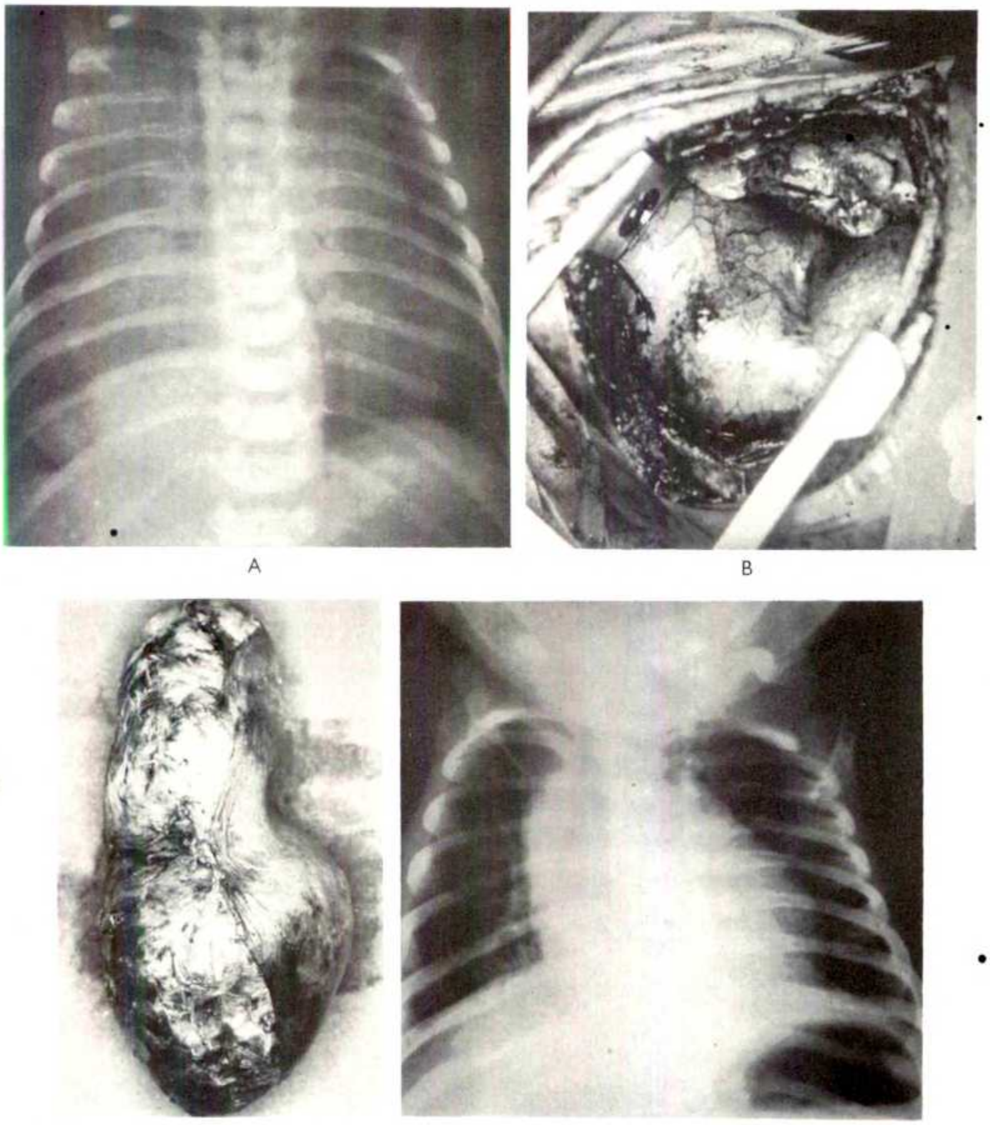


FIG. 7.—*Case* 6. A, Preoperative chest radiograph showing a large opaque mass occupying the right side of the chest. B, Operative photograph showing the cyst bulging forward. C, The surgical specimen. D, Postoperative chest radiograph showing complete expansion of the right lung.

At thoracotomy (J. F. D.) through the fifth right intercostal space the findings were as follows:—

1. A large cyst (9 × 5 cm.) high in the posterior mediastinum enveloped the right main bronchus with which it communicated posteriorly. The cyst was removed and the hole in the bronchus was repaired.
2. A second cyst (4 × 2·5 cm.) lying loosely attached to the lower oesophagus was removed.
3. A third cyst was just visible protruding through the posterior part of the diaphragm. This was left.

There were considerable respiratory problems postoperatively which required a tracheostomy, but the patient eventually recovered satisfactorily.

In view of these findings and the abdominal enlargement it was surmised that an abdominal duplication was also present although it could not be demonstrated by palpation or radiographic examination. A laparotomy was undertaken 10 weeks later (A. J.). From a point 15 cm. from the duodenojejunal flexure a duplication was closely applied to the jejunum for a distance of 75 cm. It lay in the mesentery and its upper end ran upwards to the oesophageal hiatus retroperitoneally (*Fig.* 4). Both ends were blind. The duplication was removed along with the attached bowel and the child made an uneventful recovery.

He has remained well with no thoracic, abdominal, or neurological problems.

Pathological examination showed that the thoracic cysts were lined with columnar and squamous epithelium, some of which had a typical gastric pattern with ulceration in one area. Smooth muscle in the wall was infiltrated with inflammatory cells, granulation tissue, and fibrous tissue. The jejunal duplication had two layers of smooth muscle in the wall and was lined with ciliated columnar and transitional epithelium.

Case 3.—W. K., aged 2 years, was admitted with a 3-month history of fever and a cough which had not responded to antibiotics. A chest radiograph showed a left lower-lobe shadow and primary tuberculosis was suspected. An additional finding, however, was the presence of anomalies of the upper dorsal vertebrae with widening of the interpedicular spaces. Further radiographs showed the mass to be in the posterior mediastinum and the combination of these radiological features supported the alternative diagnosis of an enteric cyst.

At thoracotomy (J. F. D.) through the fifth left intercostal space a spherical cyst, 5 cm. in diameter, projecting forwards from the 4th, 5th, and 6th vertebrae was noted and removed. Postoperative recovery and follow-up were satisfactory.

Pathological examination showed an ovoid cyst containing mucoid fluid with patchy representation of circular and longitudinal muscle in its wall and a gastric mucosal lining with oxyntic cells.

Case 4.—H. B. presented with the problem of chronic constipation at the age of 5 years. Examination revealed a massive abdomen with signs of intestinal obstruction (*Fig.* 5). Abdominal radiographs supported the clinical findings, a few fluid levels being noted on the erect film. A barium-enema examination was reported as being normal. A chest radiograph showed a soft-tissue mass in the right upper mediastinum and anomalies of the bodies and posterior spines of the lower cervical and upper dorsal vertebrae. These findings were suggestive of a thoracic enteric cyst but in view of the presence of intestinal obstruction laparotomy was undertaken first.

At operation (A. J.) a large tubular duplication over 100 cm. long and 7 cm. in diameter was found. The duplication lay in the mesentery, was blind at both ends, and extended from the mid-jejunum to the mid-ileum. It was resected along with the attached bowel, the child being left with about 160 cm. of residual small bowel. Postoperative recovery was uneventful.

Three months later thoracotomy was undertaken (J.F.D.) through the fifth right intercostal space. A thick-walled cyst, 10 × 5 cm., was found lying posteriorly in the upper mediastinum. It had a pedicle which ran into a large defect in the side of an anomalous vertebral body. Further dissection revealed that it was actually two cysts, one containing cerebrospinal fluid (anterior meningocele) and the other mucoid material (enteric cyst). Both cysts were removed and a small leak of cerebrospinal fluid was controlled by the application of a patch of muscle. A good recovery followed.

There was no communication between the thoracic and abdominal cysts. All three cysts had a wall of smooth muscle. Whereas the meningocele was lined with collagenized fibrous tissue with no epithelial lining, the enteric cysts were lined with columnar and stratified epithelium, some of which was ciliated.

Case 5.—D. B. was admitted at the age of 6 months with recurrent episodes of a cough since birth. On examination he had tachypnoea with an audible wheeze and rhonchi in all areas. A chest radiograph showed a tubular shadow containing air and fluid which could be traced to below the level of the diaphragm and these findings were confirmed by a barium-meal examination. There was also an obvious anomaly of the upper dorsal spine (*Fig.* 6).

A single-stage thoraco-abdominal operation was performed, entering the chest through the fifth right intercostal space and the abdomen through a right paramedian incision (A. J.). There was a tubular posterior mediastinal duplication. Its upper blind end extended into the root of the neck. Distally the duplication pierced the diaphragm in the region of the crura and extended retroperitoneally behind the pancreas and duodenum to enter the small-bowel mesentery and join with the jejunum end to side about 15 cm. below the duodenojejunal flexure. The duplication was removed without sacrificing any of the jejunum and a Meckel's diverticulum was also removed. Postoperatively there was some degree of ileus but eventual recovery was satisfactory.

Pathological examination showed two muscle coats and a gastric mucosal lining with oxyntic cells but there was also some duodenal and squamous epithelium. There were neurons in some intermuscular areas but in others compact aganglionic fibres were noted.

Case 6.—J. U. was admitted a few days after birth with a history of respiratory distress with intercostal recession. A chest radiograph showed a mass in the right side (*Fig.* 7 A) without an obvious vertebral anomaly. A barium-meal examination was normal. The symptoms steadily got worse until operation (J. F. D.) at the age of 6 weeks (right thoracotomy through the bed of the sixth rib). A bilobar cyst, 11 × 5 × 7·5 cm. (*Fig.* 7 B), was lying retropleurally in the right paravertebral gutter with the azygos vein lying across its waist. One hundred and sixty ml. of mucoid fluid were aspirated from the cyst which was closely applied to the oesophagus and descending aorta with numerous vascular adhesions. The cyst was removed with some difficulty (*Fig.* 7 C) but it had no obvious connexion with the spinal column. Postoperative recovery was uneventful (*Fig.* 7 D).

Pathological examination demonstrated that the cyst wall consisted of two layers of intestinal muscle and a muscularis mucosa but the mucosal lining was not evident and had presumably been destroyed.

DISCUSSION

The 6 cases described in this paper illustrate the varied spectrum as regards symptomatology, radiological anatomy, and surgical anatomy in cases of thoracic enteric cysts and diverticulae.

The clinical presentation was primarily as a respiratory problem in some cases but in others abdominal symptoms were predominant; occasionally respiratory and abdominal symptoms were present in the same patient.

The respiratory symptoms were commonly dyspnoea and cyanosis, recurrent bronchitis or pneumonia, and haemoptysis in 1 case. In the 2 neonates (*Cases* 1 and 6) there was severe respiratory distress and it may be difficult to differentiate such cases from congenital diaphragmatic hernia (Ravitch and Sabiston, 1962). It is important that these patients be operated upon as a matter of some urgency as the respiratory problem is liable to be aggravated with increasing accumulation of fluid in the cyst.

Case 3 presented with recurrent bronchitis and was the only case with an enteric cyst in the left side of the chest. Although tuberculosis had been suspected, localization of the mass to the posterior mediastinum in association with a spinal anomaly clinched the diagnosis. *Case* 5 also presented with a history of recurrent bronchitis since birth. Presumably mucous secretions produced by the tubular diverticulum discharged spontaneously into the jejunum with which it communicated, thereby preventing development of acute respiratory symptoms.

Case 2 presented primarily with abdominal symptoms at the age of 2 years, although there had been recurrent episodes of respiratory infections since birth. By the time he came to surgery a year later respiratory symptoms overshadowed the persisting abdominal problem. The occurrence of haemoptysis as a complication of thoracic enteric cyst has been reported previously (Ravitch and Sabiston, 1962), but because of extensive damage to the lung from peptic ulceration lobectomy may sometimes be necessary (Le Roux, 1962). The diagnosis in our case was delayed and illustrated the difficulty that may arise in differentiating haemoptysis from haematemesis in the paediatric age-group. It seems advisable that apart from radiological evaluation of the chest and spine such cases should be subjected to oesophagoscopy as well as bronchoscopy to enable an earlier diagnosis to be made. Melaena was a late manifestation in this case although occult blood had been noted in the stool some months earlier. A thoraco-abdominal duplication may, however, present primarily with alimentary-tract bleeding, as has been reported frequently (Davis and Barnes, 1952; Beardmore and Wiglesworth, 1958).

Cases 2 and 4 demonstrated the association of extensive intra-abdominal duplications with separate thoracic lesions and also emphasized the need to consider intestinal duplication in the differential diagnosis of abdominal enlargement in childhood. The importance of radiological evaluation of the chest and spine in patients with abdominal duplication is illustrated. In 1 case the thoracic cyst was asymptomatic and similar cases have been observed by several writers (Fallon, Gordon, and Lendrum, 1954; Forshall, 1961).

The radiological features of the 6 cases form an interesting study. A posterior mediastinal shadow in a child with respiratory symptoms but occasionally with only abdominal symptoms is usually the first positive finding. Apart from being aware of the possible 'enteric' origin of the mass, the most important supportive investigation is radiological evaluation of the spine. The mediastinal shadow may contain air if a communication exists with some part of the alimentary tract (a diverticulum) and this may be demonstrated by radio-opaque studies which should always be performed.

Spinal radiographs were normal in 1 of our cases but in the others there was an anomaly which ranged from a single hemivertebra to a complex anomaly of the cervicodorsal spine. Veenaklass (1952) advised tomograms to demonstrate the spinal defect. Beardmore and Wiglesworth (1958) pointed out that the cysts may be considerably caudal to the vertebral anomaly and may therefore be missed on routine radiographs. In our cases, however, the anomalous spine and the cysts were in close proximity although they did extend caudally to a variable degree.

Thoracic enteric masses are not common. Morrison (1958) found only 15 out of 1055 published cases of mediastinal masses to be enteric in origin and 5 of his 6 cases of enteric cysts were in the paediatric age-group. In a review of mediastinal masses in childhood, Haller, Mazur, and Morgan (1969) found 10 out of 80 cases to be enteric in origin and Ravitch and Sabiston (1962) have quoted similar figures.

According to the operative findings the clinical material reported in this paper can be divided into three groups:—

1. Prevertebral thoracic enteric cysts (*Cases* 3 and 6).
2. Prevertebral thoracic enteric cysts with abdominal duplications in the same patient (*Cases* 2 and 4).
3. Communicating thoraco-abdominal enteric diverticulae (*Cases* 1 and 5).

The non-communicating thoracic cysts, with increasing accumulation of mucous secretions, are likely to enlarge with corresponding deterioration in the clinical picture. This is not usually observed with bronchogenic mediastinal cysts which are usually diagnosed later in life (Ravitch and Sabiston, 1962). As the cyst enlarges it may eventually burst or erode into the lung or the bronchus, when the patient will present with chest pain or haemoptysis.

In the communicating thoraco-abdominal diverticulae air and barium-filled segments were seen on chest radiographs. In both the cases described the diverticulum was tubular and joined the jejunum end to side, as in the original description by Gross, Neuhauser, and Longino (1950). Barlow (1965) described in detail the surgical anatomical course taken by such a case. Elwood (1959) described the autopsy findings in a similar case in a neonate with the stump of the diverticulum attached to the spinal cord. This and similar cases in the literature and the association of a large anterior meningocele with the enteric cyst in *Case* 4 are understandable if it is accepted that they are of common derivation as part of the split notochord syndrome. Such an association has also been observed in duplications of the anal canal (Smith, 1969).

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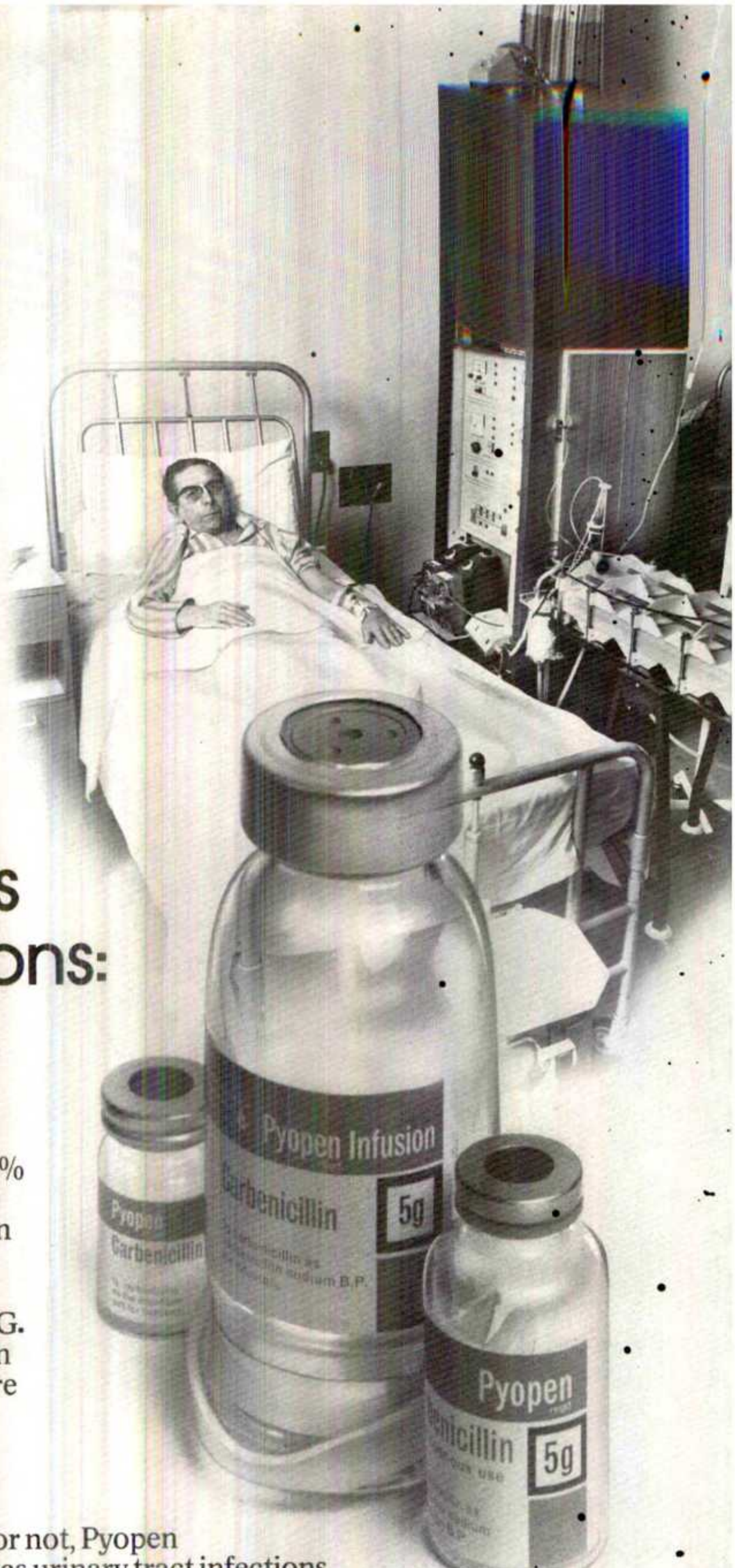

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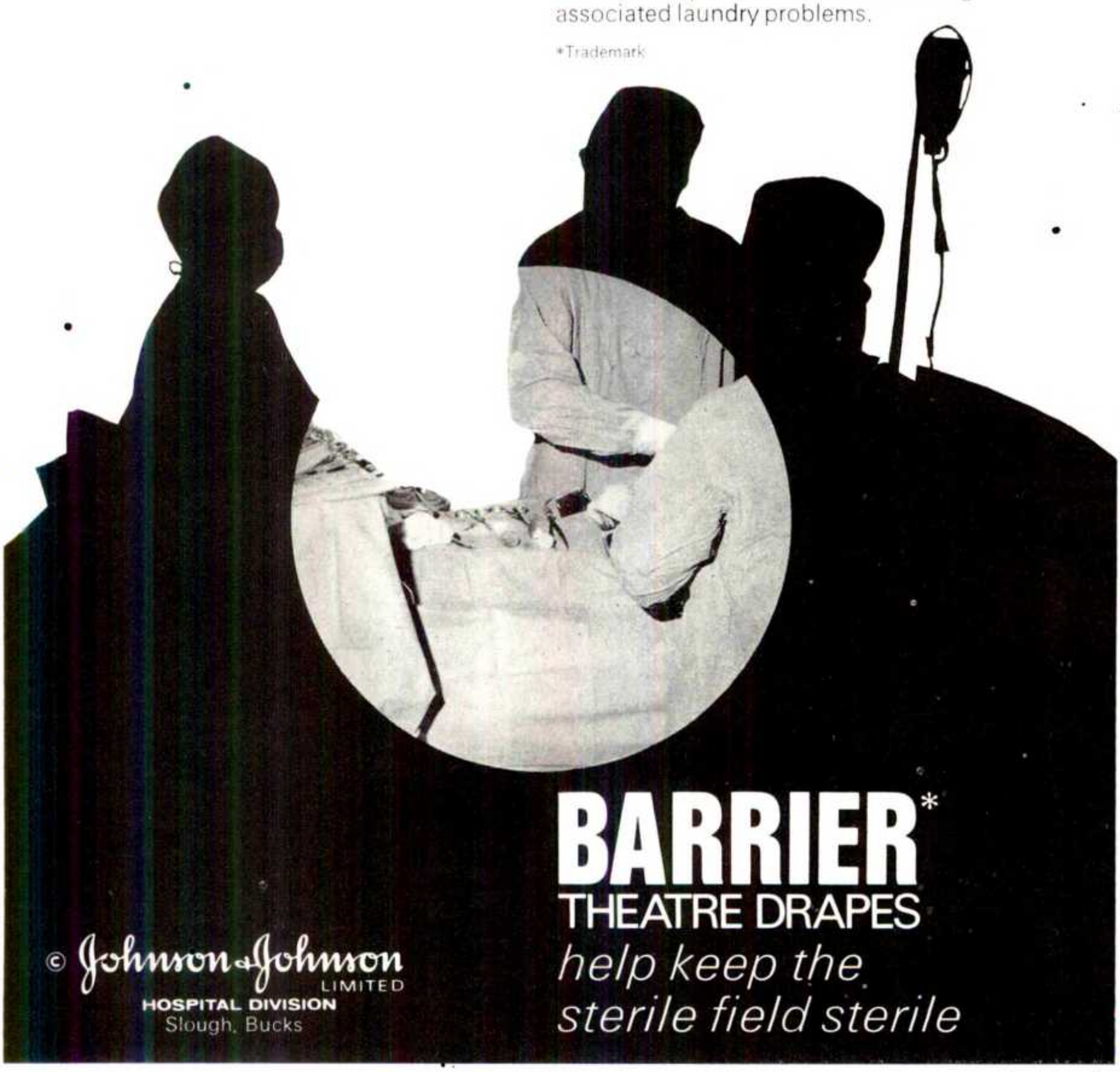

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At this stage the specimen was retained only by the ureter, the lower inferior vena cava, and the aorta, and the liver was well cooled by the perfusion. The crura were split and the thoracic aorta was exposed. Intercostal arteries were secured and the aorta was cut across obliquely with an anterior bevel about 2 cm. above the coeliac origin. The ureter and lower cava were divided and the specimen was freed. The last 500 ml. of perfusate with added papaverine (50 mg.) were injected into the aorta to flush out the kidney and pancreas; care was taken to avoid introducing air. The aortic cannula was removed and the aorta was ligated at its lower end, but the portal cannula was left in place to facilitate identification of the collapsed portal vein (*Fig.* 7).

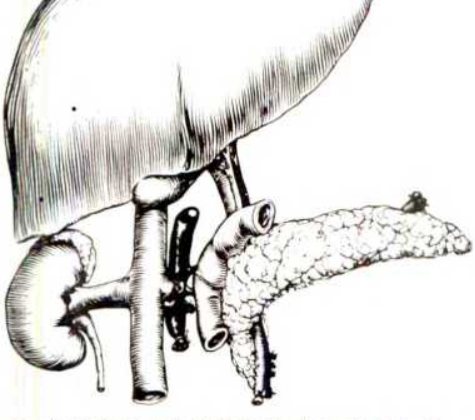

FIG. 7.—A specimen excised from the donor for simultaneous orthotopic transplantation of the pancreas, liver, and kidney.

Recipient.—This is very similar to that described for the orthotopic liver and pancreas transplantation, except that the additional transplantation of the kidney required that the inferior vena caval anastomosis was performed caudal to the renal veins and the recipient's kidneys were removed. The ureter was anastomosed obliquely end to end with a running 0000 chromic catgut suture. The aortic segment containing the orifices of the coeliac, the superior mesenteric, and the right renal arteries was anastomosed to the recipient aorta above the renal vessels end to side with a running 0000 silk suture (*Fig.* 8).

RESULTS

There were survivors following all the operative procedures described above. Some of the details are summarized in the tables.

1. Heterotopic Liver Transplantation (*Table I*).—Of the 6 allografted animals, 2 survived under a week. The grafts showed mononuclear-cell infiltration. The 4 remaining animals survived between 78 and 525 days. Early biopsies showed liver-cell atrophy and mononuclear-cell infiltration. The 3 animals surviving more than 500 days had completely absorbed the liver allografts which could not be found at autopsy.

2. Heterotopic Cardiac Transplantation (*Table II*).—The 3 animals survived for between 6 and 47 days. The 2 that died at 6 and 7 days after transplantation had marked changes of rejection. The animal that lived 47 days had the cardiac allograft biopsied at 7 and 18 days. On each occasion there was slight mononuclear-cell infiltration. At autopsy at 47 days there was marked cellular infiltration and aneurysmal dilatation of the left ventricle.

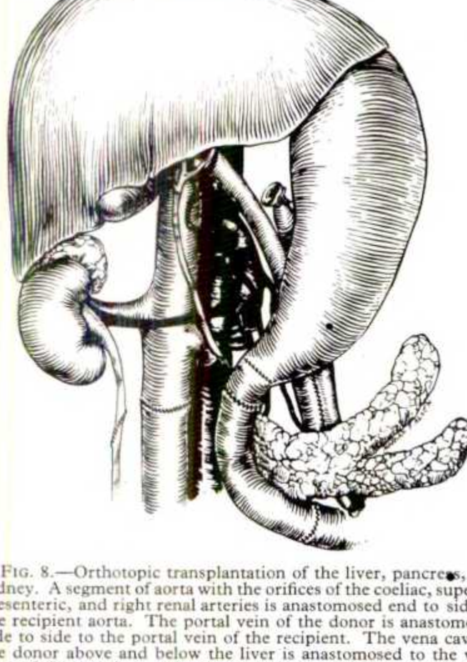

FIG. 8.—Orthotopic transplantation of the liver, pancreas, and kidney. A segment of aorta with the orifices of the coeliac, superior mesenteric, and right renal arteries is anastomosed end to side to the recipient aorta. The portal vein of the donor is anastomosed side to side to the portal vein of the recipient. The vena cava of the donor above and below the liver is anastomosed to the vena cava of the recipient. The ureter of the donor is anastomosed to the ureter of the recipient obliquely. The second part of the donor duodenum is anastomosed to the first and third parts of the recipient duodenum. Biliary and pancreatic drainage is into the donor second part of the duodenum. Vagotomy and pyloroplasty have been performed.

3. Heterotopic Heart and Liver Transplantation from Same Donor (*Table III*).—The 4 animals survived for between 7 and 203 days. The 2 that died at 7 and 22 days had changes of rejection in both the heart and liver allografts. The liver allograft was removed after 6 days in the animal which lived for 69 days, at which time there were changes of rejection in both the liver and the cardiac allografts. The 69-day autopsy showed marked changes of rejection with necrosis of the myocardium. The animal that lived for 203 days had the liver allograft removed at 15 days, at which time both the liver and heart allografts had marked changes of rejection. Similar changes were shown in a biopsy of the heart allograft at 36 days. At autopsy the heart had been completely absorbed.

4. Orthotopic Renal Transplantation.—Thirty grafts were performed and these were examined between 5 and 33 days after operation; 29 showed moderate to severe macroscopical and microscopical features of rejection. One allograft had a normal appearance after 12 days.

5. Heterotopic Liver and Orthotopic Kidney Transplantation from the Same Donor (*Table IV*).—Three animals died within a week. One of these died from rejection of the kidney; the liver was removed after 2¼ hours in the recipient. The animal that lived for 4 days had the liver allograft removed after 24·hours. The kidney at autopsy had slight mononuclear-cell infiltration. The animal that lived for 6 days had moderate mononuclear-cell infiltration of the liver and slight infiltration of the kidney. One animal died at 23 days with rejection changes in both the liver and kidney allografts. One animal in which the liver was removed after 24 hours died from uraemia with rejection of the kidney after 55 days. One animal lived for 95 days, dying of peritonitis. The liver was removed after 14 days, when it showed considerable mononuclear-cell infiltration. The renal biopsy at that time was normal. At autopsy, however, the kidney had substantial mononuclear-cell infiltration. Two animals are alive after 2½ and 3¼ years. The first of these had the liver allograft removed after 24 hours and is now surviving on the renal allograft. The second had a biopsy of both allografts at 20 days and there was moderate mononuclear-cell infiltration in the kidney and slight infiltration in the liver. Further biopsy at 96 days showed slight mononuclear-cell infiltration of the liver and a normal appearance of the kidney. Biopsy at 581 days showed marked atrophy and fibrosis of the liver and occasional foci of mononuclear cells in the kidney which was providing normal renal function.

Table I.—RESULTS OF HETEROTOPIC LIVER TRANSPLANTATION

PIG	SURVIVAL (days)	CAUSE OF DEATH	HISTOLOGY
1	4	Intestinal obstruction	Considerable mononuclear-cell infiltrate
2	6	Intestinal obstruction	Moderate mononuclear-cell infiltrate
3	78	Intestinal obstruction	Centrilobular degeneration—moderate mononuclear-cell infiltrate
4	512	Killed. Allograft absorbed	Biopsy of allograft at 38 days showed liver-cell atrophy and moderate mononuclear-cell infiltrate
5	519	Killed. Allograft absorbed	Biopsy of allograft at 105 days showed liver-cell atrophy, severe chronic vascular lesions. Moderate mononuclear-cell infiltrate
6	525	Killed. Allograft absorbed	Biopsy of allograft at 55 days showed substantial mononuclear-cell infiltrate. Biopsy at 138 days showed liver-cell atrophy and slight mononuclear-cell infiltrate

Table II.—RESULTS OF HETEROTOPIC CARDIAC TRANSPLANTATION

PIG	SURVIVAL (days)	CAUSE OF DEATH	HISTOLOGY
1	6	Killed	Marked mononuclear-cell infiltrate. Necrosis of heart muscle. Fibrinous pericarditis. Endocardial thrombus
2	7	Killed	Marked mononuclear-cell infiltrate. Necrosis of heart muscle
3	47	Killed	Biopsy at 7 days: Slight mononuclear-cell infiltrate Biopsy at 18 days: Slight mononuclear-cell infiltrate Autopsy at 47 days: Marked mononuclear-cell infiltrate. Aneurysm of left ventricle

Table III.—RESULTS OF HETEROTOPIC HEART AND LIVER TRANSPLANTATION FROM THE SAME DONOR

PIG	SURVIVAL (days)	CAUSE OF DEATH	HISTOLOGY	
			Heart	Liver
1	7	Gastric haemorrhage	Slight mononuclear-cell infiltrate. Some areas of degenerate muscle	Moderate mononuclear-cell infiltrate
2	22	Cardiac arrest	Biopsy at 8 days: Substantial mononuclear-cell infiltrate Autopsy: Moderate mononuclear-cell infiltrate	Moderate mononuclear-cell infiltrate. Severe liver-cell atrophy Moderate mononuclear-cell infiltrate. Severe liver-cell atrophy
	69	Killed	Biopsy at 6 days: Moderate mononuclear-cell infiltrate. Areas of degenerating muscle Autopsy: Substantial mononuclear-cell infiltrate. Extensive muscle necrosis	Removal at 6 days showed substantial mononuclear-cell infiltrate
4	203	Gastric haemorrhage	Biopsy at 15 days: Moderate mononuclear-cell infiltrate Biopsy at 36 days: Moderate mononuclear-cell infiltrate Autopsy: Heart absorbed	Removal at 15 days showed substantial mononuclear-cell infiltrate

6. Heterotopic Pancreatic Transplantation (*Table V*).—Four animals survived for between 16 and 49 days. The longest survivor had slight mononuclear-cell infiltration in the pancreatic allograft, as did the animal that survived 16 days. The graft in the 22-day survivor was infected. The animal that died after 37 days was emaciated and had an infarcted allograft. The control animals which had pancreatectomy alone became ill after a week, suffered great weight-loss, and died emaciated with ketosis. Of 5 control pancreatectomies, the longest survival was 26 days.

7. Orthotopic Pancreatic Transplantation (*Table VI*).—Four animals survived for between 2 weeks and 50 days. The animal that lived for 14 days died from bronchopneumonia with haemorrhagic pancreatitis. The other animals had moderate mononuclear-cell infiltration of the pancreas. The longest survivor died emaciated with necrosis and atrophy of the pancreatic parenchyma in addition to the cellular infiltration.

Table IV.—RESULTS OF AUXILIARY LIVER AND ORTHOTOPIC KIDNEY TRANSPLANTATION FROM THE SAME DONOR

PIG	SURVIVAL	CAUSE OF DEATH	HISTOLOGY	
			Liver	Kidney
1	4 days	Intestinal obstruction	Removed after 24 hours. Normal	Slight mononuclear-cell infiltrate
2	6 days	Intestinal obstruction	Moderate mononuclear-cell infiltrate	Slight mononuclear-cell infiltrate
3	7 days	Uraemia	Removed after 2½ hours. Normal	Severe mononuclear-cell infiltrate and pyelonephritis
4	22 days	Wound dehiscence	Biopsy at 13 days: Moderate mononuclear-cell infiltrate. Areas of necrosis	Moderate mononuclear-cell infiltrate
			Autopsy: Centrilobular liver-cell necrosis. Slight neutrophil infiltrate	Substantial mononuclear-cell infiltrate
5	55 days	Uraemia	Removed after 24 hours. Normal	Substantial mononuclear-cell infiltrate
6	95 days	Peritonitis	Removed after 14 days. Considerable mononuclear-cell infiltrate. Liver-cell atrophy. Portal vein thrombus	Biopsy at 14 days: Normal Autopsy: Substantial mononuclear-cell infiltrate
7	2½ years	Alive	Removed after 24 hours. Normal	
8	3½ years	Alive	Biopsy at 20 days: Slight mononuclear-cell infiltrate and increase in connective tissue	Moderate mononuclear-cell infiltrate
			Biopsy at 96 days: Slight mononuclear-cell infiltrate	Normal
			Biopsy at 581 days: Marked atrophy, fibrosis, and slight mononuclear-cell infiltrate	Occasional foci of mononuclear cells

Table V.— RESULTS OF HETEROTOPIC PANCREATIC TRANSPLANTATION

PIG	SURVIVAL (days)	CAUSE OF DEATH	HISTOLOGY
1	16	Pyelonephritis	Patchy mononuclear-cell infiltrate
2	22	Pneumonia	Infected allograft
3	37	Emaciation	Infarcted allograft
4	49	Intestinal obstruction	Slight mononuclear-cell infiltrate

Table VI.—RESULTS OF ORTHOTOPIC PANCREATIC TRANSPLANTATION

PIG	SURVIVAL (days)	CAUSE OF DEATH	HISTOLOGY
1	14	Bronchopneumonia	Haemorrhagic pancreatitis
2	17	Peritonitis	Moderate mononuclear-cell infiltrate
3	44	Purulent pneumonia	Moderate mononuclear-cell infiltrate. Atrophy of exocrine tissue with fibrosis
4	50	Emaciation	Moderate mononuclear-cell infiltrate. Necrotic and atrophic parenchyma

Table VII.—RESULTS OF ORTHOTOPIC KIDNEY AND PANCREATIC TRANSPLANTATION

PIG	SURVIVAL (days)	CAUSE OF DEATH	HISTOLOGY	
			Kidney	Pancreas
1	11	Uraemia	Severe mononuclear-cell infiltrate Stigmata of severe rejection	Slight to moderate mononuclear-cell infiltrate

8. Orthotopic Kidney and Pancreas Transplantation from the Same Donor (*Table VII*).—One animal survived for 11 days, dying of uraemia with severe mononuclear-cell infiltration of the kidney indicating marked rejection. The pancreas, however, showed slight to moderate mononuclear-cell infiltration.

9. Orthotopic Transplantation of the Pancreas and Liver (*Table VIII*).—One animal survived for 38 days, dying of intestinal obstruction. The liver at autopsy showed slight mononuclear cell infiltration and portal-tract fibrosis. The pancreas showed a minimal mononuclear-cell infiltrate and a slight increase in fibrous tissue.

10. Orthotopic Transplantation of the Liver, Pancreas, and Kidney (*Table IX*).—Eight animals survived for between 4 and 57 days. Six died from intestinal obstruction, 1 from a biliary fistula, and 1 from peritonitis. The longest survivor had normal histological appearances of the liver, pancreas, and kidney allografts. The two animals which died at 4 and 10 days had microscopical cholangitis in the liver allografts. In the remaining animals there was mononuclear-cell infiltration present in all the allografts but the liver and pancreatic grafts had less intense infiltration than the kidney grafts.

DISCUSSION

The purpose of this paper is to describe technical aspects of organ allografts in the pig that have not previously been published. It is clear that the pig is an excellent experimental animal for organ transplantation research and can survive even the extensive procedure of simultaneous orthotopic transplantation of the liver, kidney, and pancreas. Certain tentative conclusions about the rejection pattern of the various organs can be made. These experiments confirm the previous data from this laboratory showing that, in the pig, heart and kidney allografts are rejected more aggressively than the liver. Rejection of pancreatic allografts, whether orthotopic or heterotopic, appears to be slower and milder than that of the kidney or heart. The liver, whether allografted heterotopically or orthotopically, appears to slow down the process of rejection of other organs. This can be demonstrated after 24 hours' residence of an accessory liver allograft which is subsequently removed. In 1 experiment, however, where the accessory liver allograft was removed after 2½ hours, aggressive rejection of the kidney occurred. Accessory livers and hearts undergo severe atrophy which seems to be independent of rejection. Similar changes have been reported in other species with accessory grafts of these organs. Orthotopic liver grafts in the pig frequently show microscopical changes of rejection which disappear spontaneously after 3 to 4 weeks. Similar changes have been observed in the rejection pattern of the organ allografts reported in this paper. The data here show quite clearly that liver allografts in the pig exhibit an immunosuppressive effect against themselves and other donor tissue which varies in individual experiments but cannot be related to the amount of tissue grafted. In fact, transplantation of the liver and pancreas together appears to increase the immune reaction in the liver.

Table VIII.—RESULTS OF ORTHOTOPIC LIVER AND PANCREATIC TRANSPLANTATION

PIG	SURVIVAL (days)	CAUSE OF DEATH	HISTOLOGY	
			Liver	Pancreas
1	38	Intestinal obstruction	Slight mononuclear-cell infiltrate and portal-tract fibrosis	Minimal mononuclear-cell infiltrate Slight increase in fibrous tissue

Table IX.—RESULTS OF ORTHOTOPIC LIVER, KIDNEY, AND PANCREATIC TRANSPLANTATION

PIG	SURVIVAL (days)	CAUSE OF DEATH	HISTOLOGY
1	4	Intestinal obstruction	Liver: Cholangitis Kidney: Normal Pancreas: Oedematous
2	10	Intestinal obstruction	Liver: Cholangitis Kidney: Moderate mononuclear-cell infiltrate Pancreas: Necrotic
3	12	Intestinal obstruction	Liver: Slight mononuclear-cell infiltrate Kidney: Moderate mononuclear-cell infiltrate Pancreas: Normal
4	17	Intestinal obstruction	Liver: Moderate mononuclear-cell infiltrate Kidney: Substantial mononuclear-cell infiltrate Pancreas: Moderate mononuclear-cell infiltrate
5	18	Biliary fistula	Liver: Slight mononuclear-cell infiltrate Kidney: Substantial mononuclear-cell infiltrate Pancreas: Necrotic
6	19	Peritonitis	Liver: Slight mononuclear-cell infiltrate Kidney: Moderate mononuclear-cell infiltrate Pancreas: Slight mononuclear-cell infiltrate
7	30	Intestinal obstruction	Liver: Moderate mononuclear-cell infiltrate; scattered areas of necrosis Kidney: Moderate mononuclear-cell infiltrate Pancreas: No infiltrate; occasional small foci of atrophy and necrosis
8	57	Intestinal obstruction	Liver: Normal Kidney: Normal Pancreas: Normal

Studies of glucose and insulin metabolism following pancreatic transplantation in the pig are reported elsewhere (Sells, Calne, Hadjiyannakis, and Marshall, 1972). It was found that apancreatic pigs developed hyperglycaemia and ketosis. Both orthotopic and heterotopic allografts prevent hyperglycaemia. The recipients of functioning orthotopic pancreatic allografts have normal glucose-tolerance curves with raised plasma-insulin levels, whilst the glucose-tolerance tests on heteroropic liver-graft recipients showed hypoglycaemia and there was marked hyperinsulinaemia. Denervation and ischaemic damage of the grafted pancreas could explain the high plasma-insulin levels. It is possible that the diversion of insulin and glucagon from the liver in the heterotopic grafts may have accentuated the hypoglycaemia.

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PREDICTION OF 1-YEAR SURVIVAL AFTER RESECTION OF LUNG TUMOURS FROM THE PREOPERATIVE STEROID EXCRETION PATTERN

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SUMMARY

A prospective study of 50 patients with lung cancer who were treated by surgical resection of their tumour has shown that most of those who died within 1 year after resection had abnormalities in preoperative steroid excretion whereas most of those who are alive had normal steroid excretion. Of the 21 patients who died within 1 year, 5 died in hospital, mainly as a result of surgical complications, and were found to have an abnormally low androsterone to aetiocholanolone ratio and a high total 17-oxosteroid excretion. Those who were discharged alive and well from hospital but who died within 1 year as a result of metastasis to other organs had a low androsterone level in relation to aetiocholanolone and to total 17-hydroxycorticosteroids. Thus, it has been possible to identify by their preoperative steroid excretion 12 out of 14 patients who died within 1 year although they had had a successful resection.

ALTHOUGH radical surgery offers the best chance of survival for patients with lung cancer compared with other methods of treatment, nearly half of the surgically treated patients die within 1 year. Therefore a method of prediction of the prognosis might be useful for the management of these patients. If the technique of prediction has a biochemical basis it might provide clues to the pathogenesis of this disease and might even lead to a therapeutic application. Such a chemical method of predicting prognosis has already been shown to be effective for patients with inoperable lung cancer (Rao and Hewit, 1970). The present report deals with the prognosis of patients whose lung tumours have been resected by a lobectomy or pneumonectomy.

PATIENTS AND METHODS

Fifty male patients, aged 36–68 years (mean 55·7 years), who had undergone a resection of their lung tumour were followed up for a period of at least 1 year from the date of surgery; 27 had had a pneumonectomy and 23 a lobectomy. Two early morning specimens of urine had been collected for steroid assay about 3 days before surgery. Details of patients and laboratory methods have been described elsewhere (Rao, 1970).

RESULTS

Twenty-one patients died within 1 year after resection and, of these, 5 died in hospital mainly as a result of surgical complications such as haemoptysis, peripheral shock, or pulmonary embolism (group 1). Of the remaining 16 patients, 2 died of heart failure and kidney failure 4 and 7 months respectively after surgery and had no obvious evidence of metastases. The remaining 14 patients left hospital after surgery in a reasonable condition but died within 1 year mainly as a result of metastasis to the other lung or to other organs (group 2). Twenty-nine of the patients were alive and most of these were well 1 year after resection (group 3). Steroid excretion before resection was compared in the three groups and showed some striking differences (*Table I*). Among the patients who died within 1 year, those who died in hospital showed some differences in steroid excretion compared with those who left hospital alive and well; the former patients had a lower androsterone (A) to aetiocholanolone (E) ratio than the mean for group 2, and they also had higher 17-oxosteroid (KS) and 17-hydroxycorticosteroid (17-OHcs) excretion levels compared with those in groups 2 and 3. Patients in group 2 had significantly lower excretion of A and E compared with that in group 3. In group 2, 12 out of 14 patients had a 17-OHcs : A ratio of more than 10, whereas in group 3 only 5 out of 29 patients had such a high ratio. Thus most of the patients in group 2 could be identified by their abnormal steroid excretion (*Fig.* 1). Two patients in group 2 died of heart failure and kidney failure respectively and these did not have any marked abnormalities in steroid excretion.

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DISCUSSION

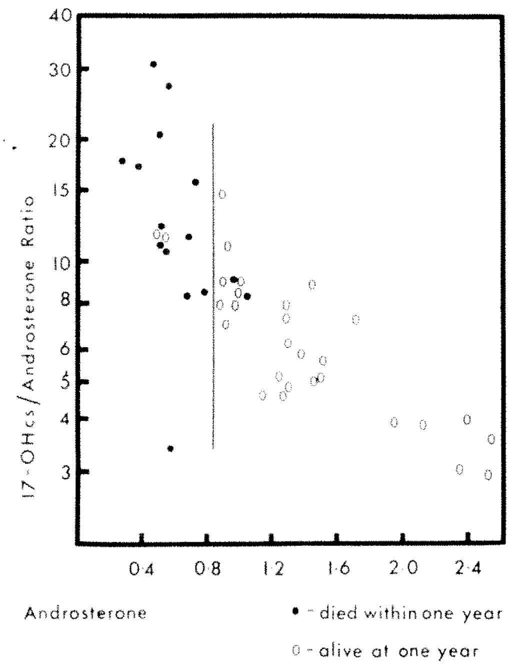

FIG. 1.—The survival of surgically treated patients.

Table I.—PREOPERATIVE STEROID EXCRETION IN GROUPS 1, 2, AND 3

GROUP	NO. OF PATIENTS	STEROID EXCRETION (mg. per g. creatinine per litre)			
		A	E	KS	17-OHcs
1	5	1·29 ± 0·46	2·90 ± 0·16*	7·02 ± 0·77	10·39 ± 3·56
2	16	0·72 ± 0·31*	1·19 ± 0·46*	4·18 ± 1·44*	8·26 ± 2·71
3	29	1·42 ± 0·66	2·11 ± 1·15	5·83 ± 1·93	8·11 ± 2·29

A, Androsterone; E, aetiocholanolone; KS, 17-oxosteroids; 17-OHcs, hydroxycorticosteroid.
* Significantly different from the mean of group 3 ($P < 0·01$).

The results indicate that it is possible to identify using a chemical method, even before surgical treatment, those lung cancer patients who have a poor prognosis despite resection of their lung tumours. The significance of these findings could be considerable in the management of these patients if it can be established that their abnormalities are of aetiological significance and are not merely a reflection of the stage of the disease. The latter possibility arises because in patients with inoperable lung cancer the same steroid abnormalities are significantly related to the prognosis (Rao and Hewit, 1970). Thus, in these patients the greater the 17-OHcs : A ratio the shorter is the survival time. The present results show that this ratio is equally useful in predicting the 1-year survival in patients whose lung tumours have been surgically removed. Therefore, it is possible that the 17-OHcs : A ratio indicates the presence of metastases which were not clinically recognizable, and thus reflects only the stage of the disease. An alternative possibility in surgically treated patients is that a high 17-OHcs : A ratio indicates a greater susceptibility to metastasis after surgery. Previous work (Rao, 1970) has shown that removal of the lung tumour does not result in the disappearance of these steroid abnormalities and therefore they cannot be considered as being due to the presence of the lung tumours. It is not likely that these abnormalities are the effects of the clinically unrecognizable secondary tumours, since the removal of the primary tumour did not result in the decrease of the abnormalities. Therefore it appears that these abnormalities in lung cancer are the characteristics not of the tumour but rather of the host, which may be involved in the defence against the growth and spread of the tumour. Some indications are already available of the possible ways in which steroid abnormalities may be involved in the defence mechanisms of the host against the tumour. These can be considered under three main aspects.

1. Metabolic Effects.—Corticosteroids are mainly catabolic (Symington, 1969) and androsterone is anabolic (Furman and Howard, 1959). The high 17-OHcs : A ratio found in patients with a poor prognosis might shift the metabolic balance towards increased catabolism and lead to the cachexia found in many patients with a poor prognosis.

2. Haemostatic Effects.—It is known that cancer patients have an increased coagulability of their blood and this has been suggested as favouring the establishment of blood-borne metastasis (Thornes, 1967). Evidence for this view has come from the finding that the death-rate from cancer among persons receiving anticoagulant therapy is significantly lower than that in the general population (Thornes, 1967). It is known that corticosteroids increase coagulation by increasing the free fatty acids in the blood (Hoak and Robinson, 1963), whereas androsterone reduces coagulation by its ability to reduce platelet stickiness (Dufault, Tremblay, Nowaczynski, and Genest, 1961) and to increase fibrinolysis (Thornes, 1970). In fact, androsterone has been used prophylactically for this purpose in cardiovascular disease. Aetiocholanolone administration results in the increase of fibrinogen (Kimball, Vogel, Perry, and Wolff, 1967) and may thus enhance the tendency to coagulation. Thus, the low A : E ratio found in patients with a poor prognosis might have resulted in increased blood coagulation, favouring the establishment of blood-borne metastasis. Increased coagulability may also result in the formation of fatal pulmonary emboli.

3. Immunological Effects.—The importance of immunological mechanisms in the defence against cancer is now widely recognized (Editorial, *British*

Medical Journal, 1970). The immunosuppressive effects of corticosteroids are well known and these steroids are used extensively for this purpose in tissue transplantation. It is likely that androsterone may enhance the immune response because of its anabolic effects. Thus, the high 17-OHcs : A ratio seen in patients with a poor prognosis may lead to a reduced immune response against the tumour.

It must be emphasized that although the above mechanisms are discussed separately two or more of these may be operating in unison to enhance the effect of steroid abnormalities. A careful investigation of these mechanisms in the prognosis of cancer would be a rewarding study.

A convincing method of proving that the steroid abnormalities in lung cancer are of aetiological significance would be to study the effects of correction of these abnormalities on the prognosis of these patients. Since the abnormalities in steroid excretion centre around a deficiency of androsterone these could be corrected by the administration of this steroid or a suitable precursor. Testosterone would not be a suitable steroid because the A : E ratio is not altered by its administration (Johnsen, 1968). Dehydroepiandrosterone also would not be a suitable precursor because this steroid is converted mainly to aetiocholanolone and thus would increase the abnormality found in lung cancer (Kirschner and Lipsett, 1964). It may therefore be necessary to administer androsterone or some other 5-alpha-androstane compound. Since the correction of the deficiency of androsterone could be carried out in conjunction with the existing methods of therapy it should be entirely feasible to conduct such a clinical trial.

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INVESTIGATION OF OEDEMA OF THE LOWER LIMB FOLLOWING SUCCESSFUL FEMOROPOPLITEAL BY-PASS SURGERY: THE ROLE OF PHLEBOGRAPHY IN DEMONSTRATING VENOUS THROMBOSIS

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SUMMARY

Of 21 limbs having successful femoropopliteal vein by-pass grafts, 20 showed peripheral oedema 7 days after operation. Circumferential enlargement of more than 4·5 cm. was associated with thrombosis of the popliteal or tibial veins, whereas legs enlarging less than 1·5 cm. did not show radiological evidence of venous thrombosis.

Venous thrombosis is less likely after surgery for intermittent claudication than for rest pain or gangrene of the toes.

Distal anastomosis of the vein-graft to the popliteal artery is more often accompanied by venous thrombosis than anastomosis above the knee-joint.

OEDEMA of the leg and foot following successful reconstructive surgery to the arteries of the lower limb has been observed ever since such procedures were introduced (Eastcott, 1953; Rob, 1953). Whereas hyperaemia occurs after reconstruction of both aorto-iliac and superficial femoral segments, appreciable peripheral oedema appears to be most frequently encountered after surgery to the femoral and popliteal arteries. Peripheral oedema is not necessarily associated with hyperaemia and in such cases it is possible that lymphatic or venous occlusion may be contributory factors.

Damage to large lymphatic trunks accompanying the long saphenous vein has been described in patients having femoropopliteal vein by-pass grafts and a close correlation was found between the presence of oedema and lymphatic occlusion (Vaughan, Slavotinek, and Jepson, 1970). Husni (1967) was unable to confirm an association between oedema and deep-vein thrombosis.

The present investigation has been undertaken in order to determine the true incidence of oedema after femoropopliteal reconstructions, and by means of a precise technique of phlebography to study the incidence of thrombosis within the tibial, popliteal, and femoral veins.

EXPERIMENTAL PROTOCOL AND METHODS

Twenty-two consecutive patients undergoing autogenous saphenous by-pass grafting for atherosclerotic occlusive disease of the superficial femoral artery have been studied.

Several techniques for detecting the presence of venous thrombosis are available and the suitability of each has been considered in the context of this investigation. Preferential localization of ^{125}I- and ^{131}I-labelled fibrinogen in venous thrombi is well documented but is unsuitable for detecting thrombosis in the vicinity of a surgical operation in view of the deposition of isotope in fibrin laid down during the early stages of wound healing, leading to a 'blurred' scan. The ultrasonic 'Doppler-effect' flowmeter has been widely used to measure femoral venous flow by Sigel, Popky, and Boland (1967) and Sumner, Baker, and Strandness (1968), but this technique is less reliable in its present stage of development for demonstrating flow in venous plexuses such as those related to the soleus muscle. Such techniques as infra-red photography (thermography) and plethysmography are not sufficiently precise to allow demonstration of thrombosis in the small deep veins in the leg.

For these reasons phlebography appeared to be the most appropriate technique for use in this study. The rationale of the investigation and its risks were fully discussed with all the patients consenting to take part in the study.

Technique of Phlebography.—Phlebography was performed on the seventh postoperative day, oedema related to the surgical procedure rarely appearing later than this. Dietary intake on the morning of the investigation was restricted to fluids in order to minimize the tendency of contrast media to induce nausea. The technique employed was that described by Rogoff and De Weese (1960) and modified by Wesolowski, Greenfield, Sawyer, Fries, Shaefer, and Martinez (1965).

Hypaque 45 per cent (Bayer) was employed as the contrast medium and was introduced by direct transcutaneous venepuncture on the dorsum of the foot, facilitated by the placement of a tourniquet just above the ankle. 'Cut-down' exposure of a superficial vein is entirely unethical in a potentially ischaemic foot, and in this series direct venepuncture was perfectly satisfactory on each occasion. The leg under investigation was held in steep dependency at 45° downwards. Many authors attribute poor opacification of the deep veins to failure in observing this particular point. Retrograde venous flow was also encouraged by the use of the Valsalva manœuvre. A tourniquet, 8·0 cm. in width, was placed just above the ankle and inflated to 80 mm. Hg in order to direct the venous blood-flow from the dorsum of the foot into the deep veins of the calf. Radiographs were taken in both the anteroposterior and lateral planes.

The protocol in this investigation included information with regard to the severity of symptoms and the existence of coexisting disease such as diabetes mellitus or superficial thrombophlebitis, and, in addition, the exact position of proximal and distal artery-to-vein anastomosis was recorded.

The result of each operation at the seventh postoperative day was recorded according to the following grading:—

A. Restored tibial pulses.
B. Graft pulsatile but no tibial pulses.
C. Foot warmer but graft not palpable.
D. Graft palpable but not pulsatile.
E. Foot worse.

The circumference of both legs was measured before operation and again on the seventh postoperative day 25 cm. above and 20 cm. below the tubercle of the tibia. Although it has been found possible to measure limb circumference to an accuracy of ± 0·2 cm., measurements have been recorded to the nearest 0·5 cm.

RESULTS

Clinical details of the 22 patients studied are summarized in *Table I*. The result of surgery in each limb studied was very satisfactory, being graded A or B, thus eliminating immediate graft failure as a possible cause for oedema.

Surgery was undertaken for intermittent claudication in 12 limbs, rest pain in the foot in 6 limbs, and gangrene of the toes in 3 limbs. In 9 instances the lower anastomosis between the vein-graft and the artery was situated above the knee-joint and in 12 below the joint.

When measured on the seventh postoperative day 1 patient showed no difference in calf circumference in comparison with the contralateral limb, but the remaining 20 patients showed an increase on the operated side, with a range from 0·5 to 7·5 cm.

Venography performed on the seventh postoperative day showed no evidence of venous thrombosis in 12 patients but revealed occlusive or non-occlusive thrombosis in 9. No features suggesting pulmonary embolism occurred in these patients.

Relation of Oedema to Venous Thrombosis.—*Table II* includes the results from all the patients studied, placing each limb into one of five categories according to the severity of oedema. Eight limbs enlarged circumferentially by 0–1·4 cm., all being free from venous thrombosis. Clinical oedema was present above 1·5 cm. enlargement, but venous thrombosis occurred only twice with a circumferential increase of less than 4·5 cm. Seven limbs were found to have enlarged by more than 4·5 cm. and all showed popliteal or tibial venous thrombosis.

The importance of carrying out phlebography in both the lateral and anteroposterior planes was illustrated in several instances in which non-occlusive thrombus was clearly seen in one plane but not in radiographs taken at a right-angle.

Factors influencing Venous Thrombosis.—*Table III* relates presence or absence of venous thrombosis to the severity of preoperative limb ischaemia.

Of the 12 limbs in which intermittent claudication was the preoperative indication for surgery, only 4 subsequently developed venous thrombosis. Nine limbs showed more severe ischaemia, however, and postoperatively 5 of this group were found to have popliteal or tibial venous thrombosis.

Table IV compares the incidence of venous thrombosis with the level of anastomosis of the vein-graft to the popliteal artery.

Table I.—SUMMARY OF THE CLINICAL DETAILS

CASE	SYMPTOMS	LEVEL OF LOWER ANASTOMOSIS	RESULT OF OPERATION (Grade)	CIRCUMFERENCE DIFFERENCE 7 DAYS AFTER OPERATION (cm.)	RESULT OF VENOGRAM
1	Claudication: 100 yd.	5·0 cm. A.K.	A	Unchanged	Normal
2	Rest pain	1·0 cm. B.K.	B	4·5	Tibial thrombosis
3	Claudication: 150 yd.	2·0 cm. B.K.	B	0·5	Normal
4	Severe rest pain	Posterior tibial artery	B	6·5	Tibial thrombosis
5	Claudication: 150 yd.	2·0 cm. B.K.	B	6·0	Tibial thrombosis
6	Gangrene of toes	1·5 cm. B.K.	A	0·5	Normal
7	Claudication: 100 yd.	1·5 cm. A.K.	B	0·5	Normal
8	Gangrene of toe	2·0 cm. B.K.	B	7·5	Tibial and popliteal thrombosis
9	Claudication: 100 yd.	5·0 cm. A.K.	A	3·5	Tibial thrombosis
10	Claudication: 200 yd	0·5 cm. A.K.	A	0·5	Normal
11	Claudication: 100 yd.	2·0 cm. B.K.	A	4·5	Popliteal thrombosis
12	Claudication: 200 yd.	2·0 cm. A.K.	A	1·5	Popliteal thrombosis
13	Claudication: 100 yd.	1·0 cm. B.K.	A	1·5	Normal
14	Rest pain	0·5 cm. A.K.	A	0·5	Normal
15	Claudication: 100 yd.	3·0 cm. A.K.	A	1·0	Normal
16	Rest pain	0·5 cm. B.K.	A	6·0	Popliteal and tibial thrombosis
17	Gangrene	3·0 cm. B.K.	A	4·5	Popliteal thrombosis
18	Claudication: 60 yd.	6·0 cm. A.K.	B	1·0	Normal
19	Claudication: 100 yd.	2·0 cm. A.K.	A	3·0	Normal
20	Rest pain	3·0 cm. B.K.	A	2·0	Normal
21	Rest pain	2·5 cm. B.K.	A	1·5	Normal

A.K. = Above knee-joint; B.K. = below knee-joint. *See* text for explanation of grading.

Table II.—RELATION BETWEEN OEDEMA AND PRESENCE OF VENOUS THROMBOSIS

	INCREASE IN CALF CIRCUMFERENCE					TOTAL
	0–1·4 cm.	1·5–2·9 cm.	3·0–4·4 cm.	4·5–5·9 cm.	6·0–7·5 cm.	
Thrombosis	—	1	1	3	4	9
No thrombosis	8	3	1	—	—	12

Table III.—RELATION BETWEEN VENOUS THROMBOSIS AND SEVERITY OF PREOPERATIVE SYMPTOMS

	PREOPERATIVE SYMPTOMS			TOTAL
	Intermittent Claudication	Rest Pain	Gangrene	
Thrombosis	4	3	2	9
No thrombosis	8	3	1	12

Anastomosis above the knee-joint was carried out in 9 cases and was accompanied by thrombosis only twice. Twelve operations were carried out below the joint, however, and of these, 7 developed venous thrombosis.

None of the patients in this series was diabetic and there were no cases of existing superficial thrombophlebitis or pre-existing deep-vein thrombosis, as judged clinically. In all the cases the preoperative measurements of thigh and calf circumference showed no difference between the symptomatic and the contralateral limb.

DISCUSSION

The results of this investigation confirm that oedematous swelling of the leg below the knee may be expected 7 days after successful femoropopliteal by-pass grafting. It would appear that an increase in circumference of 0·5–1·5 cm. above the preoperative measurement is most unlikely to be associated with venous thrombosis. A circumferential increase of 4·5 cm. or more is, however, strongly suggestive of thrombosis in the tibial or popliteal veins.

Table IV.—RELATION BETWEEN THROMBOSIS AND LEVEL OF POPLITEAL ANASTOMOSIS

	LEVEL OF POPLITEAL ANASTOMOSIS		TOTAL
	Above Knee	Below Knee	
Thrombosis	2	7	9
No thrombosis	7	5	12

It would also appear that venous thrombosis occurs less frequently after surgery for the relief of intermittent claudication than for rest pain and ischaemic gangrene. Thrombosis was noted in 5 out of 9 limbs treated for severe ischaemia, whereas only 4 out of 12 limbs in the claudication group showed thrombosis.

The explanation for this apparent association between venous thrombosis and surgery for relief of severe symptoms may lie in the observation that thrombosis of the popliteal vein occurs more frequently following anastomosis of a vein-graft to the popliteal artery below the level of the knee-joint than after procedures concentrated above the joint. Distal dissection of the popliteal artery was necessary in 8 out of the 9 patients presenting with rest pain or gangrene.

Mobilization of the popliteal artery high in the popliteal fossa is generally less likely to involve trauma to the popliteal vein than more distal dissection.

As the popliteal artery descends through the popliteal fossa it is crossed posteriorly by the popliteal vein and medial popliteal nerve, the vein being closely applied to the artery. Using the medial approach to the fossa the artery is at its most accessible 4–5 cm. above the knee-joint, lying deep to the muscular portion of the semimembranosus just above the origin of the tendinous part of the muscle. At this point the popliteal vein can be separated from the artery with very little difficulty.

In contrast, adequate exposure of the popliteal artery below the knee-joint line, as it lies lateral to the medial popliteal nerve between the two heads of the gastrocnemius, is only possible after freeing the adherent vein together with the venae comitantes which so frequently accompany the distal portion of the artery. It is frequently necessary to divide one or two cross connexions of the venae comitantes to the main popliteal vein and care is necessary to avoid narrowing the vein at these points. Division of veins entering the popliteal vein from the surrounding muscles may also be necessary.

It is, therefore, likely that the critical factor leading to popliteal vein thrombosis is the level at which the lower end of the graft must be anastomosed to the popliteal artery.

Anastomosis of the vein-graft above the knee-joint also confers considerable advantages in terms of sustained patency compared with distal anastomoses (Baddeley, Ashton, Slaney, and Barnes, 1970). Thus it is clear that wherever possible the anastomosis of the vein-graft to the popliteal artery should be carried out above the knee-joint.

Although it would seem that marked oedema is commonly associated with venous thrombosis the aetiology of less obvious swelling remains obscure. Simeone and Husni (1959) associate oedema and hyperaemia after reconstructive surgery with changes in the physiological response of arterioles to increased intraluminal pressure. Controversy surrounds the understanding of the regulation of arterial tone. Bayliss (1902) suggested that the normal constrictor response of small arteries to increased intraluminal pressure depends on a local response of smooth muscle in the vessel wall to the stimulant action of each pulse wave. Following circulatory arrest, this response is lost as a consequence of functional failure of ischaemic smooth muscle. Anrep (1912) regarded post-ischaemic vasodilatation and oedema as manifestations of local release of vasodilator metabolites, but Folkow (1949) showed that vasodilatation can occur after arterial occlusion for periods of less than 3 seconds, rather vitiating a chemical cause for lack of smooth-muscle response. Essex, Herrick, Baldes, and Mann (1943) showed that muscle-cells in the walls of canine arteries exposed to reduced intraluminal pressure undergo atrophy. This work awaits clinical confirmation, but changes specific to ischaemia are very difficult to separate from the degenerative processes seen in atherosclerosis. It is thought that the prolonged low-flow state distal to a coarctation of the aorta leads to changes in peripheral vessels to the extent that, after resection of the coarctation aneurysm formation, non-specific arteritis and fibrinoid necrosis may involve peripheral arteries (Perez-Alvarez and Oudkerk, 1955).

Thus, evidence does exist that peripheral arteries may be incapable of a normal physiological response to restored intraluminal pressure following a prolonged period of reduced flow. Excessive transudation of fluid across capillary membranes consequent upon sustained elevation of capillary hydrostatic pressure, in the absence of pre-capillary arteriolar constriction, may contribute to peripheral oedema after successful reconstructive arterial surgery.

Although we are unable to comment upon the findings of Vaughan and others (1970) with regard to the contribution of lymphatic obstruction to leg oedema after femoropopliteal by-pass procedures, it seems probable that excessive extracellular fluid accumulates to a limited extent in response to impaired vasoconstrictor activity, but in patients with more marked swelling thrombosis of the tibial or popliteal veins must be considered.

Acknowledgements.—It is a pleasure to record my gratitude to Professor G. Slaney and Mr. F. Ashton who allowed me to study their patients and gave encouragement and helpful criticism. I am also indebted to colleagues in the X-ray Department of the Queen Elizabeth Hospital for their helpful co-operation.

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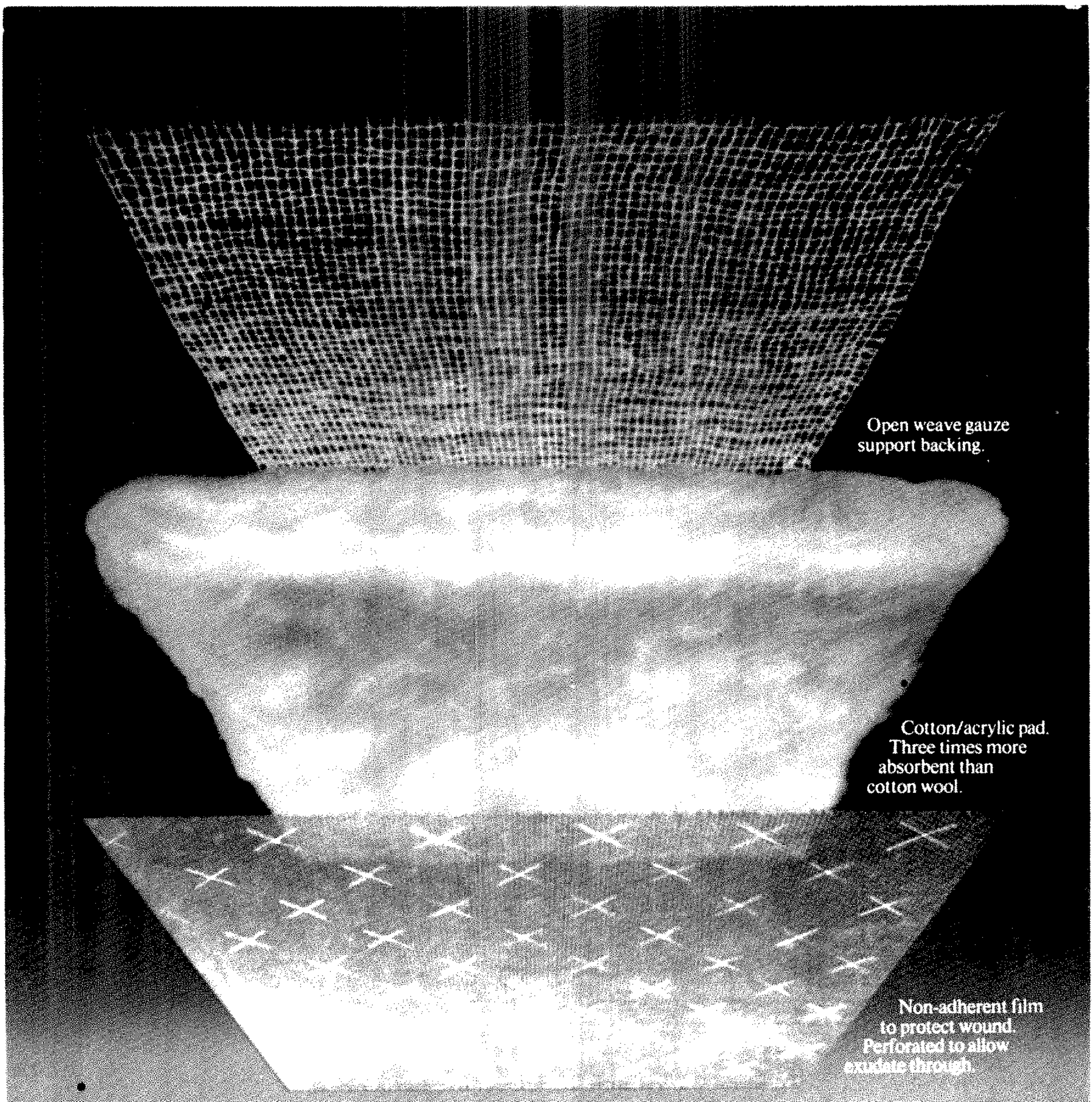
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SHORT NOTES OF RARE OR OBSCURE CASES

RECURRENT SPONTANEOUS RUPTURE OF THE URINARY BLADDER

By M. H. WHEELER*
SURGICAL UNIT, CARDIFF ROYAL INFIRMARY

SUMMARY

Only 5 cases of recurrent spontaneous bladder rupture have been reported in the literature. The present report is of a patient who developed a spontaneous rupture on two occasions within 5 years. The first rupture was treated without bladder suture. A pelvic fracture 12 months before the first episode is considered to be a probable aetiological factor.

SPONTANEOUS rupture of the urinary bladder is uncommon but recurrent spontaneous rupture is very rare. The present report is of a patient who developed a spontaneous rupture on two occasions within 5 years.

CASE REPORT

In January, 1968, Mrs. M. S., a 32-year-old housewife, was admitted to hospital as an emergency with severe generalized abdominal pain which had commenced suddenly 12 hours previously when she had risen from bed to micturate. She had failed to reach the toilet because of the severity of the pain and had subsequently been unable to micturate although she had felt the desire to do so. There was no history of recent trauma, excessive alcoholic intake, or other urinary symptoms.

On examination the patient was ill and in considerable pain. There was generalized abdominal tenderness and rigidity with absent bowel-sounds. A diagnosis of perforated abdominal viscus was made and a laparotomy was performed. Urine was found in the peritoneal cavity. There was a small circular perforation through a linear scar approximately 2·5 cm. in length on the posterior aspect of the bladder.

This perforation was closed in two layers with catgut and a Foley balloon catheter was inserted into the bladder per urethram. Ampicillin was prescribed for 1 week. The postoperative course was uneventful and a subsequent intravenous pyelogram and micturating cystogram were normal. The patient was discharged on the tenth postoperative day.

PAST HISTORY.—In March, 1962, the patient had been involved in a motor accident, suffering concussion, a fractured left tibia, and also fractures of the right horizontal and vertical pubic rami. At this time there had been no evidence of any injury to the urinary bladder and recovery had been uneventful.

Twelve months later in March, 1963, she had been admitted to another hospital with a history of severe generalized abdominal pain of sudden onset. A diagnosis of peritonitis secondary to a perforated peptic ulcer had been made and a laparotomy had been performed. At operation the only abnormal finding had been that of 300 ml. of slightly blood-stained fluid in the peritoneal cavity. The source of the fluid had not been established.

Postoperatively the patient had developed what had been thought to be ascites and at abdominal paracentesis 3·5 litres of straw-coloured fluid with a specific gravity of 1012 had been obtained. Cytology of the fluid had demonstrated numerous endothelial and squamous cells. At this stage a urethral catheter had been inserted because of suspected retention of urine. The ascites had regressed spontaneously, the catheter had later been removed, and the patient had recovered.

DISCUSSION

The first recorded case of spontaneous rupture of the urinary bladder was as long ago as 1279 by Pierus (Stone, 1931). Whenever spontaneous rupture occurs there is almost invariably a predisposing factor recognizable (*Table I*). Stone (1931) reviewed 40 cases and added 2 of his own. He stressed the importance of chronic or acute urinary obstruction and also of destructive lesions of the bladder as aetiological factors. Stone's second case was due to a vesical calculus eroding the bladder wall and possibly causing obstruction. A similar case was also reported by Innis in 1961.

Table I.—CAUSES OF SPONTANEOUS BLADDER RUPTURE

1. Obstruction
    - Prostatic hypertrophy (Thomas, 1956)
    - Papilloma (MacAlister, 1955)
    - Neurogenic
2. Scarring, inflammation, or malignant disease of the bladder wall (Altman and Horsburgh, 1966)
3. Over-distension, e.g., by alcohol (Feigal and Polzak, 1946)
4. Drugs, e.g., Carbachol (MacAlister, 1955)
5. Straining, e.g., stool, labour
6. Idiopathic

The commonest cause of urinary obstruction is prostatic hypertrophy and this has frequently been a factor in the causation of rupture. Prostatectomy has been carried out with success at the same time as the bladder repair (Thomas, 1956).

Over-distension of the bladder which is frequently associated with excessive alcoholic intake has also been recognized as a predisposing cause (Feigal and Polzak, 1946; Clinton-Thomas, 1955).

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Drugs used in the treatment of urinary retention may lead to bladder rupture and MacAlister in 1955 reported such a case with the use of Carbachol.

Hershman and Allen (1954) described a case of spontaneous rupture occurring in a patient suffering from syphilis. The authors felt that they had excluded a neurogenic bladder, however, from the cystoscopic and cystometric findings.

It has also been thought that spontaneous rupture may be precipitated by increased abdominal pressure, e.g., straining at stool and micturition or during labour. Graves (1960) recorded a case occurring during the 3rd month of pregnancy. Nevertheless, spontaneous rupture in the female is far less common than in the male.

Finally, the condition may occur without a predisposing cause. Such a case was reported by Barnes and Steele (1935).

Recurrent spontaneous rupture of the urinary bladder is a rare phenomenon. Crastnopol, Artz, and Rosett (1950) reviewed 3 cases and added 1 of their own. All 4 patients were male and in all the rupture was intraperitoneal. The patient of Crastnopol and others (1950) gave a history of pelvic trauma 27 months before rupture occurred, but they thought it justifiable to include this as a case of spontaneous rupture in view of the considerable time interval which had elapsed.

The patient of Bliss, Clark, and Saunders (1964) was a female who experienced two episodes of rupture after a subarachnoid haemorrhage. It was considered that there was retention with neuromuscular incoordination as an aetiological factor in the first instance and an epileptic fit in the second episode. Both ruptures in each of the 5 patients mentioned above were treated by suture and bladder drainage.

The case reported here is believed to have suffered recurrent spontaneous rupture of the urinary bladder. The first episode occurred 12 months after a motor accident which had resulted in a fractured pelvis. Although at the time of the first rupture the correct diagnosis was not made the exact nature of the illness is clear in retrospect. What was diagnosed as being ascitic fluid must have been urine in the peritoneal cavity. This rupture was therefore successfully treated by bladder drainage alone, but this is obviously not to be recommended as a method of management as a second rupture can occur later through a thin scar.

The present case is similar to the case reported by Crastnopol and others (1950) in that there was a history of pelvic trauma and a long delay before rupture occurred.

The correct management of spontaneous rupture consists of laparotomy, repair of the bladder—in two layers if possible—peritoneal toilet, adequate bladder drainage by means of urethral catheterization, and antibiotic cover.

The condition is still a serious one with a mortality-rate of up to 47 per cent (Bastable, de Jode, and Warren, 1959; Yarwood, 1959). Misdiagnosis is common, the usual diagnosis being peritonitis secondary to a perforated peptic ulcer (Yarwood, 1959).

Acknowledgement.—I should like to thank Professor A. P. M. Forrest, under whose care this patient was admitted, for permission to publish details of this case.

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MASSIVE HAEMORRHAGE IN ELEPHANTIASIS NEUROFIBROMA

BY P. MCMASTER

ADDENBROOKE'S HOSPITAL, CAMBRIDGE

SUMMARY

An unusual case of elephantiasis neurofibroma associated with massive haemorrhage occurring in an elderly man is reported.

NEUROFIBROMATOSIS (Von Recklinghausen's disease) is a condition occurring once in 3000 births and is an abnormality of neuro-ectoderm inherited by a dominant gene.

Elephantiasis neurofibroma is a rare feature of the disease and massive life-threatening haemorrhage into it has not previously been reported.

CASE REPORT

Mr. J. C., aged 61 years, was a patient who was known to have Von Recklinghausen's disease. His father had also suffered from this condition and had died of a cerebral tumour.

For a number of years the patient had been noted to have a large pendulous overgrowth of subcutaneous tissue (elephantiasis neurofibroma) situated in the lumbar region. This had caused him no trouble. However, he did have epilepsy, possibly due to cerebral glomal lesions.

The patient was admitted as an emergency in a state of collapse. He was semiconscious, pale, and sweating; his pulse was 140 per minute and blood-pressure 70/40. The central venous pressure was −2 cm. of saline. On his back in the lumbar region was a massive, fluctuant, and tender swelling. It measured approximately 45 cm. in diameter and there were signs of early cutaneous necrosis at its centre (*Fig.* 1).

Immediate resuscitative measures were taken. The patient was transfused with 2 units of plasma and 4 units of blood over the next hour.

Investigations revealed the following: haemoglobin, 6·8 g. per cent; haematocrit, 21; serum sodium, 125 mEq./l.; potassium, 4·5 mEq./l.; bicarbonate, 19 mEq./l.; blood-urea, 64 mg. per cent; serum creatinine, 1·3 mg. per 100 ml. Urine examination was normal. A chest radiograph showed the patchy appearance of bronchopneumonia. In spite of intensive efforts at resuscitation his condition did not improve and the lumbar swelling was clearly increasing in size. An emergency operation was therefore undertaken.

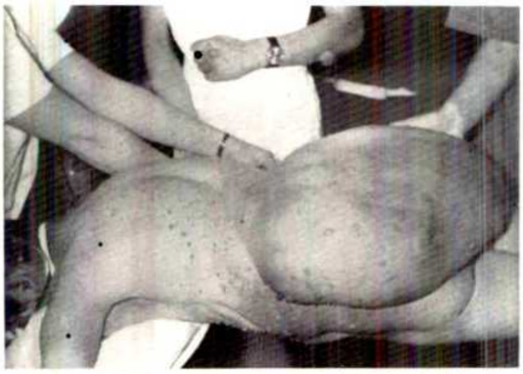

FIG. 1.—Patient prone and anaesthetized, showing the elephantiasis neurofibroma.

With the patient in the prone position the large lumbar swelling was explored through a transverse incision. An enormous superficial cavity was opened and 2·5 litres of blood were evacuated.

At the base of this cavity numerous vessels were found to be bleeding freely and were individually ligated. The neurofibroma was then excised. Redundant skin was also removed and four Redivac drains were left in situ. The transverse incision was closed with interrupted silk. A total of 14 units of blood was transfused during this procedure.

At the end of the operation the patient's condition had improved considerably—blood-pressure 150/90 and central venous pressure +5. His respiration was, however, laboured and he was subsequently bronchoscoped when large quantities of mucopurulent sputum were removed. His pneumonia was treated with ampicillin, 500 mg. 6-hourly for 10 days.

Apart from a small area of skin necrosis in the lower flaps the patient's postoperative recovery was uneventful. He was discharged to convalescence after 3 weeks and remains well 1 year later.

Histological examination confirmed the benign character of the neurofibroma (*Fig.* 2).

DISCUSSION

There have been a number of reports of elephantiasis neurofibroma (Hadil, 1928; Spittal, 1929; Anzinger, 1931; Westcott and Ackerman, 1947) since it was first described (Virchow, 1863).

The typical picture is that of a child presenting with neurofibromatosis (one of whose parents may also have the condition) in whom there appears a slowly developing, large, diffuse overgrowth of subcutaneous tissue and skin of the affected part. The overlying skin may be normal but often it is thickened and pigmented. The lesions are frequently situated around the neck or extremities (Bruns, 1891).

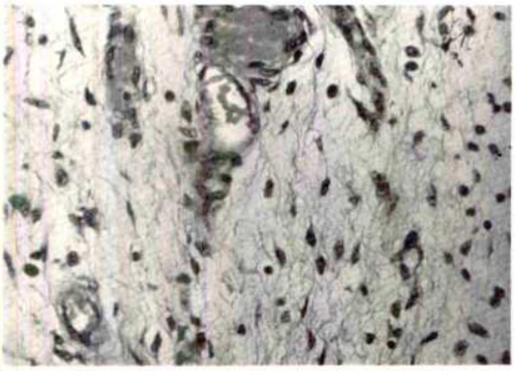

FIG. 2.—Histological appearance, showing oedematous neurofibrous stroma and numerous blood-vessels.

Elephantiasis neurofibromatosis is usually progressive and disfiguring and sarcomatous malignant change occurs in 5–15 per cent of cases (D'Agestino, 1963).

The case described here was associated with an unusual complication requiring vigorous resuscitation and emergency surgery.

Acknowledgements.—I am indebted to Mr. W. G. Everett for his help and encouragement in the preparation of this case and to Mrs. Richardson for her secretarial assistance.

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Orthopaedic Surgery in Spasticity. By HAROLD M. FROST, M.D., A.O.A., A.A.O.S., A.B.J.S., Detroit. 9 × 6 in. Pp. 216 + xi. Illustrated. 1972. Springfield: Ill.: Charles C. Thomas. $13.00.

THIS is a stimulating monograph and the author, Dr. Harold Frost, is the ideal man to write such a book because of his mature clinical experience over the past two decades. He has written many books and articles on orthopaedic problems and his background can be seen in the text of this book.

The book is divided into two sections. The first deals with the functional and operational viewpoints. Neurophysiology is portrayed in an original manner. The clinical problems of upper- and lower-extremity spasticity are discussed in an interesting and lively manner. The various corrective surgical procedures are explained in a very practical way. The line drawings throughout the book are original and easy to understand.

Section 2 is mainly clinical. The author describes his experience of many years of working with spastic children at the Crippled Children's Clinic at the Henry Ford Hospital. In this section the author describes some new procedures which in his hands have given excellent results.

Anyone who has to deal with spastics should read this book.

Urologische Operationslehre, Vol. 8. By G. W. MÜLLER, Magdeburg, W. WELRHEIM, Magdeburg, and G. W. HEISE, Magdeburg. 10½ × 7¼ in. Pp. 172. Illustrated. 1971. Leipzig: Georg Thieme. 53 M.

VOLUME 8 of this excellent series on urological surgery deals with plastic operations on the renal pelvis, tuberculosis of the urinary system, and pediatric urology.

Numerous operative methods are demonstrated for keeping vital kidney tissue viable by plastic reduction of the renal pelvis. The theory of aberrant blood-vessels causing hydronephrosis with the consequence of resection of those vessels is obsolete. Indeed, when blood-vessels are compressing the ureter transposition of the ureter is the operation of choice.

In the treatment of tuberculosis nephrectomy is unusual; the aim is to save as much kidney tissue as possible. The treatment by anti-tuberculous antibiotics as mentioned in this book is questionable. Stenosis of calices and the pelvis is more dangerous than the tuberculous infection itself; surgical therapy is started according to this principle, while partial kidney resection may be necessary.

In the section on paediatric urology vesico-ureteral reflux, which is often accompanied by a mega-ureter, gets ample attention; reconstructive operations are promising in such cases.

Operative treatment of ectopia and exstrophia of the bladder is more successful when implantation of the ureters with a roof of bladder-mucosa in the sigmoid colon is performed than in the cosmetically more satisfying plastic reconstruction of Marshall.

An excellent reference book.

INDEX TO VOLUME 59

PAGE

ABDOMINAL aorta, inflammatory aneurysms of 609
— aortic aneurysm(s) and horse-shoe kidney 513
— — — ruptured, neurological complications of 707
— — — uncommon complication of: aorto-caval fistulae 461
— — — — — aorto-enteric fistulae 458
— incisional hernia, pneumoperitoneum in management of 372
— tuberculosis 597
ABEYATUNGE, L. R.: A modified technique of colostomy 99
Abscess, acute intramural, of pyloric antrum—localized phlegmon 197
— amoebic liver, peritonitis from 179
Achalasia, treatment of, by cardiomyotomy 281
Acid burns, corrosive, squamous carcinoma of stomach following 382
Acid-fundic selective vagotomy of stomach without drainage in treatment of duodenal ulcer: Technique and results 602
ACLAND, ROBERT: New instruments for microvascular surgery 181
ADELOYE, ADELOLA: Mortality in missile wounds of the head 201
Agenesis, lumbrosacral, in 60-year-old man 577
AHMED, ALI, and METCALFE-GIBSON, C.: Haemoperitoneum complicating secondary carcinoma in the liver 576
AHMED, SAEED, JOLLEYS, AMBROSE, and DARK, JOHN F.: Thoracic enteric cysts and diverticulae 963
Alkaline reflux gastritis, postgastrectomy, reversibility of, by Roux-en-Y loop 13
ALLAN, J. S.: *See* TERRY, H. J., jt. auth.
Allografts, porcine renal, comparison of portal and systemic venous drainage in 541
Amoebic liver abscess, peritonitis from 179
Amputation(s), assessment of above- and through-knee 873
— neuroma of great auricular nerve after parotidectomy 735
— through-knee 260
Anal canal, prolapse of ileum through rectum and 149
— sphincter, external, anatomy of 717
Anastomosis(es), intestinal, omental reinforcement of 129
— splenorectal, ligation of left renal vein in, without impairment of renal function 170
Anatomy of external anal sphincter 717
ANDERS, C. J.: *See* JACKSON, B. T., jt. auth.
Aneurysm(s), abdominal aortic, and horse-shoe kidney 513
— — — uncommon complication of: aorto-caval fistulae 461
— — — — — aorto-enteric fistulae 458
— aortic, following external cardiac massage 238
— femoral 614
— inflammatory, of abdominal aorta 609
— post-irradiation femoral, treated by iliopopliteal by-pass via obturator foramen 400
— ruptured abdominal aortic, neurological complications of 707
— — mycotic, of spleen 572
Angiomatous spleen, ruptured, presenting as severe coagulation defect 492
Anteroposition of portal vein and spontaneous passage of gall-stones 737

PAGE

Antibiotic(s), effect of single-dose parenteral, in prevention of wound infection 98
— wound, in gastro-intestinal surgery 184
Aorta, abdominal, inflammatory aneurysms of 609
— thoracic, associated with hypothermia, case of traumatic rupture of 243
Aortic aneurysm(s), abdominal, and horse-shoe kidney 513
— — — uncommon complication of: aorto-caval fistulae 461
— — — — — aorto-enteric fistulae 458
— — following external cardiac massage 238
— — ruptured abdominal, neurological complications of 707
— valve homografts, fate of 231
Aortoduodenal fistula, spontaneous 368
Aorto-caval fistulae: uncommon complication of abdominal aortic aneurysms 461
Aorto-enteric fistulae: uncommon complication of aortic aneurysms 458
Aorto-iliac occlusive disease, axillary-femoral by-pass grafts in treatment of 704
Appendicectomy, development of right inguinal hernia following 352
— incidence of right inguinal hernia following 623
Appendicitis, chronic schistosomal 743
Appendix, leiomyoma of 579
ARCHAMPONG, E. Q.: Peritonitis from amoebic liver abscess 179
Argentaffin-cell tumour of Meckel's diverticulum 213
Arterial anastomosis of renal allografts, secondary haemorrhage from 890
— embolectomy, routine operative arteriography in 482
— flow, bilateral traumatic renal artery occlusion with survival after late reconstitution of 915
— surgery, femoropopliteal reconstructive, relationship between failure of, and blood-flow 549
Arteriography, routine operative, in arterial embolectomy 482
Arteriovenous fistulae for chronic intermittent haemodialysis, modified surgical technique for 953
— — post-angiographic vertebral 627
— — single congenital, of hand 76
— malformation, treatment of, by endarterial electrocoagulation 146
Artery disease, coronary, surgery for 801
— occlusion, bilateral traumatic renal, with survival after late reconstitution of arterial flow 915
— superficial femoral, new non-invasive technique for assessment of obstruction 226
Ascaris lumbricoides, adult, movements of 437
ASHKEN, M. HANDLEY: *See* CASTRO, J. E., jt. auth.
Asphyxia, traumatic, brachial plexus lesions associated with 539
Atrophy following testicular torsion 422
D'AURIA, D.: *See* HENNESSY, T. P. J., jt. auth.
Auricular nerve, great, after parotidectomy, amputation neuroma of 735
Axillary lymph-nodes in cancer of breast, regression of 776
Axillary-femoral by-pass grafts in treatment of aorto-iliac occlusive disease 704
Azathioprine in treatment of Crohn's disease 819

PAGE
BACTERIA in operating theatres, effect of clothing on dissemination of - - - - - - 878
Bacterial content of gastric juice - - - - 443
Bailie, H. W. C.: *See* Strahan, J., jt. auth.
Baker, Jane M.: *See* Blamey, R. W., jt. auth.
Baker, R., and Parker, E. J. C.: Femoro-femoral cross-over grafts - - - - - - - 701
Balfour, Tom W.: Does squamous carcinoma of the colon exist? - - - - - - 410
Bannister, Carys M.: A method of repair of myelomeningoceles - - - - - - - 445
Barst, Henry H.: Pneumoperitoneum as an aid in the surgical treatment of giant herniae - - 360
Bartram, Clive, and Jagelman, David: A case of xanthogranulomatous pyelonephritis - - 319
Battered buttock syndrome—fat fractures - - 165
Baum, M.: *See* Edwards, M. H., jt. auth.
Baxter, Thelma J., O'Brien, B. McC., Henderson, P. N., and Bennett, R. C.: Histopathology of small vessels following microvascular repair - - - - - - 617
Beeley, A. H.: *See* Roberts, V. C., jt. auth.
Behçet's disease, rectal and colonic ulceration in - 173
Bell, Graham, and Short, Douglas W.: Muscle blood-flow following insertion of a by-pass vein-graft in femoropopliteal occlusive disease - - - - - - - - - 429
Bell, P. R. F.: *See* Calman, K. C., jt. auth.
Benign pelvic lipomatosis, bilateral ureteric obstruction caused by - - - - - - - 69
Bennett, R. C., Hughes, E. S. R., and Cuthbertson, A. M.: Long-term review of function following pull-through operations of the rectum - - - - - - - - - 723
— — *See also* Baxter, Thelma J., jt. auth.
Bentley, R. J.: The obliteration of perforating veins in the leg - - - - - - - 197
Berg, Derek: Tumoral calcinosis - - - - 570
Bergdahl, Leif, and Boquist, Lennart: Tuberculosis of the gall-bladder - - - - - 289
Bilateral double nipples - - - - - - 55
Bile in reflux oesophagitis and success in prevention by surgical means, importance of - - 794
Bile-duct(s), malignant tumours of - - - - 501
— obstruction, experimental, effect of, on critical biosynthetic functions of liver - - - 564
Biliary drainage, extrahepatic, in experimental liver injury - - - - - - - - 136
Biliary-enteric fistula, case of gall-stone ileus in absence of - - - - - - - - - 573
Biliary-pressure studies during cholecystectomy - 267
Biliary-tract disease, comparative evaluation of preoperative and operative radiology in - - 205
Biosynthetic functions, critical, of liver, effect of experimental bile-duct obstruction on - - 564
Birkenstock, W. E., and Louw, J. H.: Malakoplakia of the colon - - - - - - 662
— — Rabkin, R., and Stables, D. P.: Bilateral traumatic renal artery occlusion with survival after late reconstruction of arterial flow - - - - - - - - - 915
Bladder, recurrent spontaneous rupture of - - 985
Blamey, R. W., Baker, Jane M., and Crosby, D. L.: Reticulo-endothelial system activity during homograft rejection and immunosuppression 62
Block, J.: *See* Glover, G. W., jt. auth.
Blood viscosity, postoperative changes in, and influence of haematocrit and plasma-fibrinogen 629
Blood-flow and failure of femoropopliteal reconstructive arterial surgery, relationship between - - - - - - - - - 549
— muscle, following insertion of by-pass vein-graft in femoropopliteal occlusive disease - 429
Bloor, K.: *See* Walker, D. I., jt. auth.
Blumgart, L. H.: *See* Bolton, P. M., jt. auth.

PAGE
Boerhaave syndrome - - - - - - - - 41
Bolton, P. M., and Blumgart, L. H.: Neurological complications of ruptured abdominal aortic aneurysm - - - - - - - 707
Bombeck, C. T.: *See* Gillison, E. W., jt. auth.
Boquist, Lennart: *See* Bergdahl, Leif, jt. auth.
Bouch, D. C., Julian, D. J., Kitchin, A. H., Oliver, M. F., and Wade, J. D.: Surgery for coronary artery disease - - - - - 801
Bowden, W. M.: *See* Cleator, I. G. M., jt. auth.
Bowel herniation through defect of broad ligament 151
— large, Crohn's disease of - - - - - - 823
— — ileostomy and excision of, for Crohn's disease, ileal recurrence after - - - 253
— — lesion of second cancer of large bowel - - 16
Boyle, Ian T.: *See* Scott, Roy, jt. auth.
Brachial plexus lesions associated with traumatic asphyxia - - - - - - - - - 539
Bradfield, W. J. D.: *See* Hall, J. H., jt. auth.
Bradley, J. W. P., and Fielding, L. P.: Hydropneumothorax complicating perforated peptic ulcer - - - - - - - - - - 72
Bramley, P. A., and Norman, J. E. DeB.: Secondary enlargement of mandibular coronoid process 426
Breast, cancer of, regression of axillary lymph-nodes in - - - - - - - - - - 776
— carcinoma, primary, delayed hypersensitivity response in - - - - - - - 505
— subcutaneous rupture of: a seat-belt injury - 491
— tissue, aberrant, carcinoma of - - - - 89
— tumour sex chromatin (Barr body) as index of survival and response to pituitary ablation, evaluation of - - - - - - - 731
Brightmore, Terence: Bilateral double nipples - 55
— — Perianal gas-producing infection of non-clostridial origin - - - - - - 109
Brook, Wilfred, and Gardner, Michael: Anteroposition of the portal vein and spontaneous passage of gall-stones - - - - - 737
Brown, Alastair R.: Non-gangrenous ischaemic colitis - - - - - - - - - 463
Brown, Ashley A.: *See* Simon, John S., jt. auth.
Brown, K. N.: *See* Deutsch, A. A., jt. auth.
Brown, P. P.: *See* Williams, J. Alexander, jt. auth.
Brown, R. F., and Simmonds, F. A.: An unusual dislocation of the hip - - - - - - 326
Browne, Hyacinth I.: *See* MacGowan, W. A. L., jt. auth.
Burden, D. W.: *See* Williams, J. Alexander, jt. auth.
Burton, James A.: Atrophy following testicular torsion - - - - - - - - - 422
Buttock, battered, syndrome—fat fractures - - 165
By-pass surgery, successful femoropopliteal, investigation of oedema of lower limb following: role of phlebography in demonstrating venous thrombosis - - - - - - - - 979
Byrnes, Dermot P.: *See* MacGowan, W. A. L., jt. auth.

CALCIFICATION, leiomyoma of oesophagus with 239
Calcifying epithelioma of Malherbe - - - - 387
Calcinosis, tumoral - - - - - - - 570
Calculi, effects of, on ureteral function - - - 45
Callaghan, Joseph: The Boerhaave syndrome - 41
Calman, K. C., and Bell, P. R. F.: Experimental organ preservation - - - - - - 758
Calnan, J. S.: *See* Greenhalgh, R. M., jt. auth.
Calne, R. Y., Sells, R. A., Marshall, V. C., Millard, P. R., Herbertson, B. M., Hadjiyannakis, E. J., Dunn, D. C., Robson, A. J., and Davis, D. R.: Multiple organ grafts in the pig - - - - - - 969
— — *See also* Robson, A. J., jt. auth.

PAGE
Cancer of breast, regression of axillary lymph-nodes in 776
— mammary, response to therapy of skeletal metastases from 85
— second, of large bowel, lesion of 16
— unresected, of head of pancreas, surgical objectives in 508
Carcinoma of aberrant breast tissue 89
— colon in association with neurofibromatosis, case of 322
— — involving duodenum, 'curative' surgery in 932
— — simulating Crohn's disease 484
— duodenum 50
— primary breast, delayed hypersensitivity response in, as index of host resistance 505
— of renal pelvis, crossed renal ectopia without fusion associated with 235
— secondary, in liver, haemoperitoneum complicating 576
— squamous, of colon, does it exist? 410
— — stomach following corrosive acid burns 382
Cardiac massage, external, aortic aneurysm following 238
Cardiomyotomy, treatment of achalasia by 281
CARTER, D. C., JENKINS, D. H. R., and WHITFIELD, H. N.: Omental reinforcement of intestinal anastomoses 129
CASTRO, J. E., and ASHKEN, M. HANDLEY: Crossed renal ectopia without fusion associated with carcinoma of the renal pelvis 235
Catheter, Fogarty balloon, damage from 389
Cervical oesophagus and laryngopharynx, repair of, after irradiation 524
— swelling, lateral, ectopic thymic tissue presenting as 885
CHAIMOVITZ, C.: *See* HASHMONAI, M., jt. auth.
CHANT, A. D. B.: The effects of posture, exercise, and bandage pressure on the clearance of ^{24}Na from the subcutaneous tissues of the foot 552
Childhood, mesenteric neurofibromatosis in 739
— perforated duodenal ulcer in 288
CHILDS, PETER: Dietary fat, dyspepsia, diarrhoea, and diabetes 669
Chloral hydrate intoxication, rare complication of: gastric necrosis 317
Cholecystectomy, biliary-pressure studies during 267
— drainage following 293
Choledochoduodenostomy 277
Chronic osteomyelitis, primary skin-grafting in treatment of 117
Circulation times, erythrocyte and plasma, in haemorrhagic shock 957
Circumferential oesophageal myotomy 938
CLARK, C. G.: *See* COWIE, A. G. A., jt. auth.
CLARK, ORLO, and TAYLOR, SELWYN: Persistent and recurrent hyperparathyroidism 555
CLARKE, M. B.: *See* NICOLAIDES, A. N., jt. auth.
Claudication, intermittent, simultaneous flow and pressure measurements in 418
CLAYTON JONES, D. G.: *See* SAVAGE, P. E. A., jt. auth.
CLEATOR, I. G. M., and BOWDEN, W. M.: Bowel herniation through a defect of the broad ligament 151
CLUNIE, GORDON J. A.: *See* COLLINS, GEOFFREY M., jt. auth.
Coagulation defect, severe, ruptured angiomatous spleen presenting as 492
COHEN, M.: *See* CUSHIERI, A., jt. auth.
COLCOCK, BENTLEY P.: *See* STEWART, GEORGE R., jt. auth.
Colitis, idiopathic pseudomembranous, successfully treated by surgical excision 154
— non-gangrenous ischaemic 463
COLLINS, C. D.: Perforation of a peptic ulcer in duplicated ileum 159

PAGE
COLLINS, GEOFFREY M., HARTLEY, LIONEL C. J., and CLUNIE, GORDON J. A.: Kidney preservation for transportation 187
Colon, carcinoma of, in association with neurofibromatosis, case of 322
— — involving duodenum, 'curative' surgery in 932
— — simulating Crohn's disease 484
— malakoplakia of 662
— squamous carcinoma of, does it exist? 410
Colonic ileus, spastic, acute myelitis presenting as 918
— ulceration, rectal and, in Behçet's disease 173
Colostomy, modified technique 99
Congenital arteriovenous fistula, single, of hand 76
— oesophago-bronchial fistula in adult 921
Coronary artery disease, surgery for 801
Coronoid process, mandibular, secondary enlargement of 426
COTTON, L. T.: *See* ROBERTS, V. C., jt. auth.; SABRI, S., jt. auth.
COWIE, A. G. A., and CLARK, C. G.: The lithogenic effect of vagotomy 365
Cranial fossa, anterior, fractures of floor of 585
CRELLIN, R. Q.: *See* FIELD, E. S., jt. auth.
CROCKETT, D. J.: *See* NAYLOR, A., jt. auth.
CROFT, C. B., and WILKINSON, A. R.: Ulceration of the mouth, pharynx, and larynx in Crohn's disease of the intestine 249
Crohn's disease, aspects of radiology of 810
— — azathioprine in treatment of 819
— — carcinoma of colon simulating 484
— — ileal recurrence after ileostomy and excision of large bowel for 253
— — of intestine, ulceration of mouth, pharynx, and larynx in 249
— — large bowel 823
— — nutritional disturbances in 817
— — recurrent, surgical resection of 892
— — results of surgical treatment for 826
— — of small intestine, surgical treatment of 821
— — and ulcerative colitis, perimuscular excision of rectum for 29
— — value for diagnosis and research of special investigation on rectal biopsies in 806
CROOKS, J.: *See* HEDLEY, A. J., jt. auth.
CROSBY, D. L.: *See* BLAMEY, R. W., jt. auth.
CRUMPLIN, K. H.: *See* JONES, S. M., jt. auth.
Cryosurgery in treatment of head and neck neoplasia 709
CULLEN, T. H., and VOSS, H. J.: Leiomyoma of the appendix 579
CURRY, BERNADETTE, and GRAY, NORMAN: Visceral neurofibromatosis 494
CUSHIERI, A., HOWELL-HUGHES, J., and COHEN, M.: Biliary-pressure studies during cholecystectomy 267
CUTHBERT, HUGH: *See* LEECH, PETER, jt. auth.
CUTHBERTSON, A. M.: *See* BENNETT, R. C., jt. auth.
CUTHBERTSON, D. P., FELL, G. S., SMITH, CATHERINE M., and TILSTONE, W. J.: Metabolism after injury. I: Effects of severity, nutrition, and environmental temperature on protein potassium, zinc, and creatine 925
Cyst(s), ruptured solitary, of liver 919
— thoracic enteric, and diverticulae 963
Cystic duct ligature, non-absorbable 245
CYWES, S., and MAYELL, MARGARET J.: Mesenteric neurofibromatosis in childhood 739

DANIEL, O.: *See* SHAH, I. K., jt. auth.
DARK, JOHN F.: *See* AHMED, SAEED, jt. auth.
Dartos pouch, maintenance of maldescended testicles within scrotum using 175
DAVIDSON, JAMES S.: Circumferential oesophageal myotomy 938

PAGE
Davis, D. R.: *See* Calne, R. Y., jt. auth.
Davis, P. W., and Foster, D. B. E.: Hirschsprung's disease. A clinical review - - - - 19
Dawson, A. M.: Nutritional disturbances in Crohn's disease - - - - - - - - 817
Dawson, I. M. P.: The value for diagnosis and research of special investigation on rectal biopsies in Crohn's disease - - - 806
Deep-vein thrombosis, diagnosis of - - - 830
— — in patients with fractures of femoral neck - 377
— — postoperative, in a district general hospital, routine use of ultrasound for diagnosis of - 133
— — after prostatectomy, effect of the fibrinolytic inhibitor epsilon-aminocaproic acid on incidence of - - - - - - 522
— — and venous stasis - - - - - 713
Demofonti, A.: *See* Mazzoni, G., jt. auth.
Desmond, A. M., and Reynolds, K. W.: Erosive gastritis: its diagnosis, management, and surgical treatment - - - - - - 5
Deutsch, A. A., Brown, K. N., Freeman, N. V., and Stanley, D. A.: A case of diaphragmatic hernia, absent pericardium, and hamartoma of liver - - - - - - 156
Dhall, D. P.: *See* Mavor, G. F., jt. auth.
Diabetes, dietary fat, dyspepsia, and diarrhoea - 669
Diaphragmatic hernia, case of, absent pericardium, and hamartoma of liver - - - - - 156
Diarrhoea, dietary fat, dyspepsia, and diabetes - 669
Diastasis of the contralateral sacro-iliac joint, anterior dislocation of the hip and—the rear-seat passenger's injury - - - 296
Dickson, G. H.: *See* Frawley, John E., jt. auth.
Dietary fat, dyspepsia, diarrhoea, and diabetes - 669
Dislocation, anterior, of hip and diastasis of contralateral sacro-iliac joint—the rear-seat passenger's injury - - - - - - 296
— unusual, of hip - - - - - - - 326
Distal ileal extrinsic innervation in rabbit and dog, proximal jejunal and - - - - - 394
Diverticulum(ae), intraluminal, of duodenum, case of - - - - - - - - - - 324
— jejunal, foreign-body perforation of - - - 744
— thoracic enteric cysts and - - - - 963
Doig, Caroline M.: The effect of clothing on the dissemination of bacteria in operating theatres 878
de Dombal, F. T.: The results of surgical treatment for Crohn's disease - - - - 826
Donaldson, A. A.: *See* Sangruchi, Vira, jt. auth.
Doran, F. S. A.: A clinical trial to determine whether a Lytle's repair of a primary indirect inguinal hernia needs the addition of a rectus flap - - - - - - 339
— — White, Mary, and Drury, M.: The scope and safety of short-stay surgery in the treatment of groin herniae and varicose veins - 333
Douglas, M., and Duthie, H. L.: Pyloroplasty alone in the management of patients with a negative exploration for duodenal ulcer - - 783
Dowling, B. L.: *See* Lee, E. C. G., jt. auth.
Doyle, F. H.: *See* Galasko, C. S. B., jt. auth.
Doyle, J. C.: *See* Vellar, I. D. A., jt. auth.
Drainage, extrahepatic biliary, in experimental liver injury - - - - - - - - - 136
Drury, M.: *See* Doran, F. S. A., jt. auth.
Dryburgh, Frances: *See* Scott, Roy, jt. auth.
Dukes, Heather M., and Mynors, John M.: Ruptured mycotic aneurysm of the spleen - - 572
Duncan, T.: *See* Hedley, A. J., jt. auth.
Dunn, D. C.: *See* Calne, R. Y., jt. auth.
Duodenal ulcer, acid-fundic selective vagotomy of stomach without drainage in treatment of: technique and results - - - - - 602
— — oesophageal perforation during abdominal truncal vagotomy for - - - - 936
PAGE
Duodenal ulcer, perforated, in childhood - - 288
— prospective study of immediate and long-term results of Polya gastrectomy for - - - 849
— — pyloroplasty alone in management of patients with negative exploration for - - - 783
— — pylorus-preserving gastrectomy in treatment of - - - - - - - - - 27
— — value of preserving pylorus in surgery of - 779
Duodenum, carcinoma of - - - - - 50
— case of intraluminal diverticulum of - - 324
— 'curative' surgery in carcinoma of colon involving - - - - - - - - - 932
Duthie, H. L.: *See* Douglas, M., jt. auth.; Hamer, D. B., jt. auth.
Dyspepsia, dietary fat, diarrhoea, and diabetes - 669
— gall-stone, pyloric function, and - - - 449

Eadie, D. G. A.: *See* Hardy, D. G., jt. auth.
Eastcott, H. H. G.: *See* Frawley, John E., jt. auth.; Lewis, J. D., jt. auth.
Eastwood, D. S.: Subcutaneous rupture of the breast: a seat-belt injury - - - - 491
Eaton, Henry, and Tennekoon, G. E.: Squamous carcinoma of the stomach following corrosive acid burns - - - - - - - 382
Ectopia, crossed renal, without fusion associated with carcinoma of renal pelvis - - - 235
Ectopic kidney, solitary crossed, giant hydronephrosis in - - - - - - - - - 104
— thymic tissue presenting as lateral cervical swelling - - - - - - - - 885
Edmond, P.: *See* Ross, J. A., jt. auth.
Edwards, J. M., Peachey, R. D. G., and Kinmonth, J. B.: Lymphangiography and surgery in lymphangioma of the skin - - 36
Edwards, M. H., Baum, M., and Magarey, C. J.: Regression of axillary lymph-nodes in cancer of the breast - - - - - - - 776
Electrical stimulation of legs, effect of, on postoperative thrombosis - - - - - 65
Electrocoagulation, endarterial, treatment of arteriovenous malformation by - - - - 146
El Masri, S. H.: *See* Gordon-Smith, I. C., jt. auth.
El-Katib, Y.: Pedunculated teratoma of rectum infested with bilharziasis - - - - 655
Elephantiasis neurofibroma, massive haemorrhage in 987
Ellis, Harold, Morgan, N. Naunton, and Wastell, Christopher: 'Curative' surgery in carcinoma of the colon involving duodenum 932
— — *See also* Stoker, T. A. M., jt. auth.
Elmslie, R. G., and Slavotinek, A. H.: Surgical objectives in unresected cancer of the head of the pancreas - - - - - - - 508
Embolectomy, arterial, routine operative arteriography in - - - - - - - - 482
Empey, D. W.: Rectal and colonic ulceration in Behçet's disease - - - - - - 173
Endarterial electrocoagulation, treatment of arteriovenous malformation by - - - - 146
Enteric cysts, thoracic, and diverticulae - - 963
Environmental temperature and nutritional intake, effect of, on metabolic response to abdominal surgery - - - - - - - - 93
Epithelioma, calcifying, of Malherbe - - - 387
Erlik, D.: *See* Hashmonai, M., jt. auth.
Erosive gastritis, diagnosis, management, and surgical treatment of - - - - - - 5
Erythrocyte and plasma circulation times in haemorrhagic shock - - - - - - - 957
Evans, D. B.: *See* Robson, A. J., jt. auth.
Evans, D. M., and Webster, J. H. H.: Spontaneous aortoduodenal fistula - - - - - 368
Excision, perimuscular, of rectum for Crohn's disease and ulcerative colitis - - - - 29

PAGE

Excisional surgery, ulcerative colitis treated by ileostomy and - - - - - - - 345
Extrahepatic biliary drainage in experimental liver injury - - - - - - - - - 136

FARIS, IRWIN: Extrahepatic biliary drainage in experimental liver injury - - - - 136
FAWCETT, A. N., and HARRISON, D. A.: Two unusual leg ulcers - - - - - - - 478
FEGAN, W. G., and KLINE, A. L.: The cause of varicosity in superficial veins of the lower limb - 798
FELL, G. S.: *See* CUTHBERTSON, D. P., jt. auth.
FELL, R. H.: *See* MOLONEY, G. E., jt. auth.
Femoral aneurysm(s) - - - - - - - 614
— — post-irradiation, treated by iliopopliteal by-pass via obturator foramen - - - 400
— artery obstruction, superficial, new non-invasive technique for assessment of - - - 226
— neck, deep-vein thrombosis in patients with fractures of - - - - - - - 371
Femoropopliteal by-pass surgery, successful, investigation of oedema of lower limb following: the role of phlebography in demonstrating venous thrombosis - - - - - - - 979
— occlusive disease, muscle blood-flow following insertion of by-pass vein-graft in - - 429
— reconstructive arterial surgery, failure of, and blood-flow, relationship between - - 549
Femoro-femoral cross-over grafts - - - - 701
FERGUSSON, I. L. C.: Haemangiomata of skeletal muscle - - - - - - - - 634
Fibrescopy, upper gastro-intestinal, value of - - 793
Fibrinogen, radioactive, technique for detecting rejection episodes in human transplant recipients using - - - - - - - 138
Fibrinolysis, alteration in, associated with surgery and venous thrombosis - - - - 754
Fibrinolytic inhibitor epsilon-aminocaproic acid, effect of, on incidence of deep-vein thrombosis after prostatectomy - - - - 522
Fibroblasts and reticulo-endothelial cells, effect of obstructive jaundice on migration of, into early experimental granulomata - - - 875
Fibrosis, idiopathic retroperitoneal, clinical aspects of - - - - - - - - - - 58
FIDLER, MALCOLM: Foreign-body perforation of a jejunal diverticulum - - - - - - 744
FIELD, E. S., NICOLAIDES, A. N., KAKKAR, V. V., and CRELLIN, R. Q.: Deep-vein thrombosis in patients with fractures of the femoral neck - - - - - - - - - 377
— — *See also* NICOLAIDES, A. N., jt. auth.
FIELDING, L. P.: *See* BRADLEY, J. W. P., jt. auth.
FINCH, D. R. A., and GOUGH, M. H.: Ectopic thymic tissue presenting as a lateral cervical swelling - - - - - - - - 885
Finney pyloroplasty, modification of - - - 454
FISH, P.: *See* NICOLAIDES, A. N., jt. auth.
Fistulae, aorto-caval: uncommon complication of abdominal aortic aneurysms - - - 461
— aorto-enteric: uncommon complication of abdominal aortic aneurysms - - - - 458
— arteriovenous, for chronic intermittent haemodialysis, modified surgical technique for - 953
— biliary-enteric, case of gall-stone ileus in absence of - - - - - - - - - - 573
— congenital oesophago-bronchial, in adult - - 921
— post-angiographic vertebral arteriovenous - 627
— single congenital arteriovenous, of hand - - 76
— spontaneous aortoduodenal - - - - 368
— vesico-intestinal - - - - - - - 593
FITZGERALD, D. E.: *See* WOODCOCK, J. P., jt. auth.
FLUTE, P. T.: Conservative management of thrombo-embolism - - - - - - - - 834

Fogarty balloon catheter, damage from - - - 389
Foot, subcutaneous tissues of, effects of posture, exercise, and bandage pressure on clearance of ^{24}Na from - - - - - 552
Foreign-body perforation of jejunal diverticulum - 744
Fossa, anterior cranial, fractures of floor of - 585
FOSTER, D. B. E.: *See* DAVIS, P. W., jt. auth.
Fracture(s), fat—battered buttock syndrome - - 165
— of femoral neck, deep-vein thrombosis in patients with - - - - - - - - 377
— floor of anterior cranial fossa - - - - 585
FRAWLEY, JOHN E., DICKSON, G. H., JAMIESON, C. W., and EASTCOTT, H. H. G.: Abdominal aortic aneurysm and horse-shoe kidney - 513
FREEMAN, N. V.: *See* DEUTSCH, A. A., jt. auth.
Frusemide in 110 consecutive prostatectomies, value of - - - - - - - - - - 190
Fundoplication for relief of oesophageal reflux due to hiatus hernia, results of - - - - 285

GACHES, CHRISTOPHER: *See* SLADE, NORMAN, jt. auth.
GALASKO, C. S. B., and DOYLE, F. H.: The response to therapy of skeletal metastases from mammary cancer - - - - - - - 85
Gall-bladder, tuberculosis of - - - - - 289
Gall-stone(s) dyspepsia, pyloric function and - - 449
— ileus in absence of biliary-enteric fistula, case of 573
— spontaneous passage of, and anteroposition of portal vein - - - - - - - 737
GARDNER, A. M. N., and STEWART, I. A.: Treatment of arteriovenous malformation by endarterial electrocoagulation - - - - - - 146
— — *See also* BROOK, WILFRED, jt. auth.
GARNER, RICHARD W., and MOWAT, ALASTAIR G.: Joint rupture in Reiter's disease - - - 657
Gas cavity, artificially produced, ventilation of, under basal conditions - - - - - 624
Gastrectomy, pylorus-preserving, in treatment of duodenal ulcer - - - - - - - 27
Gastric decompression after vagotomy, randomized prospective trial comparing three established methods of - - - - - - 605
— juice, bacterial content of - - - - - 443
— necrosis, rare complication of chloral hydrate intoxication - - - - - - - 317
— secretion during routine secretion studies in man, assessment of value of measuring uncollected - - - - - - - - - 473
— ulcer, high, operative treatment of, with special reference to Pauchet's method - - - 1
— — treatment of, by highly selective vagotomy without a drainage procedure - - - 787
Gastritis, erosive, diagnosis, management, and surgical treatment of - - - - - - 5
— postgastrectomy alkaline reflux reversibility of, by Roux-en-Y loop - - - - - - 13
Gastro-intestinal fibroscopy, upper, value of - - 793
— surgery, wound antibiotics in - - - - - 184
GENTILI, B.: *See* MAZZONI, G., jt. auth.
GILL, W.: *See* JENKINS, D. H. R., jt. auth.
GILLESPIE, GORDON, and MACPHERSON, GORDON H.: Acute intramural abscess of the pyloric antrum—localized phlegmon - - - - 197
GILLIE, I.: *See* WALKER, D. I., jt. auth.
GILLISON, E. W., KUSAKARI, K., BOMBECK, C. T., and NYHUS, L. M.: The importance of bile in reflux oesophagitis and the success in its prevention by surgical means - - - - 794
GIRDWOOD, R. W.: *See* KEIGHLEY, M. R. B., jt. auth.
Glomus jugulare tumours—radiotherapy or surgery? 947
— tumour - - - - - - - - - 91
GLOVER, G. W., and BLOCK, J.: Glomus jugulare tumours—radiotherapy or surgery? - - 947

PAGE

GOLDING, P. L., SINGH, M., and WORTHINGTON, B.: Bilateral ureteric obstruction caused by benign pelvic lipomatosis - - - - 69
GOLIGHER, J. C.: Ileal recurrence after ileostomy and excision of the large bowel for Crohn's disease - - - - - - - - - 253
GOODWIN, N. E.: *See* HICKMAN, R., jt. auth.
GORDON, I.: *See* MILLER, D. F., jt. auth.
GORDON-SMITH, I. C., HICKMAN, J. A., and EL MASRI, S. H.: The effect of the fibrinolytic inhibitor epsilon-aminocaproic acid on the incidence of deep-vein thrombosis after prostatectomy - - - - - - - 522
GOSLING, R. G.: *See* WOODCOCK, J. P., jt. auth.
GOUGH, M. H.: *See* FINCH, D. R. A., jt. auth.
Graft(s), axillary-femoral by-pass, in treatment of aorto-iliac occlusive disease - - - 704
— femoro-femoral cross-over - - - - 701
— multiple organ, in pig - - - - - 969
GRAY, NORMAN: *See* CURRY, BERNADETTE, jt. auth.
GREEN, P. W. B., HAWKINS, B. S., IRVINE, W. T., and JAMIESON, C. W.: An assessment of above- and through-knee amputations - - - 873
GREENHALGH, R. M., ROSENGARTEN, D. S., and CALNAN, J. S.: A single congenital arteriovenous fistula of the hand - - - - 76
GREENING, W. P.: *See* SMITH, G. M. R., jt. auth.
GREGORY, M. M.: *See* VOIGT, J. C., jt. auth.
GRIFFITHS, GORDON: *See* HUDDY, PHILLIP, jt. auth.
GROGONO, J. L., and PARKS, A. G.: Surgical resection of recurrent Crohn's disease - - 892
Groin herniae and varicose veins, scope and safety of short-stay surgery in treatment of - - 333
GRUNDY, D. J., KING, P. A., and LLOYD, G.: Comparative evaluation of preoperative and operative radiology in biliary-tract disease - 205
GUE, S.: Development of right inguinal hernia following appendicectomy - - - - 352
GUERRIER, HUGH P., and TURNER, MAURICE J.: A case of intraluminal diverticulum of the duodenum - - - - - - - 324
GUNN, A.: The non-absorbable cystic duct ligature 245
— — and KEDDIE, N. C.: Abdominal tuberculosis 597
GUNSTENSEN, J., and WADE, J. D.: Mediastinoscopy 209

HADJIYANNAKIS, E. J.: *See* CALNE, R. Y., jt. auth.
Haemangioma(s), retroperitoneal, case of - - 74
— of skeletal muscle - - - - - - - 634
Haemangiosarcoma of spleen - - - - - 406
Haematocrit and plasma-fibrinogen, postoperative changes in blood viscosity and influence of - 629
Haemodialysis, chronic intermittent, arteriovenous fistulae for: modified surgical technique - 953
Haemodynamics of hind-limb in greyhound dogs, effects of intermittently applied external pressure on - - - - - - 219
— lower limb in man, effect of intermittently applied external pressure on - - - 223
Haemoperitoneum complicating secondary carcinoma in liver - - - - - - - 576
Haemorrhage, massive, in elephantiasis neurofibroma - - - - - - - - 987
— secondary, from arterial anastomosis of renal allografts - - - - - - - - 890
— shock, erythrocyte and plasma circulation times in - - - - - - - - - 957
HAINES, J. R.: *See* LEE, EMANOEL, jt. auth.
HALE, J. E., and MACKENZIE, D. H.: Subcutaneous nodular lymphohistiocytic hyperplasia - 375
HALL, G. F. M.: *See* TOGHILL, P. J., jt. auth.
HALL, J. H., and BRADFIELD, W. J. D.: Prolapse of the ileum through the rectum and anal canal - - - - - - - - 149

PAGE

HALL, R. R.: Hyperkalaemia following temporary occlusion of the portal vein and hepatic artery 125
HALPIN, D. S.: *See* WILLIAMS, C. B., jt. auth.
HAM, J. M., JONES, M., and KEMP, D.: Platelet adhesiveness and lipoprotein lipase activity in patients with benign and malignant disease of the prostate - - - - - 60
Hamartoma of liver, case of diaphragmatic hernia, absent pericardium, and - - - - 156
HAMER, D. B., and DUTHIE, H. L.: Pneumoperitoneum in the management of abdominal incisional hernia - - - - - 372
HAMER, J. D.: Investigation of oedema of the lower limb following successful femoropopliteal by-pass surgery: the role of phlebography in demonstrating venous thrombosis - - 979
HAMILTON, T.: *See* HEADING, R. C., jt. auth.
Hand, single congenital arteriovenous fistula of - 76
HARDY, D. G., and EADIE, D. G. A.: Femoral aneurysms - - - - - - - 614
HARRISON, D. A.: *See* FAWCETT, A. N., jt. auth.
HARTLEY, LIONEL C. J.: *See* COLLINS, GEOFFREY M., jt. auth.
HASHMONAI, M., SCHRAMEK, A., CHAIMOVITZ, C., and ERLIK, D.: Arteriovenous fistulae for chronic intermittent dialysis: a modified surgical technique - - - - - 953
HAWKINS, B. S.: *See* GREEN, P. W. B., jt. auth.
HAWLEY, P. R.: *See* PENFOLD, J. C. B., jt. auth.
Head, mortality in missile wounds of - - - 201
— and neck neoplasia, cryosurgery in treatment of 709
— of pancreas, unresected cancer of, surgical objectives in - - - - - - - 508
HEADING, R. C., MCCLELLAND, D. B. I., STUART, A. E., and HAMILTON, T.: Ruptured angiomatous spleen presenting as a severe coagulation defect - - - - - - - 492
HEALD, R. J., and LOCKHART-MUMMERY, H. E.: The lesion of the second cancer of the large bowel - - - - - - - - - 16
HEDLEY, A. J., MICHIE, W., DUNCAN, T., HEMS, G., and CROOKS, J.: The effect of remnant size on the outcome of subtotal thyroidectomy for thyrotoxicosis - - - - - - - 559
Hemithorax, skin-lined, technique for creating - 868
HEMS, G.: *See* HEDLEY, A. J., jt. auth.
HENDERSON, P. N.: *See* BAXTER, THELMA J., jt. auth.
HENNESSY, T. P. J., WEIR, D. G., and D'AURIA, D.: Pylorus-preserving gastrectomy in the treatment of duodenal ulcer - - - - - 27
Hepatic artery, hyperkalaemia following temporary occlusion of portal vein and - - - 125
— failure, acute, model to improve treatment of - 771
HERBERTSON, B. M.: *See* CALNE, R. Y., jt. auth.
Hernia(e), abdominal incisional, pneumoperitoneum in management of - - - - - - 372
— diaphragmatic, absent pericardium, and hamartoma of liver, case of - - - - - 156
— giant, pneumoperitoneum as aid in surgical treatment of - - - - - - - 360
— groin, and varicose veins, scope of safety of short-stay surgery in treatment of - - 333
— hiatus, results of fundoplication for relief of oesophageal reflux due to - - - - 285
— — symptomatic, results of operations for - - 432
— primary indirect inguinal, clinical trial to determine whether Lytle's repair of, needs addition of rectus flap - - - - - - 339
— right inguinal, following appendicectomy, development of - - - - - - 352
— — — — — incidence of - - - - 623
Herniation, bowel, through a defect of broad ligament - - - - - - - - - 151
Hiatus hernia, results of fundoplication for relief of oesophageal reflux due to - - - - 285

THE BRITISH JOURNAL OF SURGERY

THE BRITISH JOURNAL OF SURGERY

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CONTENTS OF VOLUME 59

Number 1

Original Papers PAGE

Operative Treatment of High Gastric Ulcer with Special Reference to Pauchet's Method *Adam Lewis and George Qvist* 1

Erosive Gastritis: Its Diagnosis, Management, and Surgical Treatment *A. M. Desmond and K. W. Reynolds* 5

The Reversibility of Postgastrectomy Alkaline Reflux Gastritis by a Roux-en-Y Loop *H. H. Lawson* 13

The Lesion of the Second Cancer of the Large Bowel - *R. J. Heald and H. E. Lockhart-Mummery* 16

Hirschsprung's Disease - - - - - - *P. W. Davis and D. B. E. Foster* 19

Pylorus-preserving Gastrectomy in the Treatment of Duodenal Ulcer *T. P. J. Hennessy, D. G. Weir, and D. D'Auria* 27

Perimuscular Excision of the Rectum for Crohn's Disease and Ulcerative Colitis *E. C. G. Lee and B. L. Dowling* 29

Vesico-ureteric Reflux following Renal Transplantation *R. V. S. Yadav, W. Johnson, P. J. Morris, P. Sprague, D. Yoffa, and V. C. Marshall* 33

Lymphangiography and Surgery in Lymphangioma of the Skin *J. M. Edwards, R. D. G. Peachey, and J. B. Kinmonth* 36

The Boerhaave Syndrome - - - - - - - - - - *Joseph Callaghan* 41

The Effects of Calculi on Ureteral Function - - - - *J. A. Ross and P. Edmond* 45

Carcinoma of the Duodenum - - - - - - - - - *John S. Kenefick* 50

Bilateral Double Nipples - - - - - - - - - - *Terence Brightmore* 55

Some Clinical Aspects of Idiopathic Retroperitoneal Fibrosis - - - *M. J. Mitchinson* 58

Platelet Adhesiveness and Lipoprotein Lipase Activity in Patients with Benign and Malignant Disease of the Prostate - - - - - - - - - *J. M. Ham, M. Jones, and D. Kemp* 60

Reticulo-endothelial System Activity during Homograft Rejection and Immunosuppression *R. W. Blamey, Jane M. Baker, and D. L. Crosby* 62

The Effect of Electrical Stimulation of the Legs on Postoperative Thrombosis *G. E. Moloney, M. Tessa Morrell, and R. H. Fell* 65

Short Notes of Rare or Obscure Cases - - - - - - - - - - 69

Reviews and Notices of Books - - - - - - - - - - 81

Number 2

Original Papers

The Response to Therapy of Skeletal Metastases from Mammary Cancer *C. S. B. Galasko and F. H. Doyle* 85

Carcinoma of Aberrant Breast Tissue - - - - - *G. M. R. Smith and W. P. Greening* 89

Glomus Tumour - - - - - - - *J. Strahan and H. W. C. Bailie* 91

The Effect of Environmental Temperature and Nutritional Intake on the Metabolic Response to Abdominal Surgery - - - - - - *John Spivey and Ivan D. A. Johnston* 93

The Effect of a Single-dose Parenteral Antibiotic in the Prevention of Wound Infection *A. V. Pollock and D. S. Tindal.* 98

A Modified Technique of Colostomy - - - - - - - *L. R. Abeyatunge* 99

PAGE
The Local Effects of Intra-arterial Injections of Sodium Tetradecyl Sulphate (S.T.D.) 3 per cent — *W. A. L. MacGowan, P. D. J. Holland, Hyacinth I. Browne, and Dermot P. Byrnes* 101
Giant Hydronephrosis in a Solitary Crossed Ectopic Kidney - *A. J. Yates-Bell and D. A. Packham* 104
Inhibition of the Growth of Tumour Cells in Culture by Noxytiolin - - - *C. W. Jamieson* 108
Perianal Gas-producing Infection of Non-clostridial Origin - - - *Terence Brightmore* 109
Primary Skin-grafting in the Treatment of Chronic Osteomyelitis - *A. Naylor and D. J. Crockett* 117
Hyperkalaemia following Temporary Occlusion of the Portal Vein and Hepatic Artery *R. R. Hall* 125
Omental Reinforcement of Intestinal Anastomoses *D. C. Carter, D. H. R. Jenkins, and H. N. Whitfield* 129
The Routine Use of Ultrasound for the Diagnosis of Postoperative Deep-vein Thrombosis in a District General Hospital - - - - - - - - - - - - - - *R. F. McIlroy* 133
Extrahepatic Biliary Drainage in Experimental Liver Injury - - - - - *Irwin Faris* 136
A Technique for detecting Rejection Episodes in Human Transplant Recipients using Radioactive Fibrinogen - - - - - - - - - - - - - - *John R. Salaman* 138
Abdominal Wound Infections and Plastic Wound Guards — *J. Alexander Williams, G. D. Oates, P. P. Brown, D. W. Burden, Jane McCall, A. G. Hutchison, and Lorna J. Lees* 142
Treatment of Arteriovenous Malformation by Endarterial Electrocoagulation — *A. M. N. Gardner and I. A. Stewart* 146
Short Notes of Rare or Obscure Cases - - - - - - - - - - 149
Reviews and Notices of Books - - - - - - - - - - - 161

Number 3

Original Papers

The Battered Buttock Syndrome—Fat Fractures - - - - - *B. F. Meggitt and J. N. Wilson* 165
Ligation of the Left Renal Vein in Splenorenal Anastomosis without Impairment of Renal Function *John S. Simon, Ashley A. Brown, and Harvey B. Ross* 170
Rectal and Colonic Ulceration in Behçet's Disease - - - - - - - *D. W. Empey* 173
The Maintenance of Maldescended Testicles within the Scrotum using a Dartos Pouch *W. J. Pryn* 175
Peritonitis from Amoebic Liver Abscess - - - - - - - - - *E. Q. Archampong* 179
New Instruments for Microvascular Surgery - - - - - - - *Robert Acland* 181
Wound Antibiotics in Gastro-intestinal Surgery - - - - *T. A. M. Stoker and Harold Ellis* 184
Kidney Preservation for Transportation *Geoffrey M. Collins, Lionel C. J. Hartley, and Gordon J. A. Clunie* 187
The Value of Frusemide in 110 Consecutive Prostatectomies - - - - - *C. R. Williams* 190
The Effect of Oral Supplementation of Zinc Sulphate on Primary Wound Healing in Rats *U. I. Lavy* 194
Acute Intramural Abscess of the Pyloric Antrum—Localized Phlegmon — *Gordon Gillespie and Gordon H. MacPherson* 197
The Obliteration of Perforating Veins in the Leg - - - - - - - - *R. J. Bentley* 199
Mortality in Missile Wounds of the Head - - - - - - - - *Adelola Adeloye* 201
Comparative Evaluation of Preoperative and Operative Radiology in Biliary-tract Disease — *D. J. Grundy, P. A. King, and G. Lloyd* 205
Mediastinoscopy - - - - - - - - - - - *J. Gunstensen and J. D. Wade* 209
Argentaffin-cell Tumour of Meckel's Diverticulum *E. L. Jones, H. Thompson, and J. Alexander Williams* 213
The Effects of Intermittently Applied External Pressure on the Haemodynamics of the Hind-limb in Greyhound Dogs - - - - - - - - - *S. Sabri, V. C. Roberts, and L. T. Cotton* 219
The Effect of Intermittently Applied External Pressure on the Haemodynamics of the Lower Limb in Man - - - - - - - *V. C. Roberts, S. Sabri, A. H. Beeley, and L. T. Cotton* 223
A New Non-invasive Technique for Assessment of Superficial Femoral Artery Obstruction — *J. P. Woodcock, R. G. Gosling, and D. E. FitzGerald* 226
The Fate of Aortic Valve Homografts — *P. E. A. Savage, D. G. Clayton Jones, A. E. Thompson, and D. N. Ross* 231
Short Notes of Rare or Obscure Cases - - - - - - - - - - 235
Reviews and Notices of Books - - - - - - - - - - - 246

NUMBER 4

Original Papers

PAGE
ULCERATION OF THE MOUTH, PHARYNX, AND LARYNX IN CROHN'S DISEASE OF THE INTESTINE *C. B. Croft and A. R. Wilkinson* 249
ILEAL RECURRENCE AFTER ILEOSTOMY AND EXCISION OF THE LARGE BOWEL FOR CROHN'S DISEASE *J. C. Goligher* 253
THROUGH-KNEE AMPUTATION *J. F. Newcombe and R. W. Marcuson* 260
BILIARY-PRESSURE STUDIES DURING CHOLECYSTECTOMY *A. Cushieri, J. Howell Hughes, and M. Cohen* 267
TWELVE-HOUR LIVER PRESERVATION IN THE PIG USING HYPOTHERMIA AND HYPERBARIC OXYGEN *Harold Spilg, C. J. Uys, Rosemary Hickman, Stuart J. Saunders, and John Terblanche* 273
CHOLEDOCHODUODENOSTOMY *A. G. Johnson and A. J. Harding Rains* 277
THE TREATMENT OF ACHALASIA BY CARDIOMYOTOMY *H. V. Wingfield and A. Karwowski* 281
THE RESULTS OF FUNDOPLICATION FOR THE RELIEF OF OESOPHAGEAL REFLUX DUE TO HIATUS HERNIA *I. K. Shah and O. Daniel* 285
PERFORATED DUODENAL ULCER IN CHILDHOOD *J. M. S. Johnstone and R. F. Rintoul* 288
TUBERCULOSIS OF THE GALL-BLADDER *Leif Bergdahl and Lennart Boquist* 289
DRAINAGE FOLLOWING CHOLECYSTECTOMY *C. B. Williams, D. S. Halpin, and A. J. S. Knox* 293
ANTERIOR DISLOCATION OF THE HIP AND DIASTASIS OF THE CONTRALATERAL SACRO-ILIAC JOINT—THE REAR-SEAT PASSENGER'S INJURY? *D. E. Markham* 296
SURGICAL RESEARCH SOCIETY 299
Short Notes of Rare or Obscure Cases 317
Reviews and Notices of Books 328

NUMBER 5

Original Papers

THE SCOPE AND SAFETY OF SHORT-STAY SURGERY IN THE TREATMENT OF GROIN HERNIAE AND VARICOSE VEINS *F. S. A. Doran, Mary White, and M. Drury* 333
A CLINICAL TRIAL TO DETERMINE WHETHER A LYTLE'S REPAIR OF A PRIMARY INDIRECT INGUINAL HERNIA NEEDS THE ADDITION OF A RECTUS FLAP *F. S. A. Doran* 339
ULCERATIVE COLITIS TREATED BY ILEOSTOMY AND EXCISIONAL SURGERY *Jean K. Ritchie* 345
DEVELOPMENT OF RIGHT INGUINAL HERNIA FOLLOWING APPENDICECTOMY *S. Gue* 352
TUBERCULOUS PERIPHERAL LYMPHADENITIS *A. A. Hooper* 353
PNEUMOPERITONEUM AS AN AID IN THE SURGICAL TREATMENT OF GIANT HERNIAE *Henry H. Barst* 360
THE LITHOGENIC EFFECT OF VAGOTOMY *A. G. A. Cowie and C. G. Clark* 365
SPONTANEOUS AORTODUODENAL FISTULA *D. M. Evans and J. H. H. Webster* 368
PNEUMOPERITONEUM IN THE MANAGEMENT OF ABDOMINAL INCISIONAL HERNIA *D. B. Hamer and H. L. Duthie* 372
SUBCUTANEOUS NODULAR LYMPHOHISTIOCYTIC HYPERPLASIA *J. E. Hale and D. H. Mackenzie* 375
DEEP-VEIN THROMBOSIS IN PATIENTS WITH FRACTURES OF THE FEMORAL NECK *E. S. Field, A. N. Nicolaides, V. V. Kakkar, and R. Q. Crellin* 377
NON-RECURRENT LARYNGEAL NERVE *George R. Stewart, John C. Mountain, and Bentley P. Colcock* 379
SQUAMOUS CARCINOMA OF THE STOMACH FOLLOWING CORROSIVE ACID BURNS *Henry Eaton and G. E. Tennekoon* 382
CALCIFYING EPITHELIOMA OF MALHERBE *S. M. Jones and K. H. Crumplin* 387
DAMAGE FROM THE FOGARTY BALLOON CATHETER *G. E. Mavor, M. G. Walker, D. P. Dahl, and C. A. S. Pegg* 389
ORBITAL HYDATID DISEASE IN IRAQ *H. Talib* 391
PROXIMAL JEJUNAL AND DISTAL ILEAL EXTRINSIC INNERVATION IN THE RABBIT AND DOG *D. H. R. Jenkins and I. B. Macleod* 394
Short Notes of Rare or Obscure Cases 400
Reviews and Notices of Books 413

Number 6

Original Papers

PAGE

Sir Cecil Wakeley 417

Simultaneous Flow and Pressure Measurements in Intermittent Claudication
J. D. Lewis, C. Papathanaiou, S. T. Yao, and H. H. G. Eastcott 418

Atrophy following Testicular Torsion *James A. Burton* 422

Secondary Enlargement of the Mandibular Coronoid Process *P. A. Bramley and J. E. DeB. Norman* 426

Muscle Blood-flow following Insertion of a By-pass Vein-graft in Femoropopliteal Occlusive Disease
Graham Bell and Douglas W. Short 429

The Results of 101 Operations for Symptomatic Hiatus Hernia *C. J. Magarey* 432

The Movements of the Adult *Ascaris Lumbricoides* *Milroy Paul* 437

Bacterial Content of the Gastric Juice *A. B. Macgregor and P. W. Ross* 443

A Method of Repair of Myelomeningoceles *Carys M. Bannister* 445

Pyloric Function and Gall-stone Dyspepsia *A. G. Johnson* 449

A Modification of the Finney Pyloroplasty *C. Wastell* 454

Aorto-enteric Fistulae: An Uncommon Complication of Abdominal Aortic Aneurysms
J. P. D. Reckless, I. McColl, and G. W. Taylor 458

Aorto-caval Fistulae: An Uncommon Complication of Abdominal Aortic Aneurysms
J. P. D. Reckless, I. McColl, and G. W. Taylor 461

Non-gangrenous Ischaemic Colitis *Alastair R. Brown* 463

An Assessment of the Value of measuring Uncollected Gastric Secretion during Routine Secretion Studies in Man *C. W. Venables* 473

Two Unusual Leg Ulcers *A. N. Fawcett and D. A. Harrison* 478

Routine Operative Arteriography in Arterial Embolectomy *G. E. Mavor, M. G. Walker, and D. P. Dhall* 482

Carcinoma of Colon simulating Crohn's Disease *B. J. Stoodley and C. V. Mann* 484

Prostatectomy and Deep-vein Thrombosis
A. N. Nicolaides, E. S. Field, V. V. Kakkar, A. J. Yates-Bell, S. Taylor, and M. B. Clarke 487

Short Notes of Rare or Obscure Cases 489

Reviews and Notices of Books 497

Number 7

Original Papers

Malignant Tumours of the Bile-ducts *Kenneth W. Warren, John C. Mountain, and William Lloyd-Jones* 501

The Delayed Hypersensitivity Response in Primary Breast Carcinoma as an Index of Host Resistance
Roger J. Mitchell 505

Surgical Objectives in Unrestricted Cancer of the Head of the Pancreas
R. G. Elmslie and A. H. Slavotinek 508

Abdominal Aortic Aneurysm and Horse-shoe Kidney
John E. Frawley, G. H. Dickson, C. W. Jamieson, and H. H. G. Eastcott 513

The Diagnosis of Parathyroid Overactivity in a Population of Renal Stone Formers
Roy Scott, Frances Dryburgh, Robert Wilson, Ian T. Boyle, and David Pollock 517

The Effect of the Fibrinolytic Inhibitor Epsilon-aminocaproic Acid on the Incidence of Deep-vein Thrombosis after Prostatectomy *I. C. Gordon-Smith, J. A. Hickman, and S. H. El Masri* 522

Repair of the Laryngopharynx and Cervical Oesophagus after Irradiation *H. J. Shaw* 524

PAGE

THE ROLE OF RADIOTHERAPY IN THE MANAGEMENT OF MALIGNANT THYMOMA *C. R. H. Penn and H. F. Hope-Stone* 533

BRACHIAL PLEXUS LESIONS ASSOCIATED WITH TRAUMATIC ASPHYXIA - - *Peter Leech and Hugh Cuthbert* 539

A COMPARISON OF PORTAL AND SYSTEMIC VENOUS DRAINAGE IN PORCINE RENAL ALLOGRAFTS *G. Mazzoni, C. Di Martino, A. Demofonti, A. Valli, S. Pellegrini, B. Gentili, and M. Melis* 541

THE SINGLE THYROID NODULE *A. Psarras, S. N. Papadopoulos, D. Livadas, A. D. Pharmakiotis, and D. A. Koutras* 545

THE RELATIONSHIP BETWEEN BLOOD-FLOW AND FAILURE OF FEMOROPOPLITEAL RECONSTRUCTIVE ARTERIAL SURGERY - - - - - - - - *H. J. Terry, J. S. Allan, and G. W. Taylor* 549

THE EFFECTS OF POSTURE, EXERCISE, AND BANDAGE PRESSURE ON THE CLEARANCE OF ^{24}Na FROM THE SUBCUTANEOUS TISSUES OF THE FOOT - - - - - - - - - - *A. D. B. Chant* 552

PERSISTENT AND RECURRENT HYPERPARATHYROIDISM - - - - *Orlo Clark and Selwyn Taylor* 555

THE EFFECT OF REMNANT SIZE ON THE OUTCOME OF SUBTOTAL THYROIDECTOMY FOR THYROTOXICOSIS *A. J. Hedley, W. Michie, T. Duncan, G. Hems, and J. Crooks* 559

THE EFFECT OF EXPERIMENTAL BILE-DUCT OBSTRUCTION ON CRITICAL BIOSYNTHETIC FUNCTIONS OF THE LIVER *Emanoel Lee, B. D. Ross, and J. R. Haines* 564

PERIPHERAL TUBERCULOUS LYMPHADENITIS IN THE ELDERLY - - - - - *A. L. G. Peel* 568

Short Notes of Rare or Obscure Cases - - - - - - - - - 570

Reviews and Notices of Books - - - - - - - - - - 581

NUMBER 8

Original Papers

FRACTURES OF THE FLOOR OF THE ANTERIOR CRANIAL FOSSA - - *Antony Jefferson and Gerald Reilly* 585

VESICO-INTESTINAL FISTULAE - - - - - - - *Norman Slade and Christopher Gaches* 593

ABDOMINAL TUBERCULOSIS - - - - - - - - *A. Gunn and N. C. Keddie* 597

ACID-FUNDIC SELECTIVE VAGOTOMY OF THE STOMACH WITHOUT DRAINAGE IN THE TREATMENT OF DUODENAL ULCER: TECHNIQUE AND RESULTS - - *Luigi Imperati, Costanzo Natale, and Francesco Marinaccio* 602

A RANDOMIZED PROSPECTIVE TRIAL COMPARING THREE ESTABLISHED METHODS OF GASTRIC DECOMPRESSION AFTER VAGOTOMY - - - - - *D. F. Miller, J. R. Mason, J. McArthur, and I. Gordon* 605

INFLAMMATORY ANEURYSMS OF THE ABDOMINAL AORTA - *D. I. Walker, K. Bloor, G. Williams, and I. Gillie* 609

FEMORAL ANEURYSMS - - - - - - - - - - *D. G. Hardy and D. G. A. Eadie* 614

THE HISTOPATHOLOGY OF SMALL VESSELS FOLLOWING MICROVASCULAR REPAIR *Thelma J. Baxter, B. McC. O'Brien, P. N. Henderson, and R. C. Bennett* 617

THE INCIDENCE OF RIGHT INGUINAL HERNIA FOLLOWING APPENDICECTOMY *Peter Leech, Gordon Waddell, and Robert G. Main* 623

VENTILATION IN AN ARTIFICIALLY PRODUCED GAS CAVITY UNDER BASAL CONDITIONS - - *Lade Wosornu* 624

POST-ANGIOGRAPHIC VERTEBRAL ARTERIOVENOUS FISTULAE *Vira Sangruchi, Edward Hitchcock, and A. A. Donaldson* 627

POSTOPERATIVE CHANGES IN BLOOD VISCOSITY AND THE INFLUENCE OF HAEMATOCRIT AND PLASMA-FIBRINOGEN *J. V. Harvey Kemble and J. A. Hickman* 629

MALIGNANT MELANOMATA: AN AID TO PREOPERATIVE DIAGNOSIS - - - - *Rona M. Mackie* 632

HAEMANGIOMATA OF SKELETAL MUSCLE - - - - - - - *I. L. C. Fergusson* 634

NASOGASTRIC TUBE MANAGEMENT - - - - - - - - - *Laurence Tinckler* 637

TREATMENT OF PERITONITIS WITH PER- AND POSTOPERATIVE IRRIGATION OF THE PERITONEAL CAVITY WITH NOXYTHIOLIN SOLUTION - - - - - - - - - - - *R. G. Pickard* 642

SPONTANEOUS RUPTURE OF THE OESOPHAGUS *M. R. B. Keighley, R. W. Girdwood, M. I. Ionescu, and G. H. Wooler* 649

Short Notes of Rare or Obscure Cases - - - - - - - - - - 653

Reviews and Notices of Books - - - - - - - - - - - 665

NUMBER 9

Original Papers PAGE

Dietary Fat, Dyspepsia, Diarrhoea, and Diabetes *Peter Childs* 669
The Origin of Phleboliths *Philip Shemilt* 695
Femoro-femoral Cross-over Grafts *R. Baker and E. J. C. Parker* 701
Axillary-femoral By-pass Grafts in the Treatment of Aorto-iliac Occlusive Disease *A. V. Pollock* 704
Neurological Complications of Ruptured Abdominal Aortic Aneurysm *P. M. Bolton and L. H. Blumgart* 707
Cryosurgery in the Treatment of Head and Neck Neoplasia *H. B. Holden and P. McKelvie* 709
Venous Stasis and Deep-vein Thrombosis *A. N. Nicolaides, V. V. Kakkar, E. S. Field, and P. Fish* 713
Anatomy of the External Anal Sphincter *Changyul Oh and Allan E. Kark* 717
Long-term Review of Function following Pull-through Operations of the Rectum *R. C. Bennett, E. S. R. Hughes, and A. M. Cuthbertson* 723
The Fate and Function of the Thyroid Remnant *H. B. Young and N. Macleod* 726
Evaluation of Breast Tumour Sex Chromatin (Barr Body) as an Index of Survival and Response to Pituitary Ablation *Michael Perry* 731
Amputation Neuroma of the Great Auricular Nerve after Parotidectomy *Michael Hobsley* 735

Short Notes of Rare or Obscure Cases 737

Reviews and Notices of Books 748

NUMBER 10

Association of Surgeons of Great Britain and Ireland

Short Papers for the Moynihan Prize

The Natural History of Venous Thrombo-embolism *M. G. Walker* 753
Alteration in Fibrinolysis associated with Surgery and Venous Thrombosis *Averil O. Mansfield* 754
Experimental Organ Preservation *K. C. Calman and P. R. F. Bell* 758
The Effect of Ischaemic Injury on Kidneys preserved for 24 Hours before Transplantation *R. W. G. Johnson* 765
A Model which can be used to improve the Treatment of Acute Hepatic Failure *John Winch* 771
Regression of Axillary Lymph-nodes in Cancer of the Breast *M. H. Edwards, M. Baum, and C. J. Magarey* 776
The Value of Preserving the Pylorus in the Surgery of Duodenal Ulcer *C. S. Humphrey and A. R. Wilkinson* 779

Short Papers

Pyloroplasty alone in the Management of Patients with a Negative Exploration for Duodenal Ulcer *M. Douglas and H. L. Duthie* 783
Treatment of Gastric Ulcer by Highly Selective Vagotomy without a Drainage Procedure: An Interim Report *D. Johnston, C. S. Humphrey, R. B. Smith, and A. R. Wilkinson* 787
The Value of Upper Gastro-intestinal Gastroscopy *Ian McColl* 793
The Importance of Bile in Reflux Oesophagitis and the Success in its Prevention by Surgical Means *E. W. Gillison, K. Kusakari, C. T. Bombeck, and L. M. Nyhus* 794
The Cause of Varicosity in Superficial Veins of the Lower Limb *W. G. Fegan and A. L. Kline* 798
Surgery for Coronary Artery Disease *D. C. Bouch, D. J. Julian, A. H. Kitchin, M. F. Oliver, and J. D. Wade* 801

Symposium on Crohn's Disease

The Value for Diagnosis and Research of Special Investigation on Rectal Biopsies in Crohn's Disease *I. M. P. Dawson* 806
Some Aspects of the Radiology of Crohn's Disease *K. C. Simpkins* 810
Nutritional Disturbances in Crohn's Disease *A. M. Dawson* 817
Azathioprine in the Treatment of Crohn's Disease *J. Rhodes* 819
Surgical Treatment of Crohn's Disease of the Small Intestine *James Kyle* 821
Crohn's Disease of the Large Bowel *H. E. Lockhart-Mummery* 823
The Results of Surgical Treatment for Crohn's Disease *F. T. de Dombal* 826

PAGE

Symposium on Thrombo-embolism—Current Management

The Diagnosis of Deep-vein Thrombosis — *David Negus* 830
Conservative Management of Thrombo-embolism — *P. T. Flute* 834
The Diagnosis and Management of Massive Pulmonary Embolism — *G. A. H. Miller* 837
Reviews and Notices of Books 840

Number 11

Original Papers

Ivalon (Polyvinyl Alcohol) Sponge in the Repair of Complete Rectal Prolapse — *Sir Clifford Naunton Morgan, Nigel H. Porter, and David J. Klugman* 841
Experiences of Ivalon-sponge Implant for Complete Rectal Prolapse at St. Mark's Hospital, 1960–70 — *J. C. B. Penfold and P. R. Hawley* 846
A Prospective Study of the Immediate and Long-term Results of Polya Gastrectomy for Duodenal Ulcer — *K. C. McKeown* 849
A Technique for creating a Skin-lined Hemithorax — *Lade Worsornu* 868
An Assessment of Above- and Through-knee Amputations — *P. W. B. Green, B. S. Hawkins, W. T. Irvine, and C. W. Jamieson* 873
The Effect of Obstructive Jaundice on the Migration of Reticulo-endothelial Cells and Fibroblasts into Early Experimental Granulomata — *Emanoel Lee* 875
The Effect of Clothing on the Dissemination of Bacteria in Operating Theatres — *Caroline M. Doig* 878
Heterologous Liver Perfusion — *R. Hickman, J. R. Parker, S. J. Saunders, N. E. Goodwin, and J. Terblanche* 881
Ectopic Thymic Tissue presenting as a Lateral Cervical Swelling — *D. R. A. Finch and M. H. Gough* 885
Twenty-four-hour Preservation of Canine Kidneys exposed to 45 and 60 Minutes of Warm Ischaemia — *M. E. Snell, W. I. Hopkinson, and K. A. Porter* 886
Secondary Haemorrhage from the Arterial Anastomosis of Renal Allografts — *A. J. Robson, D. B. Evans, and R. Y. Calne* 890
Surgical Resection of Recurrent Crohn's Disease — *J. L. Grogono and A. G. Parks* 892
The Management of Congenital Hydronephrosis in the Newborn — *H. T. Williams and K. W. Wilkinson* 894
Surgical Research Society 897
Short Notes of Rare or Obscure Cases 915
Reviews and Notices of Books 923

Number 12

Original Papers

Metabolism after Injury. I: Effects of Severity, Nutrition, and Environmental Temperature on Protein Potassium, Zinc, and Creatine — *D. P. Cuthbertson, G. S. Fell, Catherine M. Smith, and W. J. Tilstone* 925
'Curative' Surgery in Carcinoma of the Colon involving Duodenum — *Harold Ellis, M. Naunton Morgan, and Christopher Wastell* 932
Oesophageal Perforation during Abdominal Truncal Vagotomy for Duodenal Ulcer — *J. J. Price, S. J. A. Powis, and D. M. Morrissey* 936
Circumferential Oesophageal Myotomy — *James S. Davidson* 938
Glomus Jugulare Tumours—Radiotherapy or Surgery? — *G. W. Glover and J. Block* 947
Arteriovenous Fistulae for Chronic Intermittent Haemodialysis: A Modified Surgical Technique — *M. Hashmonai, A. Schramek, C. Chaimovitz, and D. Erlik* 953
Erythrocyte and Plasma Circulation Times in Haemorrhagic Shock — *D. F. L. Watkin and Jennifer Hudson* 957
Thoracic Enteric Cysts and Diverticulae — *Saeed Ahmed, Ambrose Jolleys, and John F. Dark* 963
Multiple Organ Grafts in the Pig — *R. Y. Calne, R. A. Sells, V. C. Marshall, P. R. Millard, B. M. Herbertson, E. J. Hadjiyannakis, D. C. Dunn, A. J. Robson, and D. R. Davis* 969
Prediction of 1-year Survival after Resection of Lung Tumours from the Preoperative Steroid Excretion Pattern — *L. G. S. Rao* 977
Investigation of Oedema of the Lower Limb following Successful Femoropopliteal By-pass Surgery: The Role of Phlebography in demonstrating Venous Thrombosis — *J. D. Hamer* 979
Short Notes of Rare or Obscure Cases 983
Reviews and Notices of Books 986
GENERAL INDEX TO VOLUME 59 987

PAGE

Hiatus hernia, symptomatic, results of operations for 432

HICKMAN, J. A.: *See* GORDON-SMITH, I. C., jt. auth.; KEMBLE, J. V. HARVEY, jt. auth.

HICKMAN, R., PARKERS, J. R., SAUNDERS, S. J., GOODWIN, N. E., and TERBLANCHE, J.: Heterologous liver perfusion 881

— — *See also* SPILG, HAROLD, jt. auth.

HILL, D. G., and YATES, A. K.: Congenital oesophago-bronchial fistula in adult 921

Hind-limb in greyhound dogs, effects of intermittently applied external pressure on haemodynamics of 219

Hip, anterior dislocation of, and diastasis of contralateral sacro-iliac joint—the rear-seat passenger's injury 296

— unusual dislocation of 326

Hirschsprung's disease 19

Histopathology of small vessels following microvascular repair 617

HITCHCOCK, EDWARD: *See* SANGRUCHI, VIRA, jt. auth.

HOBSLEY, MICHAEL: Amputation neuroma of the great auricular nerve after parotidectomy 735

HOLDEN, H. B., and MCKELVIE, P.: Cryosurgery in the treatment of head and neck neoplasia 709

HOLLAND, P. D. J.: *See* MACGOWAN, W. A. L., jt. auth.

Homograft(s), aortic valve, fate of 231

— rejection and immunosuppression, reticulo-endothelial system during 62

HOOPER, A. A.: Tuberculous peripheral lymphadenitis 353

HOPE-STONE, H. F.: *See* PENN, C. R. H., jt. auth.

HOPKINSON, W. I.: *See* SNELL, M. E., jt. auth.

Horse-shoe kidney, abdominal aortic aneurysm and 513

HOWELL-HUGHES, J.: *See* CUSHIERI, A., jt. auth.

HUDDY, PHILLIP, and GRIFFITHS, GORDON: Leiomyoma of the oesophagus with calcification 239

HUDSON, JENNIFER: *See* WATKIN, D. F. L., jt. auth.

HUGHES, E. S. R.: *See* BENNETT, R. C., jt. auth.

HUMPHREY, C. S., and WILKINSON, A. R.: The value of preserving the pylorus in the surgery of duodenal ulcer 779

— — *See also* JOHNSTON, D., jt. auth.

HUTCHINSON, A. G.: *See* WILLIAMS, J. ALEXANDER, jt. auth.

Hydatid disease, orbital, in Iraq 391

— — of spleen 489

Hydronephrosis, congenital, in the newborn, management of 894

— giant, in solitary crossed ectopic kidney 104

Hydropneumothorax complicating perforated peptic ulcer 72

Hyperbaric oxygen, hypothermia and, twelve-hour liver preservation in pig using 273

Hyperkalaemia following temporary occlusion of portal vein and hepatic artery 125

Hyperparathyroidism, persistent and recurrent 555

Hyperplasia, subcutaneous nodular lymphohistiocytic 375

Hypersensitivity response, delayed, in primary breast carcinoma as index of host resistance 505

Hypothermia, case of traumatic rupture of thoracic aorta associated with 243

— and hyperbaric oxygen, twelve-hour liver preservation in pig using 273

IDIOPATHIC pseudomembranous colitis successfully treated by surgical excision 154

— retroperitoneal fibrosis, clinical aspects of 58

Ileal extrinsic innervation, distal, proximal jejunal and, in rabbit and dog 394

— recurrence after ileostomy and excision of large bowel for Crohn's disease 253

PAGE

Ileostomy and excision of large bowel for Crohn's disease, ileal recurrence after 253

— and excisional surgery, ulcerative colitis treated by 345

Ileum, duplicated, perforation of peptic ulcer in 159

— prolapse of, through rectum and anal canal 149

Ileus, gall-stone, in absence of biliary-enteric fistula, case of 573

— spastic colonic, acute myelitis presenting as 918

Iliopopliteal by-pass via obturator foramen, post-irradiation femoral aneurysm treated by 400

Immunosuppression, homograft rejection and, reticulo-endothelial system activity during 62

IMPERATI, LUIGI, NATALE, COSTANZO, and MARINACCIO, FRANCESCO: Acid-fundic selective vagotomy of the stomach without drainage: technique and results 602

Infection(s), abdominal wound, and plastic wound guards 142

— perianal gas-producing, of non-clostridial origin 109

— wound, effect of a single-dose parenteral antibiotic in prevention of 98

Inguinal hernia, primary indirect, clinical trial to determine whether a Lytle's repair of, needs addition of rectus flap 339

— — right, following appendicectomy, development of 352

— — — — incidence of 623

Injury, metabolism after: effects of severity, nutrition, and environmental temperature on protein potassium, zinc, and creatine 925

Intestinal anastomoses, omental reinforcement of 129

Intestine, Crohn's disease of, ulceration of mouth, pharynx, and larynx in 249

— small, surgical treatment of Crohn's disease of 821

Intra-arterial injections of sodium tetradecyl sulphate (S.T.D.), 3 per cent, local effects of 101

Intraluminal diverticulum of duodenum, case of 324

Intramural abscess, acute, of pyloric antrum—localized phlegmon 197

IONESCU, M. I.: *See* KEIGHLEY, M. R. B., jt. auth.

Irradiation, repair of laryngopharynx and cervical oesophagus after 524

IRVINE, W. T.: *See* GREEN, P. W. B., jt. auth.

Ischaemia, warm, 24-hour preservation of canine kidneys exposed to 45 and 60 minutes of 886

Ischaemic colitis, non-gangrenous 463

— injury on kidneys preserved for 24 hours before transplantation, effect of 765

Ivalon (polyvinyl alcohol) sponge in repair of complete rectal prolapse 841

Ivalon-sponge implant for complete rectal prolapse, experiences of, at St. Mark's Hospital, 1960–70 846

JACKSON, B. T., and ANDERS, C. J.: Idiopathic pseudomembranous colitis successfully treated by surgical excision 154

JAGELMAN, D. G.: Rectal stones 405

— — *See also* BARTRAM, CLIVE, jt. auth.

JAMIESON, C. W.: Inhibition of the growth of tumour cells in culture by noxytiolin 108

— — *See also* FRAWLEY, JOHN E., jt. auth.; GREEN, P. W. B., jt. auth.

Jaundice, obstructive, effect of, on migration of reticulo-endothelial cells and fibroblasts into early experimental granulomata 875

JEFFERISS, CHRISTOPHER D.: Spontaneous rupture of the stomach in an adult 79

JEFFERSON, ANTONY, and REILLY, GERALD: Fractures of the floor of the anterior cranial fossa 585

Jejunal diverticulum, foreign-body perforation of 744

— proximal, and distal ileal extrinsic innervation in rabbit 394

PAGE

Jenkins, D. G., and Subbuswamy, S. G.: Leiomyosarcoma of the spermatic cord 408
Jenkins, D. H. R., and Gill, W.: A case of carcinoma of the colon in association with neurofibromatosis 322
— — and Macleod, I. B.: Proximal jejunal and distal ileal extrinsic innervation in the rabbit and dog 394
— — *See also* Carter, D. C., jt. auth.
Johnson, A. G.: Pyloric function and gall-stone dyspepsia 449
— — and Rains, A. J. Harding: Choledochoduodenostomy 277
Johnson, R. W. G.: The effect of ischaemic injury on kidneys preserved for 24 hours before transplantation 765
Johnson, W.: *See* Yadav, R. V. S., jt. auth.
Johnston, D., Humphrey, C. S., Smith, R. B., and Wilkinson, A. R.: Treatment of gastric ulcer by highly selective vagotomy without a drainage procedure: an interim report 787
Johnston, Ivan D. A.: *See* Spivey, John, jt. auth.
Johnstone, J. M. S., and Rintoul, R. F.: Perforated ulcer in childhood 288
Jolleys, Ambrose: *See* Ahmed, Saeed, jt. auth.
Jones, E. L., Thompson, H., and Williams, J. Alexander: Argentaffin-cell tumour of Meckel's diverticulum 213
Jones, M.: *See* Ham, J. M., jt. auth.
Jones, S. M., and Crumplin, K. H.: Calcifying epithelioma of Malherbe 387
Julian, D. J.: *See* Bouch, D. C., jt. auth.

KAKKAR, V. V.: *See* Field, E. S., jt. auth.; Nicolaides, A. N., jt. auth.
Kark, Allan E.: *See* Oh, Changyul, jt. auth.
Karwowski, A.: *See* Wingfield, H. V., jt. auth.
Keating, M.: *See* Vellar, I. D. A., jt. auth.
Keddie, N. C.: *See* Gunn, A., jt. auth.
Keighley, M. R. B., Girdwood, R. W., Ionescu, M. I., and Wooler, G. H.: Spontaneous rupture of oesophagus 649
Kemble, J. V. Harvey, and Hickman, J. A.: Postoperative changes in blood viscosity and influence of haematocrit and plasma-fibrinogen 629
Kemp, D.: *See* Ham, J. M., jt. auth.
Kenefick, John S.: Carcinoma of the duodenum 50
Kidney(s), canine, exposed to 45 and 60 minutes of warm ischaemia, 24-hr. preservation of 886
— horse-shoe, abdominal aortic aneurysm and 513
— preservation for transportation 187
— preserved for 24 hours before transplantation, effect of ischaemic injury on 765
— solitary crossed ectopic, giant hydronephrosis in 104
King, P. A.: *See* Grundy, D. J., jt. auth.
Kinmonth, J. B.: *See* Edwards, J. M., jt. auth.
Kitchin, A. H.: *See* Bouch, D. C., jt. auth.
Kline, A. L.: *See* Fegan, W. G., jt. auth.
Klugman, David J.: *See* Naunton Morgan, Sir Clifford, jt. auth.
Knee, through-, amputation 260
Knox, A. J. S.: *See* Williams, C. B., jt. auth.
Koutras, D. A.: *See* Psarras, A., jt. auth.
Kusakari, K.: *See* Gillison, E. W., jt. auth.
Kyle, James: Surgical treatment of Crohn's disease of the small intestine 821

LARGE bowel, lesion of second cancer of 16
Laryngeal nerve, non-recurrent 379
Laryngopharynx and cervical oesophagus, repair of, after irradiation 524
Larynx, mouth, and pharynx, ulceration of, in Crohn's disease of intestine 249

PAGE

Lavy, U. I.: The effect of oral supplementation of zinc sulphate on primary wound healing in rats 194
Lawson, H. H.: The reversibility of postgastrectomy alkaline reflux gastritis by a Roux-en-Y loop 13
Lee, Emanoel: The effect of obstructive jaundice on the migration of reticulo-endothelial cells and fibroblasts into early experimental granulomata 875
— — and Dowling, B. L.: Perimuscular excision of the rectum for Crohn's disease and ulcerative colitis 29
— — Ross, B. D., and Haines, J. R.: The effect of experimental bile-duct obstruction on critical biosynthetic functions of the liver 564
Leech, Peter, and Cuthbert, Hugh: Brachial plexus lesions associated with traumatic asphyxia 539
— — Waddell, Gordon, and Main, Robert G.: The incidence of right inguinal hernia following appendicectomy 623
Lees, Lorna J.: *See* Williams, J. Alexander, jt. auth.
Leg(s), effect of electrical stimulation of, on postoperative thrombosis 65
— ulcers, two unusual 478
Leiomyoma of appendix 579
— oesophagus with calcification 239
Leiomyosarcoma of spermatic cord 408
Lewis, Adam, and Qvist, George: Operative treatment of high gastric ulcer with special reference to Pauchet's method 1
Lewis, J. D., Papathanaiou, C., Yao, S. T., and Eastcott, H. H. G.: Simultaneous flow and pressure measurements in intermittent claudication 418
Lipase activity, lipoprotein, platelet adhesiveness and, in patients with benign and malignant disease of prostate 60
Lipomatosis, benign pelvic, bilateral ureteric obstruction caused by 69
Lipoprotein lipase activity, platelet adhesiveness and, in patients with benign and malignant disease of prostate 60
Lithogenic effect of vagotomy 365
Livadas, D.: *See* Psarras, A., jt. auth.
Liver abscess, amoebic, peritonitis from 179
— central rupture of, with massive liver-cell necrosis 660
— critical biosynthetic functions of, effect of experimental bile-duct obstruction on 564
— hamartoma, case of diaphragmatic hernia, absent pericardium, and 156
— injury, experimental, extrahepatic biliary drainage in 136
— perfusion, heterologous 881
— preservation, 12-hour, in pig using hypothermia and hyperbaric oxygen 273
— ruptured solitary cyst of 919
— secondary carcinoma in, haemoperitoneum complicating 576
— tumour, primary, case of, associated with porphyria 653
Liver-cell necrosis, massive, central rupture of liver with 660
Lloyd, G.: *See* Grundy, D. J., jt. auth.
Lloyd-Jones, William: *See* Warren, Kenneth W., jt. auth.
Lockhart-Mummery, H. E.: Crohn's disease of the large bowel 823
— — *See also* Heald, R. J., jt. auth.
Louw, J. H.: *See* Birkenstock, W., jt. auth.
Lumbrosacral agenesis in 60-year-old man 577
Lung tumours, prediction of 1-year survival after resection of, from preoperative steroid excretion pattern 977

PAGE

Lymph-nodes, axillary, in cancer of breast, regression of - - - - - - - - - 776
Lymphadenitis, peripheral tuberculous, in the elderly 568
— tuberculous peripheral - - - - - - 353
Lymphangiography and surgery in lymphangioma of skin - - - - - - - - - 36
Lymphangioma of skin, lymphangiography and surgery in - - - - - - - 36
Lymphohistiocytic hyperplasia, subcutaneous nodular - - - - - - - - - 375
Lytle's repair of primary indirect inguinal hernia, clinical trial to determine whether, needs addition of rectus flap - - - - - 339

McArthur, J.: *See* Miller, D. F., jt. auth.
McCall, Jane: *See* Williams, J. Alexander, jt. auth.
McClelland, D. B. L.: *See* Heading, R. C., jt. auth.
McColl, I.: *See* Reckless, J. P. D., jt. auth.
McColl, Ian: The value of upper gastro-intestinal fibroscopy - - - - - - - - 793
MacGowan, W. A. L., Holland, P. D. J., Browne, Hyacinth I., and Byrnes, Dermot P.: The local effects of intra-arterial injections of sodium tetradecyl sulphate (S.T.D.) 3 per cent - - - - - - - - - 101
MacGregor, A. B., and Ross, P. W.: Bacterial content of the gastric juice - - - - - 443
McIlroy, R. F.: The routine use of ultrasound for the diagnosis of postoperative deep-vein thrombosis in a district general hospital - 133
McKelvie, P.: *See* Holden, H. B., jt. auth.
Mackenzie, D. H.: *See* Hale, J. E., jt. auth.
McKeown, K. C.: A prospective study of the immediate and long-term results of Polya gastrectomy for duodenal ulcer - - - 846
Mackie, Rona M.: Malignant melanomata: an aid to preoperative diagnosis - - - - - 632
Macleod, I. B.: *See* Jenkins, D. H. R., jt. auth.
Macleod, N.: *See* Young, H. B., jt. auth.
McMaster, P.: Massive haemorrhage in elephantiasis neurofibroma - - - - - - 987
MacPherson, Gordon H.: *See* Gillespie, Gordon, jt. auth.
Magarey, C. J.: The results of 101 operations for symptomatic hiatus hernia - - - - - 432
— — *See also* Edwards, M. H., jt. auth.
Main, Robert G.: *See* Leech, Peter, jt. auth.
Malakoplakia of the colon - - - - - - 662
Maldescended testicles, maintenance of, within scrotum using Dartos pouch - - - 175
Malherbe, calcifying epithelioma of - - - 387
Malignant melanomata, aid to preoperative diagnosis of - - - - - - - - - 632
— thymoma, role of radiotherapy in management of 533
— tumours of bile-ducts - - - - - 501
Mammary cancer, response to therapy of skeletal metastases from - - - - - - 85
Mandibular coronoid process, secondary enlargement of - - - - - - - - - 426
Mann, C. V.: *See* Stoodley, B. J., jt. auth.
Mansfield, Averil O.: Alteration in fibrinolysis associated with surgery and venous thrombosis - - - - - - - - - 754
Marcuson, R. W.: *See* Newcombe, J. F., jt. auth.
Marinaccio, Francesco: *See* Imperati, Luigi, jt. auth.
Markham, D. E.: Anterior dislocation of the hip and diastasis of the contralateral sacro-iliac joint—the rear-seat passenger's injury - 296
Marshall, V. C.: *See* Calne, R. Y., jt. auth.; Yadav, R. V. S., jt. auth.
Di Martino, C.: *See* Mazzoni, G., jt. auth.

PAGE

Mason, J. R.: *See* Miller, D. F., jt. auth.
Mavor, G. E., Walker, M. G., and Dhall, D. P.: Routine operative arteriography in arterial embolectomy - - - - - - - 482
— — — — — — and Pegg, C. A. S.: Damage from the Fogarty balloon catheter - - - - - 389
Mayell, Margaret J.: *See* Cywes, S., jt. auth.
Mayers, C. P.: Aortic aneurysm following external cardiac massage - - - - - - 238
Mazzoni, G., Di Martino, C., Demofonti, A., Valli, A., Pellegrini, S., Gentili, B., and Melis, M.: A comparison of portal and systemic venous drainage in porcine renal allografts - - - - - - - - - 541
Meckel's diverticulum, argentaffin-cell tumour of - 213
Mediastinoscopy - - - - - - - - 209
Meggitt, B. F., and Wilson, J. N.: The battered buttock syndrome—fat fractures - - 165
Melanomata, malignant, aid to preoperative diagnosis of - - - - - - - - - 632
Melis, M.: *See* Mazzoni, G., jt. auth.
Mesenteric neurofibromatosis in childhood - - 739
Metabolic response to abdominal surgery, effect of environmental temperature and nutritional intake on - - - - - - - - 93
Metabolism after injury: effects of severity, nutrition, and environmental temperature on protein potassium, zinc, and creatine - - 925
Metcalfe-Gibson, C.: *See* Ahmed, Ali, jt. auth.
Michie, W.: *See* Hedley, A. J., jt. auth.
Microvascular repair, histopathology of small vessels following - - - - - - - - - 617
— surgery, new instruments for - - - - 181
Millard, P. R.: *See* Calne, R. Y., jt. auth.
Miller, D. F., Mason, J. R., McArthur, J., and Gordon, I.: A randomized prospective trial comparing three established methods of gastric decompression after vagotomy - - 605
Miller, G. A. H.: The diagnosis and management of massive pulmonary embolism - - 837
Missile wounds of head, mortality in - - - 201
Mitchell, Roger J.: The delayed hypersensitivity response in primary breast carcinoma as an index of host resistance - - - - - 505
Mitchinson, M. J.: Some clinical aspects of idiopathic retroperitoneal fibrosis - - - 58
Moloney, G. E., Morrell, M. Tessa, and Fell, R. H.: The effect of electrical stimulation of the legs on postoperative thrombosis - - 65
Morgan, Sir Clifford Naunton, Porter, Nigel H., and Klugman, David J.: Ivalon (polyvinyl alcohol) sponge in repair of complete rectal prolapse - - - - - - - 841
— — *See also* Ellis, Harold, jt. auth.
Morrell, M. Tessa: *See* Moloney, G. E., jt. auth.
Morris, P. J.: *See* Yadav, R. V. S., jt. auth.
Morrissey, D. M.: *See* Price, J. J., jt. auth.
Mountain, John C.: *See* Stewart, George R., jt. auth.; Warren, Kenneth W., jt. auth.
Mouth, pharynx, and larynx, ulceration of, in Crohn's disease of intestine - - - - - - 249
Mowat, Alastair G.: *See* Garner, Richard W., jt. auth.
Muscle blood-flow following insertion of by-pass vein-graft in femoropopliteal occlusive disease - - - - - - - - - 429
— skeletal, haemangiomata of - - - - 634
Mycotic aneurysm, ruptured, of spleen - - - 572
Myelitis, acute, presenting as spastic colonic ileus - 918
Myelomeningoceles, method of repair of - - 445
Mynors, John M.: *See* Dukes, Heather M., jt. auth.
Myotomy, circumferential oesophageal - - - 938

PAGE

^{24}Na, CLEARANCE of, from subcutaneous tissues of foot, effects of posture, exercise, and bandage on - - - - - - 552
Nasogastric tube management - - - - 637
NATALE, COSTANZO: *See* IMPERATI, LUIGI, jt. auth.
NAYLOR, A., and CROCKETT, D. J.: Primary skin-grafting in the treatment of chronic osteomyelitis - - - - - - - - 117
Neck and head neoplasia, cryosurgery in treatment of - - - - - - - - - - 709
Necrosis, gastric, rare complication of chloral hydrate intoxication - - - - - - - 317
— massive liver-cell, central rupture of liver with - 660
NEGUS, DAVID: The diagnosis of deep-vein thrombosis - - - - - - - - 830
Neoplasia, head and neck, cryosurgery in treatment of - - - - - - - - - 709
Nerve, non-recurrent laryngeal - - - - 379
Neurofibromatosis, case of carcinoma of colon in association with - - - - - - 322
— mesenteric, in childhood - - - - 739
— visceral - - - - - - - - - - 494
Neurological complications of ruptured abdominal aortic aneurysm - - - - - - 707
Neuroma, amputation, of great auricular nerve after parotidectomy - - - - - - - 735
NEWCOMBE, J. F., and MARCUSON, R. W.: Through-knee amputation - - - - - - 260
NEWMAN, J. H.: A case of gall-stone ileus in the absence of a biliary-enteric fistula - - 573
Nickel sensitivity to surgical skin clips - - - 745
NICOL, W.: Lumbrosacral agenesis in a 60-year-old man - - - - - - - - 577
NICOLAIDES, A. N., FIELD, E. S., KAKKAR, V. V., YATES-BELL, A. J., TAYLOR, S., and CLARKE, M. B.: Prostatectomy and deep-vein thrombosis - - - - - - - - 487
— — KAKKAR, V. V., FIELD, E. S., and FISH, P.: Venous stasis and deep-vein thrombosis - 713
— — *See also* FIELD, E. S., jt. auth.
Nipples, bilateral double - - - - - - 55
Nodular lymphohistiocytic hyperplasia, subcutaneous - - - - - - - - 375
Nodule, single thyroid - - - - - - 545
Non-clostridial origin, perianal gas-producing infection of - - - - - - - - - 109
Non-gangrenous ischaemic colitis - - - 463
NORMAN, J. E. DEB.: *See* BRAMLEY, P. A., jt. auth.
Noxytiolin, inhibition of growth of tumour cells in culture by - - - - - - - - 108
— solution, treatment of peritonitis with per- and postoperative irrigation of the peritoneal cavity with - - - - - - - 642
Nutritional disturbances in Crohn's disease - - 817
— intake effect of environmental temperature and, on metabolic response to abdominal surgery 93
NYHUS, L. W.: *See* GILLISON, E. W., jt. auth.

OATES, G. D.: *See* WILLIAMS, J. ALEXANDER, jt. auth.
Obliteration of perforating veins in leg - - - 197
O'BRIEN, B. McC.: *See* BAXTER, THELMA J., jt. auth.
Obturator foramen, post-irradiation femoral aneurysm treated by iliopopliteal by-pass via 400
Occlusion, temporary, of portal vein and hepatic artery, hyperkalaemia following - - - 125
Oedema of lower limb, investigation of, following successful femoropopliteal by-pass surgery: role of phlebography in demonstrating venous thrombosis - - - - - - - - 979
Oesophageal myotomy, circumferential - - - 938
— perforation during abdominal truncal vagotomy for duodenal ulcer - - - - - - 936
Oesophageal reflux due to hiatus hernia, results of fundoplication for relief of - - - - - 285
Oesophagitis, reflux, and success in its prevention by surgical means, importance of bile in - 794
Oesophago-bronchial fistula, congenital, in adult - 921
Oesophagus, cervical, and laryngopharynx, repair of, after irradiation - - - - - - 524
— leiomyoma of, with calcification - - - 239
— spontaneous rupture of - - - - - - 649
OH, CHANGYUL, and KARK, ALLAN E.: Anatomy of the external anal sphincter - - - - 717
OLIVER, M. F.: *See* BOUCH, D. C., jt. auth.
Omental reinforcement of intestinal anastomoses - 129
Oral supplementation of zinc sulphate on primary wound healing in rats, effect of - - - 194
Orbital hydatid disease in Iraq - - - - 391
Organ preservation, experimental - - - - 758
Osteomyelitis, chronic, primary skin-grafting in treatment of - - - - - - - - 117

PACKHAM, D. A.: *See* YATES-BELL, A. J., jt. auth.
Pancreas, head of, surgical objectives in unresected cancer of - - - - - - - - - 508
PAPADOPOULIS, S. N.: *See* PSARRAS, A., jt. auth.
PAPATHANAIOU, C.: *See* LEWIS, J. D., jt. auth.
Parathyroid overactivity, diagnosis of, in population of renal stone formers - - - - - 517
Parenteral antibiotic, effect of single-dose, in prevention of wound infection - - - - 98
PARKER, E. J. C.: *See* BAKER, R., jt. auth.
PARKERS, J. R.: *See* HICKMAN, R., jt. auth.
PARKS, A. G.: *See* GROGONO, J. L., jt. auth.
Parotidectomy, amputation neuroma of great auricular nerve after - - - - - - 735
Pauchet's method, operative treatment of high gastric ulcer with special reference to - - 1
PAUL, MILROY: The movements of the adult *Ascaris lumbricoides* - - - - - - - - 437
PEACHEY, R. D. G.: *See* EDWARDS, J. M., jt. auth.
Pedunculated teratoma of rectum infested with bilharziasis - - - - - - - - - 655
PEEL, A. L. G.: Peripheral tuberculous lymphadenitis in the elderly - - - - - 568
PEGG, C. A. S.: *See* MAVOR, G. E., jt. auth.
PELLEGRINI, S.: *See* MAZZONI, G., jt. auth.
Pelvic lipomatosis, benign, bilateral ureteric obstruction caused by - - - - - - - 69
Pelvis, renal, carcinoma of, crossed renal ectopia without fusion associated with - - - 235
PENFOLD, J. C. B., and HAWLEY, P. R.: Experiences of Ivalon-sponge implant for complete rectal prolapse at St. Mark's Hospital, 1960–70 - 846
PENN, C. R. H., and HOPE-STONE, H. F.: The role of radiotherapy in the management of malignant thymoma - - - - - - - - 533
Peptic ulcer in duplicated ileum, perforation of - 159
— — hydropneumothorax complicating perforated 72
Perforated duodenal ulcer in childhood - - - 288
Perforating veins in leg, obliteration of - - - 197
Perforation, foreign-body, of jejunal diverticulum - 744
— oesophageal, during abdominal truncal vagotomy for duodenal ulcer - - - - - - 936
— of peptic ulcer in duplicated ileum - - - 159
Perianal gas-producing infection of non-clostridial origin - - - - - - - - - - 109
Pericardium, absent, diaphragmatic hernia, and hamartoma of liver - - - - - - 156
Perimuscular excision of rectum for Crohn's disease and ulcerative colitis - - - - - - 29
Peripheral lymphadenitis, tuberculous - - - 353
— tuberculous lymphadenitis in elderly - - 568
Peritoneal cavity, treatment of peritonitis with per- and postoperative irrigation of, with noxythiolin solution - - - - - - - 642

PAGE

Peritonitis from amoebic liver abscess - - - - 179
— treatment of, with per- and postoperative irrigation of the peritoneal cavity with noxythiolin solution - - - - - - - - - 642
PERRY, MICHAEL: Evaluation of breast tumour sex chromatin (Barr body) as an index of survival and response to pituitary ablation - - 731
PERSAUD, V.: *See* SONI, S. R., jt. auth.
PHARMAKIOTIS, A. D.: *See* PSARRAS, A., jt. auth.
Pharynx, mouth, and larynx, ulceration of, in Crohn's disease of intestine - - - - - - 249
Phlebography, role of, in demonstrating venous thrombosis: investigation of oedema of lower limb following successful femoropopliteal by-pass surgery - - - - - - 979
Phleboliths, origin of - - - - - - - 695
Phlegmon, localized—acute intramural abscess of the pyloric antrum - - - - - - 197
PICKARD, R. G.: Treatment of peritonitis with per- and postoperative irrigation of the peritoneal cavity with noxythiolin solution - - - 642
Pituitary ablation, evaluation of breast tumour sex chromatin (Barr body) as index of survival and response to - - - - - - 731
Plasma circulation times in haemorrhagic shock, erythrocyte and - - - - - - - - 957
Plastic wound guards, abdominal wound infections and - - - - - - - - - - 142
Platelet adhesiveness and lipoprotein lipase activity in patients with benign and malignant disease of prostate - - - - - - - 60
Plexus lesions, brachial, associated with traumatic asphyxia - - - - - - - - - 539
Pneumoperitoneum as aid in surgical treatment of giant herniae - - - - - - - 360
— in management of abdominal incisional hernia - 372
POLLOCK, A. V.: Axillary-femoral by-pass grafts in the treatment of aorto-iliac occlusive disease 704
— — and TINDAL, D. S.: The effect of a single-dose parenteral antibiotic in the prevention of wound infection - - - - - - 98
POLLOCK, DAVID: *See* SCOTT, ROY, jt. auth.
Polya gastrectomy for duodenal ulcer, prospective study of immediate and long-term results of - - - - - - - - - - 849
Porcine renal allografts, comparison of portal and systemic venous drainage in- - - - 541
Porphyria, case of primary liver tumour associated with - - - - - - - - - 653
Portal and systemic venous drainage, comparison of, in porcine renal allografts - - - - 541
— vein, anteroposition of, and spontaneous passage of gall-stones - - - - - - - 737
— — and hepatic artery, hyperkalaemia following temporary occlusion of - - - - 125
PORTER, K. A.: *See* SNELL, M. E., jt. auth.
PORTER, NIGEL H.: *See* MORGAN, Sir CLIFFORD NAUNTON, jt. auth.
Post-angiographic vertebral arteriovenous fistulae - 627
Postgastrectomy alkaline reflux gastritis by Roux-en-Y loop, reversibility of - - - - 13
Post-irradiation femoral aneurysm treated by ilio-popliteal by-pass via obturator foramen - 400
Postoperative deep-vein thrombosis, routine use of ultrasound for diagnosis of - - - 133
— thrombosis, effect of electrical stimulation of legs on - - - - - - - - - 65
POWIS, S. J. A., and RUSHTON, D. I.: A case of retroperitoneal haemangioma - - - 74
— — *See also* PRICE, J. J., jt. auth.
PRICE, J. J., POWIS, S. J. A., and MORRISSEY, D. M.: Oesophageal perforation during abdominal truncal vagotomy for duodenal ulcer - - 936
Prolapse of ileum through rectum and anal canal - 149

PAGE

Prostate, benign and malignant disease of, platelet adhesiveness and lipoprotein lipase activity in patients with - - - - - - 60
Prostatectomy(ies) and deep-vein thrombosis - - 487
— effect of fibrinolytic inhibitor epsilon-aminocaproic acid on incidence of deep-vein thrombosis after - - - - - - 522
— value of frusemide in - - - - - - 190
PRYN, W. J.: The maintenance of maldescended testicles within the scrotum using a Dartos pouch - - - - - - - - - 175
PSARRAS, A., PAPADOPOULOS, S. N., LIVADAS, D., PHARMAKIOTIS, A. D., and KOUTRAS, D. A.: The single thyroid nodule - - - - 545
Pseudomembranous colitis, idiopathic, successfully treated by surgical excision - - - 154
Pulmonary embolism, massive, diagnosis and management of - - - - - - 837
Pyelonephritis, xanthogranulomatous, case of - 319
Pyloric antrum, acute intramural abscess of—localized phlegmon - - - - - - 197
— function and gall-stone dyspepsia - - - 449
Pyloroplasty alone in management of patients with negative exploration for duodenal ulcer - 783
— Finney, modification of - - - - - 454
Pylorus in surgery of duodenal ulcer, value of preserving - - - - - - - - - 77
Pylorus-preserving gastrectomy in treatment of duodenal ulcer - - - - - - - 27

QVIST, GEORGE: *see* LEWIS, ADAM, jt. auth.

RABKIN, R.: *See* BIRKENSTOCK, W. E., jt. auth.
Radioactive fibrinogen, technique for detecting rejection episodes in human transplant recipients using - - - - - - - 138
Radiology of Crohn's disease, aspects of - - 810
— preoperative and operative, comparative evaluation of, in biliary-tract disease - - - 205
Radiotherapy, role of, in management of malignant thymoma - - - - - - - - - 533
RAINS, A. J. HARDING: *See* JOHNSON, A. G., jt. auth.
RAO, L. G. S.: Prediction of 1-year survival after resection of lung tumours from the steroid excretion pattern - - - - - - 977
Rare Cases:—
  Acute myelitis presenting as spastic colonic ileus 918
  Anteroposition of the portal vein and spontaneous passage of gall-stones - - - 737
  Aortic aneurysm following external cardiac massage - - - - - - - - 238
  Bilateral traumatic renal artery occlusion with survival after late reconstitution of arterial flow - - - - - - - - - 915
  — ureteric obstruction caused by benign pelvic lipomatosis - - - - - - - 69
  Bowel herniation through a defect of the broad ligament - - - - - - - - 151
  A case of carcinoma of the colon in association with neurofibromatosis - - - - 322
  — diaphragmatic hernia, absent pericardium, and hamartoma of the liver - - - 156
  — gall-stone ileus in the absence of a biliary-enteric fistula - - - - - - 573
  — intraluminal diverticulum of the duodenum 324
  — primary liver tumour associated with porphyria - - - - - - - - 653
  — retroperitoneal haemangioma - - - 74
  — traumatic rupture of the thoracic aorta associated with hypothermia - - - 243
  — xanthogranulomatous pyelonephritis - - - 319
  Chronic schistosomal appendicitis - - - 743

PAGE

Rare Cases (*continued*)
  Congenital oesophago-bronchial fistula in an adult - - - - - - - - - 921
  Crossed renal ectopia without fusion associated with carcinoma of the renal pelvis - - 235
  Does squamous carcinoma of the colon exist? 410
  Foreign-body perforation of a jejunal diverticulum - - - - - - - - - 744
  Gastric necrosis: A rare complication of chloral hydrate intoxication - - - - - - 317
  Haemangiosarcoma of the spleen - - - 406
  Haemoperitoneum complicating secondary carcinoma in the liver - - - - - - 576
  Hydatid disease of the spleen - - - 489
  Hydropneumothorax complicating perforated peptic ulcer - - - - - - - - 72
  Idiopathic pseudomembranous colitis successfully treated by surgical excision - - 154
  Joint rupture in Reiter's disease - - - 657
  Leiomyoma of the appendix - - - - 579
  — oesophagus with calcification - - - 239
  Leiomyosarcoma of the spermatic cord - - 408
  Lumbosacral agenesis in a 60-year-old man - 577
  Malakoplakia of the colon - - - - 662
  Massive haemorrhage in elephantiasis neurofibroma - - - - - - - - - 987
  Mesenteric neurofibromatosis in childhood - 739
  Nickel sensitivity to surgical skin clips - - 745
  The non-absorbable cystic duct ligature - - 245
  Pedunculated teratoma of rectum infected with bilharziasis - - - - - - - - 655
  Perforation of a peptic ulcer in duplicated ileum 159
  Post-irradiation femoral aneurysm treated by iliopopliteal by-pass via the obturator foramen 400
  Prolapse of the ileum through the rectum and anal canal - - - - - - - - 149
  Rectal stones - - - - - - - 405
  Recurrent spontaneous rupture of the urinary bladder - - - - - - - - - 985
  Ruptured angiomatous spleen presenting as a severe coagulation defect - - - - 492
  — mycotic aneurysm of the spleen - - 572
  — solitary cyst of the liver - - - - 919
  A single congenital arteriovenous fistula of the hand - - - - - - - - 76
  Spontaneous rupture of the stomach in an adult 79
  Subcutaneous rupture of the breast: A seat-belt injury - - - - - - - - - 491
  Tumoral calcinosis - - - - - - 570
  An unusual dislocation of the hip - - - 326
  Visceral neurofibromatosis - - - - 494
RECKLESS, J. P. D., MCCOLL, I., and TAYLOR, G. W.: Aorto-caval fistulae: An uncommon complication of abdominal aortic aneurysms 461
— — — — — — Aorto-enteric fistulae: An uncommon complication of abdominal aortic aneurysms - - - - - - - 458
Rectal biopsies in Crohn's disease, value for diagnosis and research of special investigation on 806
— and colonic ulceration in Behçet's disease - - 173
— prolapse, complete, experiences of Ivalon-sponge implant for, at St. Mark's Hospital, 1960–70 846
— — — Ivalon (polyvinyl alcohol) sponge in repair of - - - - - - - 841
— stones - - - - - - - - - - 405
Rectum and anal canal, prolapse of ileum through 149
— pedunculated teratoma of, infested with bilharziasis - - - - - - - - 655
— perimuscular excision of, for Crohn's disease and ulcerative colitis - - - - - - 29
— pull-through operations of, long-term review of function following - - - - - - 723
Rectus flap, clinical trial to determine whether a Lytle's repair of primary indirect inguinal hernia needs addition of - - - - 339

PAGE

Recurrent spontaneous rupture of the bladder - 985
Reflux gastritis, postgastrectomy alkaline, reversibility of, by Roux-en-Y loop - - - 13
— vesico-ureteric, following renal transplantation - 33
REILLY, GERALD: *See* JEFFERSON, ANTONY, jt. auth.
Reiter's disease, joint rupture in - - - - - 657
Rejection, homograft, and immunosuppression, reticulo-endothelial system during - - 62
Renal allografts, porcine, comparison of portal and systemic venous drainage in - - - 541
— — secondary haemorrhage from arterial anastomosis of - - - - - - - 890
— artery occlusion, bilateral traumatic, with survival after late reconstitution of arterial flow 915
— ectopia, crossed, without fusion associated with carcinoma of renal pelvis - - - - - 235
— function, ligation of left renal vein in splenorenal anastomosis without impairment of - - 170
— pelvis, carcinoma of, crossed renal ectopia without fusion associated with - - - - 235
— stone formers, diagnosis of parathyroid overactivity in population of - - - - - 517
— transplantation, vesico-ureteric reflux following 33
— vein, left, ligation of, in splenorenal anastomosis without impairment of renal function - - 170
Reticulo-endothelial cells and fibroblasts, effect of obstructive jaundice on migration of, into early experimental granulomata - - - - 875
— system activity during homograft rejection and immunosuppression - - - - - - 62
Retroperitoneal fibrosis, idiopathic, clinical aspects of - - - - - - - - - - - 58
— haemangioma, case of - - - - - - 74
Reviews (Titles):—
  Actions of alcohol, Vols. 1 *and* 2 (Henrich Wallgren and Herbert Barry, III) - - - - 498
  Acute cholecystitis (Clarence J. Schein) - - 923
  An aid to clinical surgery (Peter R. Scott) - 415
  Amputees and their prostheses (Mohinder A. Mital and Donald S. Pierce) - - - - 164
  Anaesthetics, resuscitation and intensive care (Walter Norriss and Donald Campbell) - 82
  Les analgésiques et la douleur (G. Vourc'h, J. de Castro, P. Gauthier-Lafaye, J. F. Giudicelli, and P. Viars) - - - - - - - 81
  The anatomical basis of medical practice (R. Frederick Becker, James W. Wilson, and John A. Gehweiler) - - - - - - 668
  Anatomy of the brain and spinal medulla (Neville G. Sutton) - - - - - - - 162
  Anatomy, regional and applied (R. J. Last) - 668
  Angiography. Techniques and procedures (Joseph E. Whitley and Nancy O'Neil Whitley) - 416
  Ano-rectal malformations in children (F. Douglas Stephens and E. Durham Smith) - 581, 840
  Aspirin, platelets and stroke. Background for a clinical trial (ed. William S. Fields and William K. Hass) - - - - - - 499
  An atlas of the anatomy of the ear (Branislav Vidić and Ronan O'Rahilly) - - - - 498
  An atlas of diseases of the eye (E. S. Perkins and Peter Hansell) - - - - - - - 668
  Atlas of ear surgery (William H. Saunders and Michael M. Paparella) - - - - - 163
  Atlas röntgenologischer Befunde am operierten Magen (E. Baudisch) - - - - - - 247
  Atlas for surgical repair of cleft lip, cleft palate, and noncleft velopharyngeal incompetence (Richard B. Yules) - - - - - - 331
  Atlas of transbronchial biopsy. Early diagnosis of peripheral pulmonary carcinomas (Eitaka Tsuboi) - - - - - - - - - 332
  Autologous transfusions (George Milles, Hiram T. Langston, and William Dalessandro) - 248

PAGE

Reviews (Titles), *continued*

Bacterial infections: Changes in their causative agents and possible basis (ed. M. Finland, W. Marget, and K. Bartmann) - - - - 923
Bailey and Love's Short practice of surgery (rev. A. J. Harding Rains and W. Melville Capper) 414
Basic practical surgery (C. Barrie Williams) - 162
Basic skills for surgical housemen (Kenneth C. Calman) - - - - - - - - 500
Biochemical consequences of chronic renal failure (M. R. Wills) - - - - - - - 248
Biological tissue in heart valve replacement (ed. M. I. Ionescu, D. N. Ross, and G. H. Wooler) 500
Blood volume and extracellular fluid volume (Solomon N. Albert) - - - - - - 665
Carcinoma of the bronchus (ed. T. J. Deeley) - 415
Cardiovascular surgery, 1969 (ed. Earle B. Mahoney) - - - - - - - 83
Cardiovascular surgery, 1970 (ed. Earle B. Mahoney) - - - - - - - 161
Care of the surgical cardiopulmonary patient (ed. William E. Neville) - - - - 499
Chest injuries (Roshan Lall Gupta) - - - 667
Chest injuries. Physiologic principles and emergency management (Emil A. Naclerio) - - 331
La chimiothérapie regional des cancers de l'appareil digestif (P. Kissel, M. Bessot, A. Duprez, and G. Mauuary) - - - - 924
Chirurgische differential-diagnostik (ed. Karl Vosschulte and Ludwig Zukschwerdt) - 667
Cleft lip and palate. Surgical, dental and speech aspects (ed. William C. Grabb, Sheldon W. Rosenstein, and Kenneth R. Bzoch) - - 331
Clinical anatomy (Harold Ellis) - - - - 328
Clinical heart disease (Samuel Oram) - - 498
Clinical organ transplantation (ed. R. Y. Calne) 415
Clinical otology. An international symposium (ed. Michael M. Paparella, Albert Hohmann, and John S. Huff) - - - - - - - 499
Color atlas of cancer cytology (Masayoshi Takahashi) - - - - - - 499
Colposcopy. A scientific and practical approach to the cervix in health and disease (Malcolm Coppleston, Ellis Pixley, and Bevan Reid) - 247
The complete handbook for medical secretaries and assistants (Robert Lee Dennis and Jean Monty Doyle) - - - - - - - 500
Concepts of disease (ed. Joel G. Brunson and Edward A. Gall) - - - - - - 499
Conférences de séméiologie chirurgicale, Vol. 5 (Jean Mouïel and Claude Regensberg) - 497
Congenital deformities of the testis and epididymis (C. Gordon Scorer and Graham H. Farrington) - - - - - - - - - - 582
Contemporary burn management (ed. Hiram C. Polk and H. Harlan Stone) - - - - 666
The continuing education of the surgeon (ed. Harold G. Barker) - - - - - - 82
The craft of surgery, Vols. 1–3 (ed. Philip Cooper) - - - - - - - - - 330
Critical surgical illness (ed. James D. Hardy) - 498
Current concepts of the histology of oral mucosa (ed. C. A. Squier and Julia Meyer) - - 583
Current concepts in the management of leukemia and lymphoma (ed. J. E. Ultmann, M. L. Griem, W. H. Kusten, and R. W. Wissler) 328
The detective-physician. The life and work of Sir William Willcox, K.C.I.E., C.B., C.M.G., M.D., F.R.C.P. (Phillip H. A. Willcox) - 665
Diagnosis and treatment of abdominal abscesses (Irving M. Ariel and Kirk K. Kazarian) - 416
Diagnostische und therapeutische Fortschritte in der Krebschirurgie (F. Linder, G. Ott, and H. Rudolph) - - - - - - - - 666
Diseases of the breast (C. D. Haagensen) - - 163

PAGE

Reviews (Titles), *continued*

Diseases of the ear, nose, and throat (ed. John Ballantyne and John Groves) - - - - 329
Diseases of the urinary tract (British Medical Journal) - - - - - - - - - 328
Die einfachen Kreislaufgrössen beim chirurgischen Patienten (C. Burri) - - - - - 413
The elephant man (Ashley Montagu) - - 924
Ellison's atlas of surgery of the stomach and duodenum (Larry C. Carey and Robert H. Albertin) - - - - - - - - - 748
Emergency room care (ed. Charles Eckert) - 752
Encyclopedia of urology (ed. C. E. Alken, V. W. Dix, W. E. Goodwin, and E. Wildbolz) - 332
Endocrine therapy in malignant disease (ed. Basil A. Stoll) - - - - - - - - - 840
Engineering and living systems. Interfaces and opportunities (D. R. Rutstein and M. Eden) 162
Les entretiens de Bichat 1971 (ed. P. L. Chigot and A. Bellin) - - - - - - - 415
Ergebnisse der Bluttransfusionsforschung, Vol. II (ed. M. Matthes, N. Kleine, and L. P. Hollander) - - - - - - - - - - 500
Essentials of artificial ventilation of the lungs (A. R. Hunter) - - - - - - 989
Examination of the hand (George L. Lucas) - 750
Facial prostheses (Alan Clive Roberts) - - 582
Die Fettembolie (Dr. Gyorgy Szabo) - - 583
A first notebook of head injury (Kenneth G. Jamieson) - - - - - - - - 329
Fortschritte der Kiefer- und Gesichts-Chirurgie (ed. K. Schuchardt) - - - - - - 246
Fractures of the mandible (H. C. Killey) - - 162
Fractures of the middle third of the facial skeleton (H. C. Killey) - - - - - - - 162
Frontiers of nuclear medicine (ed. Wolfgang Horst) - - - - - - - - - 332
Frontobasale Verletezungen (C. Probst) - - 752
Frozen section in surgical diagnosis (Andrew A. Shivas and Suzanne G. Fraser) - - - - 81
Full dentures. The treatment of the edentulous patient (Alan Mack) - - - - - 162
Fundamental physics of radiology (W. J. Meredith and J. B. Massey) - - - - - - 750
Fundamental skills in surgery (Thomas F. Nealon) - - - - - - - 583
Gathorne Robert Girdlestone (J. Trueta) - - 161
Geburtshilfliche Operationen (Heinrich Martius and Gehard Martius) - - - - - 500
Glossaire d'histopathologie des tumeurs humaines (Réne Gérard-Marchant) - - - - - 16[illegible]
Gynaecological cancer (ed. T. J. Deeley) - - 414
Gynaecology. Essentials of clinical practice (Thomas H. Green) - - - - - - 331
Die gynäkologischen Operationen (Heinrich Martius and Hugo Husslein) - - - - 413
The hand (Lee Milford) - - - - - 248
Handbook of orthoptic principles (G. T. Willoughby Cashell and Isobel M. Durran) - 497
Handbuch der experimentelle Pharmakologie. Anticoagulantien (ed. F. Markwardt) - - 83
Handbuch der Kinderheilkunde, Vol. VIII, Part 2 (ed. H. Opitz and F. Schmid) - - - 751
Handbuch der medizinischen Radiologie, Vol. 5 (ed. L. Diethelm) - - - - - - - 924
Handbuch der medizinischen Radiologie: Encyclopedia of medical radiology. Part 3. Spezielle Strahlentherapie maligner Tumoren (ed. A. Zuppinger) - - - - - - 582
Head injuries. Proceedings of an international symposium held in Edinburgh and Madrid 2nd to 10th April, 1970 - - - - - - 665
Hepatic encephalopathy (Frederick Steigmann and Bernard F. Clowdus) - - - - - 81
Hirschsprung's disease (Theodor Ehrenpreis) - 413

PAGE

Reviews (Titles), *continued*
Human organ support and replacement (ed. James D. Hardy) - - - - - - 84
Idiopathic ischemic necrosis of the femoral head in adults (ed. W. M. Zinn) - - - - 414
Ileostomy care (Marshall Sparberg) - - 584
The illness of trauma (Garbett Pipkin and Victor Buhler) - - - - - - - - 330
Instructional course lectures, Vol. XX (The American Academy of Orthopaedic Surgeons) 749
Intensive care of the surgical patient (ed. Marshall D. Goldin) - - - - - - 329
International encyclopedia of pharmacology and therapeutics. Section 8: Local anaesthetics (ed. P. Lechat) - - - - - - - 84
Intestinal absorption and its derangements (ed. A. M. Dawson) - - - - - - - 415
An introduction to clinical research (W. P. Small and Urban Krause) - - - - - - 748
Immunobiology (ed. Robert A. Good and David W. Fisher) - - - - - - - 248
The immunobiology of transplantation (Rupert Billingham and Willy Silvers) - - - 163
Ischemic forms of venous thrombosis (Henry Haimovici) - - - - - - - 246
Klinische Sudeckprophylaxe und Therapie (Jost L. Bircher) - - - - - - - 331
Kurzer Leitfaden der praktischen Infusionstherapie (W. Seifart) - - - - - - 414
The laboratory animal—Principles and practice (W. Lane-Petter and A. E. G. Pearson) - 989
The lacrimal system (ed. Everett R. Veirs) - 583
Lumbar disc disease (ed. Blaine S. Nashold and Zderek Hrubec) - - - - - - 748
Malignant tumours in organ transplant recipients (I. Penn) - - - - - - - - 161
Management of arterial occlusive disease (ed. W. Andrew Dale) - - - - - - 749
Management of constipation (ed. Sir Francis Avery Jones and Edmund W. Godding) - 497
Manual of preoperative and postoperative care (ed. John M. Kinney, Richard H. Egdahl, and George D. Zuidema) - - - - - 666
A manual of respiratory failure. Tracheostomy, endotracheal intubation and mechanical ventilation (Eli Rush Crews and Leopoldo Lapuerta) 750
Manuel de l'aide en chirurgie (P. Orsoni) - - 414
Manuel d'ostéosynthèse. Technique A.O. (M. E. Müller, M. Allgöwer, and H. Willenegger) - 161
Mechanical devices for cardiopulmonary assistance (ed. R. H. Bartlett, P. A. Drinker, and P. M. Galletti) - - - - - - - - - 328
Mediastinoscopy (ed. Otto Jepsen and H. Rahbeth Sørensen) - - - - - - 416
Methods in mammalian embryology (ed. Joseph C. Daniel) - - - - - - - 247
Methods of ossiculoplasty (James R. Tabor) - 330
Modern trends in diseases of the ear, nose and throat—2 (ed. P. Maxwell Ellis) - - - 751
Modern trends in orthopaedics—6 (ed. A Graham Apley) - - - - - - - - 924
Modern trends in surgery—3 (ed. W. T. Irvine) 163
Myoplastic amputation, immediate prosthesis and early amputation (Marian Weiss) - - - 84
Neonatal emergencies and other problems (John Black) - - - - - - - - - 924
Neoplasms of the gastrointestinal tract (William C. Lowe) - - - - - - - - 752
Nephron failure: Conservation, substitution, replacement (John B. Dossetor and M. Henry Gault) - - - - - - - - - 164
Non-specific mesenteric lymphadenitis (V. Tuchel) 748
Notes on dental materials (E. C. Combe) - - 583
Nouvelle practique chirurgicale illustrée, Vol. 4 (ed. J. Quénu) - - - - - - - 414

Reviews (Titles), *continued*
Occult traumatic lesions of the cervical vertebrae (Martin A. Abel) - - - - - - 331
Oral diagnosis. Oral medicine (David F. Mitchell, S. Miles Standish, and Thomas B. Fast) 163
Oral pathology (Donald A. Kerr and Major M. Ash) - - - - - - - - - - 328
Orthopädische Therapie (G. Chapchal and D. Waigand) - - - - - - - - 81
Orthopaedic surgery in spasticity (Harold M. Frost) - - - - - - - - - 989
Orthopaedics for the undergraduate. Fractures (W. A. Crabbe) - - - - - - - 581
Orthopédie traumatologie (Société Française de Chirurgie Orthopédique et Traumatologie) - 84
Orthopédie et traumatologie. Conférences d'enseignement 1970 - - - - - - 840
Outline of orthopaedics (J. Crawford Adams) - 329
Pädiatrischer EKG-Atlas (J. Stoermer and W. Heck) - - - - - - - - - 497
Pathogenese und Klinik des akuten Nierenversagens (ed. Ulrich Gessler, Karl Schröder, and Horst Weidinger) - - - - - 247
Pathologie du pied (Jean Lelièvre) - - - 82
Pathology of tumours of the oral tissues (R. B. Lucas) - - - - - - - - - 749
Patients, hospitals and operational research (G. M. Luck, J. Luckman, B. W. Smith, and J. Stringer) - - - - - - - - 581
Perspectives in surgery (Clare Gray Peterson) - 840
Physics applied to anaesthesia (D. W. Hill) - 749
Physiology of the eye (Hugh Davson) - - 582
The plain X-ray in the diagnosis of the acute abdomen (M. H. Gough and Michael W. L. Gear) - - - - - - - - - - 248
Plastic and reconstructive surgery (ed. J. T. Hueston) - - - - - - - - 162
The polycythemic disorders (Baruch Modan) - 416
Postoperative cardiac intensive care (M. V. Braimbridge) - - - - - - - 749
A practice of anaesthesia (ed. W. D. Wylie and H. C. Churchill-Davidson) - - - - 667
Praxis der Schockbehandlung (ed. Theodor Ott Lindenschmidt, Erich Rugheimer, and Hans Willenegger) - - - - - - - - 668
Principles of medical statistics (Sir Austin Bradford Hill) - - - - - - - - - 81
Proceedings of the fourth annual leucocyte culture conference (ed. O. Ross McIntyre) - - 247
Progress in pediatric surgery, Vol. 2 (ed. P. P. Rickham, W. Ch. Hecker, and J. Prévot) - 161
Progress in pediatric surgery, Vol. 3 (ed. P. P. Rickman, W. Ch. Hecker, and J. Prévot) - 581
Progress in surgery, Vol. 10 (ed. M. Allgöwer, S. E. Bergentz, R. Y. Calne, and U. F. Gruber) - - - - - - - - - 751
Prosthetic replacement of the aortic valve (Lester R. Sauvage, Robert F. Viggers, Knute Berger, Stephen B. Robel, Philip N. Sawyer, and Stephen J. Wood) - - - - 752
Psychiatric aspects of organ transplantation (ed. Pietro Castelnuovo-Tedesco) - - - 161
Questions and answers in orthopaedics (Floyd G. Goodman and George R. Schoedinger) - 748
Radiation effect and tolerance, normal tissue. Basic concepts in radiation pathology (ed. J. M. Vaeth) - - - - - - - - - - 989
Radiology of the skull and brain, Vols. 1 and 2 (ed. T. H. Newton and D. Gordon Potts) - 752
Recent advances in cancer and radiotherapeutics (ed. Keith E. Halnan) - - - - 666
Recent advances in haematology (ed. A. Goldberg and M. C. Brain) - - - - - - 82
Regeneration of liver and kidney (Nancy L. R. Bucher and Ronald A. Malt) - - - 330

PAGE

Reviews (Titles), *continued*
  Regionale Anästhesie mit dem Langzeitanästhetikum Bupivacain (Hans Nolte and Justus Meyer) - - - - - - - - 566
  Resistance to trauma (Zdenek Hruza) - - 924
  Schweitzer. A biography (George Marshall and David Poling) - - - - - - - - 582
  The scientific basis of medicine. Annual reviews, 1971 (ed. Ian Gilliland and Jill Francis) - 84
  Scoliosis and growth (ed. P. A. Zorab) - - 329
  Sectional anatomy and tomography of the head (Guy D. Potter) - - - - - - 751
  Septic shock in man (ed. S. G. Hersky, Louis R. M. Del Guercio, and Rita McConn) - 667
  Shands' Handbook of orthopaedic surgery (ed. R. Beverly Rancy, and H. Robert Brashear) - 583
  Shaw's textbook of gynaecology (John Hawkins and Gordon Bourne) - - - - - - 83
  A short textbook. Ear, nose, and throat (R. Pracy, J. Siegler, and P. M. Stell) - - 413
  The shoulder and neck (James E. Bateman) - 923
  Simultaneous prostatectomy and inguinal herniorrhaphy (Sidney R. Weinberg, Albert Kovetiz, and Stephen M. Lazarus) - - - - - 83
  Special topics in stereotaxis, epilepsy, disorders of behaviour, and autonomic balance (ed. W. Umbach) - - - - - - - - - 330
  Spezielle pathologische Anatomie, Volume 2, *Part I: Oesophagus und Magen* (Wilhelm Doerr, Gerhard Seifert, and Erwin Uehlinger) 923
  Spinal dysraphism. Spina bifida occulta (C. C. Michael James and L. P. Lassman) - - 500
  Stapedectomy (Harold F. Schuknecht) - - 667
  The structure and support of contemporary residency programs in surgery (ed. Harold G. Barker) - - - - - - - - - 164
  Surface and radiological anatomy (ed. W. J. Hamilton, G. Simon, and S. G. Ian Hamilton) 164
  Surgeon to soldiers (Edward D. Churchill) - 750
  Surgeons' decisions (H. L. Duthie) - - - 161
  Surgery and the allergic patient (ed. Claude A. Frazier) - - - - - - - - - 584
  Surgery annual 1971 (ed. Philip Cooper and Lloyd M. Nyhus) - - - - - - 748
  Surgery for nurses (James Moroney) - - 247
  Surgery of the oesophagus. The Coventry conference (ed. R. Abbey Smith and R. E. Smith) - - - - - - - - - 751
  Surgery of rheumatoid arthritis (ed. Richard L. Cruess and Nelson S. Mitchell)- - - 666
  Surgical anatomy, Vols. 1 *and* 2 (B. J. Anson and C. B. McVay) - - - - - - 82
  Surgical departments in hospitals. The surgeon's view (ed. D. M. Douglas) - - - - 668
  Surgical disorders of the peripheral nerves (Sir Herbert Seddon) - - - - - - 749
  Surgical treatment of coronary arteriosclerosis (Rene G. Favaloro) - - - - - - 84
  Symposium on the hand, Vol. 3 (ed. Lester M. Cramer and Robert A. Chase) - - - 668
  Technique des plâtres et corsets de scolioses (Marc Ollier) - - - - - - - - - 82
  Testicular tumours (ed. Douglas E. Johnson) - 751
  A textbook of nursing. A compendium of nursing knowledge (Evelyn Pearce) - - - - 416
  A text-book of X-ray diagnosis, Vol. 6 (ed. S. Cockrane Shanks and Peter Kerley) - - 497
  Theatre nurses handbook (Alice B. Cranfield) - 840
  The thyroid. A fundamental and clinical text (ed. Sidney C. Werner and Sidney H. Ingbar) - - - - - - - - - 667
  Today's drugs, Vol. 2 (British Medical Journal) 329
  Total hip replacement (ed. Malcolm Joyson) - 414
  Tracheostomy and artificial ventilation (ed. Stanley A. Feldman and Brian W. Cramley) 581

PAGE

Reviews (Titles), *continued*
  Transperikardiale Operationen an den Hauptbronchien und Lungengefassen (L. K. Bogusch, A. A. Travin, and J. L. Semenenkow) - 163
  Transplantation today (ed. Hans Balner, D. W. van Bekkum, and Felix T. Rapaport) - - 246
  Trauma to the liver (Gordon F. Madding and Paul A. Kennedy) - - - - - - 413
  Traumatismes ostéo-articulaires de la main (ed. R. Vilain) - - - - - - - - 332
  Tumours of bone and cartilage, Vol. 5 (Harlan J. Spjut, Howard D. Doffman, Robert E. Fechner, and Lauren V. Ackerman) - - 415
  Urologische Operationslehre, Vol. 8 (G. W. Müller, W. Welrheim, and G. W. Heise) - 989
  Urology and renal medicine (J. E. Newsam and J. J. B. Petrie) - - - - - - - 83
  Vascular disorders of the intestine (ed. Scott J. Boley) - - - - - - - - 498
  Der vena cava-Katheter (C. Burri and D. Gasser) 750
  Venous thrombosis and pulmonary embolism (Michael Hume, Simon Sevitt, and Duncan P. Thomas) - - - - - - - 83
  1971 *Year book of surgery* (ed. Seymour I. Schwartz) - - - - - - - - 750

Reviews (**Authors**):—
  Abel, Martin S.: *Occult traumatic lesions of the cervical vertebrae* - - - - - 331
  Ackerman, Lauren V.: *See* Spjut, Harlan J., jt. auth.
  Albert, Solomon N.: *Blood volume and extracellular fluid volume* - - - - - - 665
  Albertin, Robert H.: *See* Carey, Larry C., jt. auth.
  Alken, C. E., Dix, V. W., Goodwin, W. E., and Wildbolz, E.: *Encyclopedia of urology* (ed.) - - - - - - - - - 332
  Allgöwer, M., Bergentz, S. E., Calne, R. Y., and Gruber, U. F.: *Progress in surgery, Vol.* 10 (ed.) 751
  — — *See also* Müller, M. E., jt. auth.
  American Academy of Orthopaedic Surgeons: *Instructional course lectures, Vol. XX* - - 749
  Anson, B. J., and McVay, C. B.: *Surgical anatomy, Vols.* 1 *and* 2 - - - - - 82
  Apley, A. Graham: *Modern trends in orthopaedics—6* (ed.) - - - - - - - 924
  Ariel, Irving M., and Kazarian, Kirk K.: *Diagnosis and treatment of abdominal abscesses* - 416
  Ash, Major M.: *See* Kerr, Donald A., jt. auth.
  Avery Jones, Sir Francis, and Godding, Edmund W.: *Management of constipation* (ed.) 497
  Ballantyne, John, and Groves, John: *Diseases of the ear, nose and throat* (ed.) - - - 329
  Balner, Hans, van Bekkum, D. W., and Rapaport, Felix T.: *Transplantation today* (ed.) - 246
  Barker, Harold G.: *The continuing education of the surgeon* (ed.) - - - - - - 82
  — — *The structure and support of contemporary residency programs in surgery* (ed.) - 164
  Barry, III, Herbert: *See* Wallgren, Henrich, jt. auth.
  Bartlett, R. H., Drinker, P. A., and Galletti, P. M.: *Mechanical devices for cardiopulmonary assistance* (ed.) - - - - - - - - 328
  Bartmann, K.: *See* Finland, M., jt. ed.
  Bateman, James E.: *The shoulder and neck* - 923
  Baudisch, E.: *Atlas röntgenologischer Befunde am operierten Magen* - - - - - - 247
  Becker, R. Frederick, Wilson, James W., and Gehweiler, John A.: *The anatomical basis of medical practice* - - - - - - - 668
  Bellin, A.: *See* Chigot, P. L., jt. ed.
  Bergentz, S. E.: *See* Allgöwer, M., jt. ed.
  Berger, Knute: *See* Sauvage, Lester R., jt. auth.
  Bessot, M.: *See* Kissel, P., jt. auth.

PAGE
Reviews (Authors), *continued*
Billingham, Rupert, and Silvers, Willys: *The immunobiology of transplantation* 163
Bircher, Jost L.: *Klinische Sudeckprophylaxe und Therapie* 331
Black, John: *Neonatal emergencies and other problems* 924
Bogusch, L. K., Travin, A. A., and Semenenkow, J. L.: *Transperikardiale Operationen an den Hauptbronchien und Lungengefassen* 163
Boley, Scott: *Vascular disorders of the intestine* (ed.) 498
Bourne, Gordon: *See* Hawkins, John, jt. auth.
Braimbridge, M. V.: *Postoperative cardiac intensive care* 749
Brain, M. C.: *See* Goldberg, A., jt. ed.
Brashear, H. Robert: *See* Rancy, R. Beverly, jt. ed.
British Medical Journal: *Today's drugs, Vol.* 2 329
— — — *Diseases of the urinary tract* 328
Brunson, Joel G., and Gall, Edward A.: *Concepts of disease* (ed.) 499
Bucher, Nancy L. R., and Malt, Ronald A.: *Regeneration of liver and kidney* 330
Buhler, Victor: *See* Pipkin, Garbett, jt. auth.
Burri, C.: *Die einfachen Kreislaufgrössen beim chirurgischen Patienten* 413
— — and Gasser, D.: *Der vena cava-Katheter* 750
Bzoch, Kenneth R.: *See* Grabb, William C., jt. ed.
Calman, Kenneth C.: *Basic skills for surgical housemen* 500
Calne, R. Y.: *Clinical organ transplantation* (ed.) 415
— — *See also* Allgöwer, M., jt. ed.
Campbell, Donald: *See* Norris, Walter, jt. auth.
Capper, W. Melville: *See* Rains, A. J. Harding, jt. revisor
Carey, Larry C., and Albertin, Robert H.: *Ellison's atlas of surgery of the stomach and duodenum* 748
Cashell, G. T. Willoughby, and Durran, Isobel M.: *Handbook of orthoptic principles* 497
Castelnuovo-Tedesco, Pietro: *Psychiatric aspects of organ transplantation* (ed.) 161
de Castro, J.: *See* Vourc'h, G., jt. auth.
Chapchal, G., and Waigand, D.: *Orthopädische Therapie* 81
Chase, Robert A.: *See* Cramer, Lester M., jt. ed.
Chigot, P. L., and Bellin, A.: *Les entretiens de Bichat* 1971 (ed.) 415
Churchill, Edward D.: *Surgeon to soldiers* 750
Churchill-Davidson, H. C.: *See* Wylie, W. D., jt. ed.
Clowdus, Bernard F.: *See* Steigmann, Frederick, jt. auth.
Combe, E. C.: *Notes on dental materials* 583
Cooper, Philip: *The craft of surgery, Vols.* 1–3 (ed.) 330
— — and Nyhus, Lloyd M.: *Surgery annual* 1971 (ed.) 748
Coppleson, Malcolm, Pixley, Ellis, and Reid, Bevan: *Colposcopy. A scientific and practical approach to the cervix in health and disease* 247
Crabbe, W. A.: *Orthopaedics for the undergraduate. Fractures* 581
Cramer, Lester M., and Chase, Robert A.: *Symposium on the hand, Vol.* 3 (ed.) 668
Cramley, Brian W.: *See* Feldman, Stanley A., jt. ed.
Cranfield, Alice B.: *Theatre nurses handbook* 840
Crawford Adams, J.: *Outline of orthopaedics* 329
Crews, Eli Rush, and Lapuerta, Leopoldo: *A manual of respiratory failure. Tracheostomy, endotracheal intubation, and mechanical ventilation* 750

PAGE
Reviews (Authors), *continued*
Cruess, Richard L., and Mitchell, Nelson S.: *Surgery of rheumatoid arthritis* (ed.) 666
Dale, W. Andrew: *Management of arterial occlusive disease* (ed.) 749
Dalessandro, William: *See* Milles, George, jt. auth.
Daniel, Joseph C.: *Methods in mammalian embryology* (ed.) 247
Davson, Hugh: *Physiology of the eye* 582
Dawson, A. M.: *Intestinal absorption and its derangements* (ed.) 415
Deeley, T. J.: *Carcinoma of the bronchus* (ed.) 415
— — *Gynaecological cancer* (ed.) 414
Dennis, Robert Lee, and Doyle, Jean Monty: *The complete handbook for medical secretaries and assistants* 500
Diethelm, L.: *Handbuch der medizinischen Radiologie* (ed.) 924
Dix, V. W.: *See* Alken, C. E., jt. ed.
Doerr, Wilhelm, Seifert, Gerhard, and Uehlinger, Erwin: *Spezielle pathologische Anatomie, Volume* 2, *Part I: Oesophagus und Magen* 923
Doffman, Howard D.: *See* Spjut, Harlan J., jt. auth.
Dossetor, John B., and Gault, M. Henry: *Nephron failure: Conservation, substitution, replacement* 164
Douglas, D. M.: *Surgical departments in hospitals. The surgeon's view* (ed.) 668
Doyle, Jean Monty: *See* Dennis, Robert Lee, jt. auth.
Drinker, P. A.: *See* Bartlett, R. H., jt. ed.
Duprez, A.: *See* Kissel, P., jt. auth.
Durran, Isobel M.: *See* Cashell, G. T. Willoughby, jt. auth.
Duthie, H. L.: *Surgeons' decisions* 161
Eckert, Charles: *Emergency room care* (ed.) 752
Eden, M.: *See* Rutstein, D. R., jt. auth.
Egdahl, Richard H.: *See* Kinney, John M., jt. ed.
Ehrenpreis, Theodor: *Hirschsprung's disease* 413
Ellis, Harold: *Clinical anatomy* 328
Ellis, P. Maxwell: *Modern trends in diseases of the ear, nose and throat*—2 (ed.) 751
Farrington, Graham H.: *See* Scorer, C. Gordon, jt. auth.
Fast, Thomas B.: *See* Mitchell, David F., jt. auth.
Favaloro, Rene G.: *Surgical treatment of coronary arteriosclerosis* 84
Fechner, Robert E.: *See* Spjut, Harlan J., jt. auth.
Feldman, Stanley A., and Cramley, Brian W.: *Tracheostomy and artificial ventilation* (ed.) 581
Fields, William S., and Hass, William K.: *Aspirin, platelets and stroke. Background for a clinical trial* (ed.) 499
Finland, M., Marget, W., and Bartmann, K.: *Bacterial infections: Changes in their causative agents and possible basis* (ed.) 923
Fisher, David W.: *See* Good, Robert A., jt. ed.
Francis, Jill: *See* Gilliland, Ian, jt. ed.
Fraser, Suzanne G.: *See* Shivas, Andrew A., jt. auth.
Frazier, Claude A.: *Surgery and the allergic patient* (ed.) 584
Frost, Harold M.: *Orthopaedic surgery in spasticity* 989
Gall, Edward A.: *See* Brunson, Joel G., jt. ed.
Galletti, P. M.: *See* Bartlett, R. H., jt. ed.
Gasser, D.: *See* Burri, C., jt. auth.
Gault, M. Henry: *See* Dossetor, John B., jt. auth.
Gauthier-Lafaye, P.: *See* Vourc'h, G., jt. auth.

PAGE

Reviews (Authors), *continued*

Gear, Michael W. L.: *See* Gough, M. H., jt. auth.

Gehweiler, John A.: *See* Becker, R. Frederick, jt. auth.

Gérard-Marchant, Réne: *Glossaire d'histopathologie des tumeurs humaines* - - - 164

Gessler, Ulrich, Schröder, Karl, and Weidinger, Horst: *Pathogenese und Klinik des akuten Nierenversagens* (ed.) - - - - - 247

Gilliland, Ian, and Francis, Jill: *The scientific basis of medicine. Annual reviews*, 1971 (ed.) 84

Giudicelli, J. F.: *See* Vourc'h, G., jt. auth.

Godding, Edmund W.: *See* Avery Jones, Sir Francis, jt. ed.

Goldberg, A., and Brain, M. C.: *Recent advances in haematology* (ed.) - - - - - 82

Goldin, Marshall D.: *Intensive care of the surgical patient* - - - - - - - 329

Good, Robert A., and Fisher, David W.: *Immunobiology* (ed.) - - - - - 248

Goodman, Floyd, and Schoedinger, George R.: *Questions and answers in orthopaedics* - - 748

Goodwin, W. E.: *See* Alken, C. E., jt. ed.

Gough, M. H., and Gear, Michael W. L.: *The plain X-ray in the diagnosis of the acute abdomen* - - - - - - - 248

Grabb, William C., Rosenstein, Sheldon W., and Bzoch, Kenneth R.: *Cleft lip and palate. Surgical, dental and speech aspects* (ed.) - 331

Green, Thomas H.: *Gynaecology. Essentials of clinical practice* - - - - - - - 331

Griem, M. L.: *See* Ultmann, J. E., jt. ed.

Groves, John: *See* Ballantyne, John, jt. ed.

Gruber, U. F.: *See* Allgöwer, M., jt. ed.

Del Guercio, Louis R. M.: *See* Herksy, S. G., jt. ed.

Gupta, Roshan Lall: *Chest injuries* - - - - 667

Haagensen, C. D.: *Diseases of the breast* - - 163

Haimovici, Henry: *Ischemic forms of venous thrombosis* - - - - - - - - 246

Halnan, Keith E.: *Recent advances in cancer and radiotherapeutics* (ed.) - - - - 666

Hamilton, S. G. Ian: *See* Hamilton, W. J., jt. ed.

Hamilton, W. J., Simon, G., and Hamilton, S. G. Ian: *Surface and radiological anatomy* (ed.) - - - - - - - - - - 164

Hansell, Peter: *See* Perkins, E. S., jt. auth.

Hardy, James D.: *Critical surgical illness* (ed.) - 498

— — *Human organ support and replacement* (ed.) - - - - - - - 84

Hass, William K.: *See* Fields, Williams S., jt. ed.

Hawkins, John, and Bourne, Gordon: *Shaw's textbook of gynaecology* - - - - 83

Heck, W.: *See* Stoermer, J., jt. auth.

Hecker, W. Ch.: *See* Rickham, P. P., jt. ed.

Heise, G. W.: *See* Müller, G. W., jt. auth.

Hersky, S. G., del Guercio, Louis R. M., and McConn, Rita: *Septic shock in man* (ed.) - 667

Hill, Sir Austin Bradford: *Principles of medical statistics* - - - - - - - - 81

Hill, D. W.: *Physics applied to anaesthesia* - 749

Hohmann, Albert: *See* Paparella, Michael M., jt. ed.

Hollander, L. P.: *See* Matthes, M., jt. ed.

Horst, Wolfgang: *Frontiers of nuclear medicine* (ed.) - - - - - - - - - 332

Hrubec, Zderek: *See* Nashold, Blaine S., jt. ed.

Hruza, Zdenek: *Resistance to trauma* - - 924

Hueston, J. T.: *Plastic and reconstructive surgery* (ed.) - - - - - - - - - 162

Huff, John S.: *See* Paparella, Michael M., jt. ed.

PAGE

Reviews (Authors), *continued*

Hume, Michael, Sevitt, Simon, and Thomas, Duncan P.: *Venous thrombosis and pulmonary embolism* - - - - - - - - 83

Hunter, A. R.: *Essentials of artificial ventilation of the lungs* - - - - - - - 989

Husslein, Hugo: *See* Martius, Heinrich, jt. auth.

Ingbar, Sidney H.: *See* Werner, Sidney C., jt. ed.

Ionescu, M. I., Ross, D. N., and Wooler, G. H.: *Biological tissue in heart valve replacement* (ed.) 590

Irvine, W. T.: *Modern trends in surgery—3* (ed.) 163

James, C. C. Michael, and Lassman, L. P.: *Spinal dysraphism. Spina bifida occulta* - 500

Jamieson, Kenneth G.: *A first notebook of head injury* - - - - - - - - - 329

Jepsen, Otto, and Sørensen, H. Rahbeth: *Mediastinoscopy* (ed.) - - - - - 416

Johnson, Douglas E.: *Testicular tumours* (ed.) - 751

Joyson, Malcolm: *Total hip replacement* (ed.) - 414

Kazarian, Kirk K.: *See* Ariel, Irving M., jt. auth.

Kennedy, Paul A.: *See* Madding, Gordon F., jt. auth.

Kerley, Peter: *See* Shanks, S. Cockrane, jt. ed.

Kerr, Donald A., and Ash, Major M.: *Oral pathology* - - - - - - - - 328

Killey, H. C.: *Fractures of the mandible* - - 162

— — *Fractures of the middle third of the facial skeleton* - - - - - - - 162

Kinney, John M., Egdahl, Richard H., and Zuidema, George D.: *Manual of preoperative and postoperative care* (ed.) - - - 666

Kissel, P., Bessot, M., Duprez, A., and Mauuary, G.: *La chimiothérapie regional des cancers de l'appareil digestif* - - - 924

Kleine, N.: *See* Matthes, M., jt. ed.

Kovetiz, Albert: *See* Weinberg, Sidney R., jt. auth.

Krause, Urban: *See* Small, W. P., jt. auth.

Kusten, W. H.: *See* Ultmann, J. E., jt. ed.

Lane-Petter, W., and Pearson, A. E. G.: *The laboratory animal—Principles and practice* - 989

Langston, Hiram T.: *See* Milles, George, jt. auth.

Lapuerta, Leopoldo: *See* Crews, Eli Rush, jt. auth.

Lassman, L. P.: *See* James, C. C. Michael, jt. auth.

Last, R. J.: *Anatomy, regional and applied* - 668

Lazarus, Stephen M.: *See* Weinberg, Sidney R., jt. auth.

Lechat, P.: *International encyclopedia of pharmacology and therapeutics. Section 8: Local anaesthetics* (ed.) - - - - - 84

Lelièvre, Jean: *Pathologie du pied* - - - 82

Lindenschmidt, Theodor Ott, Rugheimer, Erich, and Willenegger, Hans: *Praxis der Schockbehandlung* (ed.) - - - - - 668

Linder, F., Ott, G., and Rudolph, H.: *Diagnostische und therapeutische Fortschritte in der Krebschirurgie* - - - - - - 666

Lowe, William C.: *Neoplasms of the gastrointestinal tract* - - - - - - - 752

Lucas, George L.: *Examination of the hand* - 750

Lucas, R. B.: *Pathology of tumours of the oral tissues* - - - - - - - - 749

Luck, G. M., Luckman, J., Smith, B. W., and Stringer, J.: *Patients, hospitals and operational research* - - - - - - - 581

Luckman, J.: *See* Luck, G. M., jt. auth.

McConn, Rita: *See* Hersky, S. G., jt. ed.

McIntyre, O. Ross: *Proceedings of the fourth annual leucocyte culture conference* (ed.) - 247

PAGE
Reviews (Authors), *continued*
Mack, Alan: *Full dentures. The treatment of the edentulous patient* - - - - - - 162
McVay, C. B.: *See* Anson, B. J., jt. auth.
Madding, Gordon F., and Kennedy, Paul A.: *Trauma to the liver* - - - - - - 413
Mahoney, Earle B.: *Cardiovascular surgery, 1969* (ed.) - - - - - - - - 83
— — *Cardiovascular surgery*, 1970 (ed.) - 161
Malt, Ronald A.: *See* Bucher, Nancy L. R., jt. auth.
Marget, W.: *See* Finland, M., jt. ed.
Markwardt, F.: *Handbuch der experimentelle Pharmakologie. Anticoagulantien* (ed.) - - 83
Marshall, George, and Poling, David: *Schweitzer. A biography* - - - - - 582
Martius, Gehard: *See* Martius, Heinrich, jt. auth.
Martius, Heinrich, and Husslein, Hugo: *Die gynäkoligischen Operationen* - - - - 413
— — and Martius, Gehard: *Geburtshilfliche Operationen* - - - - - - - - 500
Massey, J. B.: *See* Meredith, W. J., jt. auth.
Matthes, M., Kleine, N., and Hollander, L. P.: *Ergebnisse der Bluttransfusionsforschung, Vol. II* (ed.) - - - - - - - - - 500
Mauuary, G.: *See* Kissel, P., jt. auth.
Meredith, W. J., and Massey, J. B.: *Fundamental physics of radiology* - - - - 750
Meyer, Julia: *See* Squier, C. A., jt. ed.
Meyer, Justus: *See* Nolte, Hans, jt. auth.
Milford, Lee: *The hand* - - - - - 248
Milles, George, Langston, Hiram T., and Dalessandro, William: *Autologous transfusions* - - - - - - - - - 248
Mital, Mohinder A., and Pierce, Donald S.: *Amputees and their prostheses* - - - - 164
Mitchell, David F., Standish, S. Miles, and Fast, Thomas B: *Oral diagnosis. Oral medicine* - - - - - - - - - 163
Mitchell, Nelson S.: *See* Cruess, Richard L., jt. ed.
Modan, Baruch: *The polycythemic disorders* - 416
Montagu, Ashley: *The elephant man* - - 924
Moroney, James: *Surgery for nurses* - - 247
Mouïel, Jean, and Regensberg, Claude: *Conférences de séméiologie chirurgicale, Vol. 5* - 497
Müller, G. W., Welrheim, W., and Heise, G. W.: *Urologishe Operationslehre* - - 989
Müller, M. E., Allgöwer, M., and Willenegger, H.: *Manuel d'ostéosynthèse. Technique A.O.* 161
Naclerio, Emil A.: *Chest injuries. Physiologic principles and emergency management* - - 331
Nashold, Blaine S., and Hrubec, Zderek: *Lumbar disc disease* (ed.) - - - - - 748
Nealon, Thomas F.: *Fundamental skills in surgery* - - - - - - - - - - 583
Neville, William E.: *Care of the surgical cardiopulmonary patient* (ed.) - - - - - 499
Newsam, J. E., and Petrie, J. J. B.: *Urology and renal medicine* - - - - - - - 83
Newton, T. H., and Potts, D. Gordon: *Radiology of the skull and brain, Vols. 1 and 2* (ed.) 752
Nolte, Hans, and Meyer, Justus: *Regionale Anästhesie mit dem Langzeitanästhetikum Bupivacain* - - - - - - - 665
Norriss, Walter, and Campbell, Donald: *Anaesthetics, resuscitation and intensive care* 82
Nyhus, Lloyd M.: *See* Cooper, Philip, jt. ed.
Ollier, Marc: *Technique des plâtres et corsets de scolioses* - - - - - - - - - 82
Opitz, H., and Schmid, F.: *Handbuch der Kinderheilkunde, Vol. VIII, Part 2* (ed.) - 751
O'Rahilly, Ronan: *See* Vidić, Branislav, jt. auth.
Oram, Samuel: *Clinical heart disease* - - 498

PAGE
Reviews (Authors), *continued*
Orsoni, P.: *Manuel de l'aide en chirurgie* - - 414
Ott, G.: *See* Linder, F., jt. auth.
Paparella, Michael M., Hohmann, Albert, and Huff, John S.: *Clinical otology. An international symposium* (ed.) - - - - - 499
— — *See also* Saunders, William H., jt. auth.
Pearce, Evelyn: *A textbook of nursing. A compendium of nursing knowledge* - - - - 416
Pearson, A. E. G.: *See* Lane-Petter, W., jt. auth.
Penn, I.: *Malignant tumours in organ transplant recipients* - - - - - - - 161
Perkins, E. S., and Hansell, Peter A.: *An atlas of diseases of the eye* - - - - - - 668
Peterson, Clare Gray: *Perspectives in surgery* - 840
Petrie, J. J. B.: *See* Newsam, J. E., jt. auth.
Pierce, Donald S.: *See* Mital, Mohinder A., jt. auth.
Pipkin, Garbett, and Buhler, Victor: *The illness of trauma* - - - - - - - - 303
Pixley, Ellis: *See* Coppleston, Malcolm, jt. auth. - - - - - - - -
Poling, David: *See* Marshall, George, jt. auth.
Polk, Hiram C., and Stone, H. Harlan: *Contemporary burn management* (ed.) - - 666
Potter, Guy D.: *Sectional anatomy and tomography of the head* - - - - - - 751
Potts, D. Gordon: *See* Newton, T. H., jt. ed.
Pracy, R., Siegler, J., and Stell, P. M.: *A short textbook. Ear, nose and throat* - - - - 413
Prévot, J.: *See* Rickham, P. P., jt. ed.
Probst, C.: *Frontobasale Verletzungen* - - 752
Quénu, Jean: *Nouvelle practique chirurgicale illustrée* (ed.) - - - - - - - 414
Rains, A. J. Harding, and Capper, W. Melville: *Bailey and Love's Short practice of surgery* (rev.) - - - - - - - - - 414
Rancy, R. Beverly, and Brashear, H. Robert: *Shands' Handbook of orthopaedic surgery* (ed.) 583
Rapaport, Felix T.: *See* Balner, Hans, jt. ed.
Regensberg, Claude: *See* Mouïel, Jean, jt. auth.
Reid, Bevan: *See* Coppleson, Malcolm, jt. auth.
Rickham, P. P., Hecker, W. Ch., and Prévot, J.: *Progress in pediatric surgery, Vol. 2* (ed.) - 161
— — — — — — *Ibid., Vol.* 3 (ed.) - - 581
Robel, Stephen B.: *See* Sauvage, Lester R., jt. auth.
Roberts, Alan Clive: *Facial prostheses* - - 582
Rosenstein, Sheldon W.: *See* Grabb, William C., jt. ed.
Ross, D. N.: *See* Ionescu, M. I., jt. ed.
Rudolph, H.: *See* Linder, F., jt. auth.
Rugheimer, Erich: *See* Linderschmidt, Theodor Ott, jt. ed.
Rutstein, D. R., and Eden, M.: *Engineering and living systems. Interfaces and opportunities* - 162
Saunders, William H., and Paparella, Michael M.: *Atlas of ear surgery* - - - - - 163
Sauvage, Lester R., Viggers, Robert F., Berger, Knute, Robel, Stephen B., Sawyer, Philip N., and Wood, Stephen J.: *Prosthetic replacement of the aortic valve* - - - - - 752
Sawyer, Philip N.: *See* Sauvage, Lester R., jt. auth.
Schein, Clarence J.: *Acute cholecystitis* - - 923
Schmid, F.: *See* Opitz, H., jt. ed.
Schoedinger, George R.: *See* Goodman, Floyd G., jt. auth.
Schröder, Karl: *See* Gessler, Ulrich, jt. ed.
Schuchardt, K.: *Fortschritte der Kiefer- und Gesichts-Chirurgie* (ed.) - - - - - 246
Schuknecht, Harold F.: *Stapedectomy* - - 667
Schwartz, Seymour I.: 1971 *Year book of surgery* (ed.) - - - - - - - - 750

PAGE

Reviews (Authors), *continued*
  Scorer, C. Gordon, and Farrington, Graham H.: *Congenital deformities of the testis and epididymis* - - - - - - - - 582
  Scott, Peter R.: *An aid to clinical surgery* - 415
  Seddon, Sir Herbert: *Surgical disorders of the peripheral nerves* - - - - - - 749
  Seifart, W.: *Kurzer Leitfaden der praktischen Infusionstherapie* - - - - - - 414
  Seifert, Gerhard: *See* Doerr, Wilhelm, jt. auth.
  Semenenkow, J. L.: *See* Bogusch, L. K., jt. auth.
  Sevitt, Simon: See Hume, Michael, jt. auth.
  Shanks, S. Cockrane, and Kerley, Peter: *A textbook of X-ray diagnosis, Vol.* 6 (ed.) - - 497
  Shivas, Andrew A., and Fraser, Suzanne G.: *Frozen section in surgical diagnosis* - - 81
  Siegler, J.: *See* Pracy, R., jt. auth.
  Silvers, Willys: *See* Billingham, Rupert, jt. auth.
  Simon, G.: *See* Hamilton, W. J., jt. ed.
  Small, W. P., and Krause, Urban: *An introduction to clinical research* - - - - - 748
  Smith, B. W.: *See* Luck, G. M., jt. auth.
  Smith, E. Durham: *See* Stephens, F. Douglas, jt. auth.
  Smith, R. Abbey, and Smith, R. E.: *Surgery of the oesophagus. The Coventry conference* (ed.) - - - - - - - - 751
  Smith, R. E.: *See* Smith, R. Abbey, jt. ed.
  Société Française de Chirurgie Orthopédique et Traumatologie: *Orthopédie traumatologie* 84
  Sørensen, H. Rahbeth: *See* Jepsen, Otto, jt. ed.
  Sparberg, Marshall: *Ileostomy care* - - 584
  Spjut, Harlan J., Doffman, Howard D., Fechner, Robert E., and Ackermann, Lauren V.: *Tumours of bone and cartilage, Vol.* 5 - - 415
  Squier, C. A., and Meyer, Julia: *Current concepts of the histology of oral mucosa* (ed.) - 583
  Standish, S. Miles: *See* Mitchell, David F., jt. auth.
  Steigmann, Frederick, and Clowdus, Bernard F.: *Hepatic encephalopathy* - - - - - 81
  Stell, P. M.: *See* Pracy, R., jt. auth.
  Stephens, F. Douglas, and Smith, E. Durham: *Ano-rectal malformations in children* - 581, 840
  Stoermer, J., and Heck, W.: *Pädiatrischer EKG-Atlas* - - - - - - - - 497
  Stoll, Basil A.: *Endocrine therapy in malignant disease* (ed.) - - - - - - - 840
  Stone, H. Harlan: *See* Polk, Hiram C., jt. ed.
  Stringer, J.: *See* Luck, G. M., jt. auth.
  Sutton, Neville G.: *Anatomy of the brain and spinal medulla* - - - - - - - 162
  Szabo, Dr. Gyorgy: *Die Fettembolie* - - 583
  Tabor, James R.: *Methods of ossiculoplasty* - 330
  Takahashi, Masayoshi: *Color atlas of cancer cytology* - - - - - - - - 499
  Thomas, Duncan P.: *See* Hume, Michael, jt. auth.
  Travin, A. A.: *See* Bogusch, L. K., jt. auth.
  Trueta, J.: *Gathorne Robert Girdlestone* - - 161
  Tsuboi, Eitaka: *Atlas of transbronchial biopsy. Early diagnosis of peripheral pulmonary carcinomas* - - - - - - - - 332
  Tuchel, V.: *Non-specific mesenteric lymphadenitis* - - - - - - - - 748
  Uehlinger, Erwin: *See* Doerr, Wilhelm, jt. auth.
  Ultmann, J. E., Griem, M. L., Kusten, W. H., and Wissler, R. W.: *Current concepts in the management of leukemia and lymphoma* (ed.) 328
  Umbach, W.: *Special topics in stereotaxis, epilepsy, disorders of behaviour, and autonomic balance* (ed.) - - - - - - - 330

PAGE

Reviews (Authors), *continued*
  Vaeth, J. M.: *Radiation effect and tolerance, normal tissue. Basic concepts in radiation pathology* (ed.) - - - - - - - 989
  van Bekkum, D. W.: *See* Balner, Hans, jt. ed.
  Veirs, Everett R.: *The lacrimal system* (ed.) - 583
  Viars, P.: *See* Vourc'h, G., jt. auth.
  Vidić, Branislav, and O'Rahilly, Ronan: *An atlas of the anatomy of the ear* - - - 498
  Viggers, Robert F.: *See* Sauvage, Lester R., jt. auth.
  Vilian, R.: *Traumatismes ostéo-articulaires de la main* (ed.) - - - - - - - 332
  Vosschulte, Karl, and Zukschwerdt, Ludwig: *Chirurgische differential-diagnostik* (ed.) - 667
  Vourc'h, G., de Castro, J., Gauthier-Lafaye, P., Giudicelli, J. F., and Viars, P.: *Les analgésiques et la douleur* - - - - - 81
  Waigand, D.: *See* Chapchal, G., jt. auth.
  Wallgren, Henrich, and Barry, III, Herbert: *Actions of alcohol, Vols.* 1 *and* 2 - - - 498
  Weidinger, Horst: *See* Gessler, Ulrich, jt. ed.
  Weinberg, Sidney R., Kovetiz, Albert, and Lazarus, Stephen M.: *Simultaneous prostatectomy and inguinal herniorrhaphy* - - - 83
  Weiss, Marian: *Myoplastic amputation, immediate prosthesis and early amputation* - 84
  Welrheim, W.: *See* Müller, G. W., jt. auth.
  Werner, Sidney C., and Ingbar, Sidney H.: *The thyroid. A fundamental and clinical text* (ed.) - - - - - - - - 667
  Whitley, Joseph E., and Whitley, Nancy O'Neil: *Angiography. Techniques and procedures* - 416
  Whitley, Nancy O'Neil: *See* Whitley, Joseph E., jt. auth.
  Wildbolz, E.: *See* Alken, C. E., jt. ed.
  Willcox, Phillip H. A.: *The detective-physician. The life and work of Sir William Willcox, K.C.I.E., C.B., C.M.G., M.D., F.R.C.P.* - 665
  Willenegger, Hans: *See* Lindenschmidt, Theodor Ott, jt. ed.; Müller, M. E., jt. auth.
  Williams, C. Barrie: *Basic practical surgery* - 162
  Wills, M. R.: *Biochemical consequences of chronic renal failure* - - - - - - - 248
  Wilson, James W.: *See* Becker, R. Frederick, jt. auth.
  Wissler, R. W.: *See* Ultmann, J. E., jt. ed.
  Wood, Stephen J.: *See* Sauvage, Lester R., jt. auth.
  Wooler, G. H.: *See* Ionescu, M. I., jt. ed.
  Wylie, W. D., and Churchill-Davidson, H. C.: *A practice of anaesthesia* (ed.) - - - 667
  Yules, Richard B.: *Atlas for surgical repair of cleft lip, cleft palate, and noncleft velopharyngeal incompetence* - - - - - - 331
  Zinn, W. M.: *Idiopathic ischemic necrosis of the femoral head in adults* (ed.) - - - - 414
  Zorab, P. A.: *Scoliosis and growth* (ed.) - - 329
  Zuidema, Richard H.: *See* Kinney, John M., jt. ed.
  Zukschwerdt, Ludwig: *See* Vosschulte, Karl, jt. ed.
  Zuppinger, A.: *Handbuch der medizinischen Radiologie: Encyclopedia of medical radiology. Part* 3. *Spezielle Strahlentherapie maligner. Tumoren* (ed.) - - - - - - - 582
Reynolds, K. W.: *See* Desmond, A. M., jt. auth.
Rhodes, J.: Azathioprine in the treatment of Crohn's disease - - - - - - - - 819
Richardson, J. P.: *See* Vellar, I. D. A., jt. auth.
Rigby, C. C.: *See* Toghill, P. J., jt. auth.
Rintoul, R. F.: *See* Johnstone, J. M. S., jt. auth.
Ritchie, Jean K.: Ulcerative colitis treated by ileostomy and excisional surgery - - - 345

PAGE

Roberts, V. C., Sabri, S., Beeley, A. H., and Cotton, L. T.: The effect of intermittently applied external pressure on the haemodynamics of the lower limb in man - - 223
— — *See also* Sabri, S., jt. auth.
Robson, A. J., Evans, D. B., and Calne, R. Y.: Secondary haemorrhage from the arterial anastomosis of renal allografts - - - 890
— — *See also* Calne, R. Y., jt. auth.
Rosengarten, D. S.: *See* Greenhalgh, R. M., jt. auth.
Ross, B. D.: *See* Lee, Emanoel, jt. auth.
Ross, D. N.: *See* Savage, P. E. A., jt. auth.
Ross, Harvey B., and Sales, John E. L.: Post-irradiation femoral aneurysm treated by ilio-popliteal by-pass via the obturator foramen 400
— — *See also* Simon, John S., jt. auth.
Ross, J. A., and Edmond, P.: The effects of calculi on ureteral function - - - - - - 45
Ross, P. W.: *See* MacGregor, A. B., jt. auth.
Roux-en-Y loop, reversibility of postgastrectomy alkaline reflux gastritis by - - - - 13
Rupture of bladder, recurrent spontaneous - - 985
— central, of liver with massive liver-cell necrosis 660
— joint, in Reiter's disease - - - - - 657
— spontaneous, of stomach in adult - - - 79
— subcutaneous, of breast: a seat-belt injury - 491
— traumatic, of thoracic aorta associated with hypothermia, case of - - - - - 243
Ruptured abdominal aortic aneurysm, neurological complications of - - - - - - 707
— angiomatous spleen presenting as severe coagulation defect - - - - - - - 492
— mycotic aneurysm of spleen - - - - 572
— solitary cyst of liver - - - - - - 919
Rushton, D. I.: *See* Powis, S. J. A., jt. auth.
Russell, R. C. G.: Ruptured solitary cyst of the liver - - - - - - - - - - 919

Sabri, S., Roberts, V. C., and Cotton, L. T.: The effects of intermittently applied external pressure on the haemodynamics of the hind-limb in greyhound dogs - - - - - 219
— — *See also* Roberts, V. C., jt. auth.
Sacro-iliac joint, contralateral, diastasis of, anterior dislocation of hip and - - - - - 296
Salaman, John R.: A technique for detecting rejection episodes in human transplant recipients using radioactive fibrinogen - - - - 138
Sales, John E. L.: *See* Ross, Harvey B., jt. auth.
Sangruchi, Vira, Hitchcock, Edward, and Donaldson, A. A.: Post-angiographic vertebral arteriovenous fistulae - - - - 627
Saunders, S. J.: *See* Hickman, R., jt. auth.; Spilg, Harold, jt. auth.
Savage, P. E. A., Clayton Jones, D. G., Thompson, A. E., and Ross, D. N.: The fate of aortic valve homografts - - - - - 231
Schistosomal appendicitis, chronic - - - 743
Schramek, A.: *See* Hashmonai, M., jt. auth.
Scott, Roy, Dryburgh, Frances, Wilson, Robert, Boyle, Ian T., and Pollock, David: The diagnosis of parathyroid overactivity in a population of renal stone formers - - 517
Scrotum, maintenance of maldescended testicles within, using a Dartos pouch - - - 175
Second cancer of large bowel, lesion of - - - 16
Sells, R. A.: *See* Calne, R. Y., jt. auth.
Sex chromatin, breast tumour (Barr body), evaluation of, as index of survival and response to pituitary ablation - - - - - - 731
Shah, I. K., and Daniel, O.: The results of fundoplication for the relief of oesophageal reflux due to hiatus hernia - - - - - - 285

PAGE

Shaw, H. J.: Repair of the laryngopharynx and cervical oesophagus after irradiation - - 524
Shemilt, Philip: The origin of phleboliths - - 695
Shock, haemorrhagic, erythrocyte and plasma circulation times in - - - - - - - - 957
Short, Douglas W.: *See* Bell, Graham, jt. auth.
Simmonds, F. A.: *See* Brown, R. F., jt. auth.
Simon, John S., Brown, Ashley A., and Ross, Harvey B.: Ligation of the left renal vein in splenorenal anastomosis without impairment of renal function - - - - - - - 170
Simpkins, K. C.: Some aspects of the radiology of Crohn's disease - - - - - - 810
Singh, M.: *See* Golding, P. L., jt. auth.
Skeletal metastases from mammary cancer, response to therapy of - - - - - - 85
— muscle, haemangiomata of - - - - - 634
Skin clips, surgical, nickel sensitivity to - - 745
— lymphangiography and surgery in lymphangioma of - - - - - - - - - - - 36
Skin-grafting, primary, in treatment of chronic osteomyelitis - - - - - - - - 117
Slade, Norman, and Gaches, Christopher: Vesico-intestinal fistulae - - - - - 593
Slavotinek, A. H.: *See* Elmslie, R. G., jt. auth.
Smith, Catherine M.: *See* Cuthbertson, D. P., jt. auth.
Smith, G. M. R., and Greening, W. P.: Carcinoma of aberrant breast tissue - - - - - 89
Smith, R. B.: *See* Johnston, D., jt. auth.
Snell, M. E., Hopkinson, W. I., and Porter, K. A.: Twenty-four-hour preservation of canine kidneys exposed to 45 and 60 minutes of warm ischaemia - - - - - - - 886
Sodium tetradecyl sulphate (S.T.D.) 3 per cent, local effects of intra-arterial injections of - 101
Soni, S. R., and Persaud, V.: Central rupture of the liver with massive liver-cell necrosis - 660
Spastic colonic ileus, acute myelitis presenting as - 918
Spermatic cord, leiomyosarcoma of - - - - 408
Sphincter, external anal, anatomy of - - - - 717
Spilg, Harold, Uys, C. J., Hickman, Rosemary, Saunders, Stuart J., and Terblanche, John: Twelve-hour liver preservation in the pig using hypothermia and hyperbaric oxygen - - - - - - - - - 273
Spivey, John, and Johnston, Ivan D. A.: The effect of environmental temperature and nutritional intake on the metabolic response to abdominal surgery - - - - - 93
Spleen, haemangiosarcoma of - - - - - 406
— hydatid disease of - - - - - - - 489
— ruptured angiomatous, presenting as severe coagulation defect - - - - - - 492
— — mycotic aneurysm of - - - - - 572
Splenorenal anastomosis, ligation of left renal vein in, without impairment of renal function - 170
Sprague, P.: *See* Yadav, R. V. S., jt. auth.
Squamous carcinoma of colon, does it exist? - - 410
— — stomach following corrosive acid burns - 382
Stables, D. P.: *See* Birkenstock, W. E., jt. auth.
Stanley, D. A.: *See* Deutsch, A. A., jt. auth.
Steroid excretion pattern, preoperative, prediction of 1-year survival after resection of lung tumours from - - - - - - - - 977
Stewart, George R., Mountain, John C., and Colcock, Bentley P.: Non-recurrent laryngeal nerve - - - - - - - - - 379
Stewart, I. A.: *See* Gardner, A. M. N., jt. auth.
Stoker, T. A. M., and Ellis, Harold: Wound antibiotics in gastro-intestinal surgery - - 184
Stomach, acid-fundic selective vagotomy of, without drainage in treatment of duodenal ulcer: technique and results - - - - - 602
— spontaneous rupture of, in adult - - - - 79

PAGE
Stomach, squamous carcinoma of, following corrosive acid burns 382
Stones, rectal 405
Stoodley, B. J., and Mann, C. V.: Carcinoma of colon simulating Crohn's disease 484
Strahan, J., and Bailie, H. W. C.: Glomus tumour 91
Stuart, A. E.: *See* Heading, R. C., jt. auth.
Subbuswamy, S. G.: *See* Jenkins, D. G., jt. auth.
Subcutaneous nodular lymphohistiocytic hyperplasia 375
— rupture of breast: a seat-belt injury 491
— tissues of foot, effects of posture, exercise, and bandage on clearance of ^{24}Na from 552
Surgery, abdominal, effect of environmental temperature and nutritional intake on metabolic response to 93
— for coronary artery disease 801
— 'curative', in carcinoma of colon involving duodenum 932
— femoropopliteal reconstructive arterial, failure of, and blood-flow, relationship between 549
— gastro-intestinal, wound antibiotics in 184
— lymphangiography and, in lymphangioma of skin 36
— microvascular, new instruments for 181
— short-stay, scope and safety of, in treatment of groin herniae and varicose veins 333
— successful femoropopliteal by-pass, investigation of oedema of lower limb following: the role of phlebography in demonstrating venous thrombosis 979
— and venous thrombosis, alteration in fibrinolysis associated with 754
Surgical objectives in unresected cancer of head of pancreas 508
— Research Society 299, 897
— skin clips, nickel sensitivity to 745
Systemic venous drainage, portal and, comparison of, in porcine renal allografts 541

TALIB, H.: Orbital hydatid disease in Iraq 391
Taylor, G. W.: *See* Reckless, J. P. D., jt. auth.; Terry, H. J., jt. auth.
Taylor, S.: *See* Nicolaides, A. N., jt. auth.
Taylor, Selwyn: *See* Clark, Orlo, jt. auth.
Temperature, environmental, and nutritional intake, effect of, on metabolic response to abdominal surgery 93
Tennekoon, G. E.: *See* Eaton, Henry, jt. auth.
Teratoma, pedunculated, of rectum infested with bilharziasis 655
Terblanche, J.: *See* Hickman, R., jt. auth.; Spilg, Harold, jt. auth.
Terry, H. J., Allan, J. S., and Taylor, G. W.: The relationship between blood-flow and failure of femoropopliteal reconstructive arterial surgery 549
Testicles, maintenance of maldescended, within scrotum using a Dartos pouch 175
Testicular torsion, atrophy following 422
Thompson, A. E.: *See* Savage, P. E. A., jt. auth.
Thompson, H.: *See* Jones, E. L., jt. auth.
Thompson, M. R.: A case of traumatic rupture of the thoracic aorta associated with hypothermia 243
Thoracic aorta associated with hypothermia, traumatic rupture of 243
Thrombo-embolism, conservative management of 834
— venous, natural history of 753
Thrombosis, deep-vein, diagnosis of 830
— — effect of fibrinolytic inhibitor epsilon-aminocaproic acid on incidence of, after prostatectomy 522
— — in patients with fractures of femoral neck 377
— — prostatectomy and 487
— — venous stasis and 713
PAGE
Thrombosis, postoperative deep-vein, routine use of ultrasound for diagnosis of 133
— — effect of electrical stimulation of legs on 65
Thymic tissue, ectopic, presenting as lateral cervical swelling 885
Thymoma, malignant, role of radiotherapy in management of 533
Thyroid nodule, single 545
— remnant, fate and function of 726
Thyroidectomy, subtotal, effect of remnant size on outcome of, for thyrotoxicosis 559
Thyrotoxicosis, effect of remnant size on outcome of subtotal thyroidectomy for 559
Tilstone, W. J.: *See* Cuthbertson, D. P., jt. auth.
Tinckler, Laurence F.: Nasogastric tube management 637
— — Nickel sensitivity to surgical skin clips 745
Tindal, D. S.: *See* Pollock, A. V., jt. auth.
Toghill, P. J., Rigby, C. C., and Hall, G. F. M.: Haemangiosarcoma of the spleen 406
Torbati, M.: Hydatid disease of the spleen 489
Torsion, testicular, atrophy following 422
Transplant recipients, human, technique for detecting rejection episodes in, using radioactive fibrinogen 138
Transplantation, renal, vesico-ureteric reflux following 33
Traumatic asphyxia, brachial plexus lesions associated with 539
Truncal vagotomy, abdominal, for duodenal ulcer, oesophageal perforation during 936
Tuberculosis, abdominal 597
— of gall-bladder 289
Tuberculous lymphadenitis, peripheral, in the elderly 568
— peripheral lymphadenitis 353
Tumoral calcinosis 570
Tumour(s), argentaffin-cell, of Meckel's diverticulum 213
— breast, sex chromatin (Barr body), as index of survival and response to pituitary ablation, evaluation of 731
— cells, inhibition of growth of, in culture by noxytiolin 108
— glomus 91
— — jugulare—radiotherapy or surgery 947
— lung, prediction of 1-year survival after resection of, from preoperative steroid excretion pattern 977
— malignant, of bile-duct 504
— primary liver, associated with prophyria, case of 653
Turner, D. T. L.: *See* Williams, H. T., jt. auth.
Turner, Maurice J.: *See* Guerrier, Hugh P., jt. auth.

ULCER(S), duodenal, acid-fundic selective vagotomy of stomach without drainage in treatment of: technique and results 602
— — oesophageal perforation during abdominal truncal vagotomy for 936
— — perforated, in childhood 288
— — prospective study of immediate and long-term results of Polya gastrectomy for 849
— — pyloroplasty alone in management of patients with a negative exploration for 783
— — pylorus-preserving gastrectomy in treatment of 27
— — value of preserving pylorus in surgery of 779
— gastric, treatment of, by highly selective vagotomy without drainage procedure: an interim report 787
— high gastric, operative treatment of, with special reference to Pauchet's method 1
— peptic, in duplicated ileum, perforation of 159
— perforated peptic, hydrothorax complicating 72

PAGE
Ulcers(s), two unusual leg- 478
Ulceration of mouth, pharynx, and larynx in Crohn's disease of intestine 249
— rectal and colonic, in Behçet's disease 173
Ulcerative colitis, perimuscular excision of rectum for Crohn's disease and 29
— — treated by ileostomy and excisional surgery 345
Ultrasound, routine use of, for diagnosis of post-operative deep-vein thrombosis 133
Ureteral function, effects of calculi on 45
Ureteric obstruction, bilateral, cause by benign pelvic lipomatosis 69
Uys, C. J.: *See* Spilg, Harold, jt. auth.

VAGOTOMY, abdominal truncal, for duodenal ulcer, oesophageal perforation during 936
— acid-fundic selective, of stomach without drainage in treatment of duodenal ulcer: technique and results 602
— highly selective, without drainage procedure, treatment of gastric ulcer by: an interim report 787
— lithogenic effect of 365
— randomized prospective trial comparing three established methods of gastric decompression 605
Valli, A.: *See* Mazzoni, G., jt. auth.
Varicose veins, groin herniae and, scope and safety of short-stay surgery in treatment of 333
Varicosity in superficial veins of lower limb, cause of 798
Vein-graft, by-pass, in femoropopliteal occlusive disease, muscle blood-flow following insertion of 429
Veins, superficial, of lower limb, cause of varicosity in 798
Vellar, I. D. A., Richardson, J. P., Doyle, J. C., and Keating, M.: Gastric necrosis: a rare complication of chloral hydrate intoxication 317
Venables, C. W.: An assessment of the value of measuring uncollected gastric secretion during routine secretion studies in man 473
Venous stasis and deep-vein thrombosis 713
— thrombo-embolism, natural history of 753
— thrombosis, alteration in fibrinolysis associated with surgery and 754
— — role of phlebography in demonstrating: investigation of oedema of lower limb following successful femoropopliteal by-pass surgery 979
Vertebral, post-angiographic, arteriovenous fistulae 627
Vesico-intestinal fistulae 593
Vesico-ureteric reflux following renal transplantation 33
Vessels, small, histopathology of, following microvascular repair 617
Visceral neurofibromatosis 494
Voigt, J. C., and Gregory, M. M.: Chronic schistosomal appendicitis 743
Voss, H. J.: *See* Cullen, T. H., jt. auth.

WADDELL, GORDON: *See* Leech, Peter, jt. auth.
Waddington, R. T.: A case of primary liver tumour associated with porphyria 653
Wade, J. D.: *See* Bouch, D. C., jt. auth.; Gunstensen, J., jt. auth.
Wakeley, Sir Cecil, Bt., K.B.E., C.B. 417
Walker, D. I., Bloor, K., Williams, G., and Gillie, I.: Inflammatory aneurysms of the abdominal aorta 609
Walker, M. G.: The natural history of venous thrombo-embolism 753
— — *See also* Mavor, G. E., jt. auth.
Warren, Kenneth W., Mountain, John C., and Lloyd-Jones, William: Malignant tumours of the bile-ducts 501
Wastell, C.: A modification of the Finney pyloroplasty 454

PAGE
Wastell, C.: *See also* Ellis, Harold, jt. auth.
Watkin, D. F. L., and Hudson, Jennifer: Erythrocyte and plasma circulation times in haemorrhagic shock 957
Webster, J. H. H.: *See* Evans, D. M., jt. auth.
Weir, D. G.: *See* Hennessy, T. P. J., jt. auth.
Wheeler, M. H.: Recurrent spontaneous rupture of the bladder 985
White, Mary: *See* Doran, F. S. A., jt. auth.
Whitfield, H. N.: *See* Carter, D. C., jt. auth.
Wilkinson, A. R.: *See* Croft, C. B., jt. auth.; Humphrey, C. S., jt. auth.; Johnston, D., jt. auth.
Wilkinson, K. W.: *See* Williams, H. T., jt. auth.
Williams, C. B., Halpin, D. S., and Knox, A. J. S.: Drainage following cholecystectomy 293
Williams, C. R.: The value of frusemide in 110 consecutive prostatectomies 190
Williams, G.: *See* Walker, D. I., jt. auth.
Williams, H. T., and Turner, D. T. L.: Acute myelitis presenting as spastic colonic ileus 918
— — and Wilkinson, K. W.: The management of congenital hydronephrosis in the newborn 894
Williams, J. Alexander, Oates, G. D., Brown, P. P., Burden, D. W., McCall, Jane, Hutchison, A. G., and Lees, Lorna J.: Abdominal wound infections and plastic wound guards 142
Wilson, J. N.: *See* Meggitt, B. F., jt. auth.
— — *See also* Jones, E. L., jt. auth.
Wilson, Robert: *See* Scott, Roy, jt. auth.
Winch, John: A model which can be used to improve the treatment of acute hepatic failure 771
Wingfield, H. V., and Karwowski, A.: The treatment of achalasia by cardiomyotomy 281
Woodcock, J. P., Gosling, R. G., and Fitzgerald, D. E.: A new non-invasive technique for assessment of superficial femoral artery obstruction 226
Wooler, G. H.: *See* Keighley, M. R. B., jt. auth.
Worthington, B.: *See* Golding, P. L., jt. auth.
Wosornu, Lade: A technique for creating a skin-lined hemithorax 868
— — Ventilation in an artificially produced gas cavity under basal conditions 624
Wound(s) antibiotics in gastro-intestinal surgery 184
— guards, plastic, abdominal wound infections and 142
— healing, primary, in rats, effect of oral supplementation of zinc sulphate on 194
— infection(s), abdominal, and plastic wound guards 142
— — effect of single-dose parenteral antibiotic in prevention of 98
— missile, of head, mortality in 201

XANTHOGRANULOMATOUS pyelonephritis, case of 319

YADAV, R. V. S., Johnson, W., Morris, P. J., Sprague, P., Yoffa, D., and Marshall, V. C.: Vesico-ureteric reflux following renal transplantation 33
Yao, S. T.: *See* Lewis, J. D., jt. auth.
Yates, A. K.: *See* Hill, D. G., jt. auth.
Yates-Bell, A. J., and Packham, D. A.: Giant hydronephrosis in a solitary crossed ectopic kidney 104
— — *See also* Nicolaides, A. N., jt. auth.
Yoffa, D.: *See* Yadav, R. V. S., jt. auth.
Young, H. B., and Macleod, N.: The fate and function of the thyroid remnant 726

ZINC sulphate, effect of oral supplementation of, on primary wound healing in rats 194

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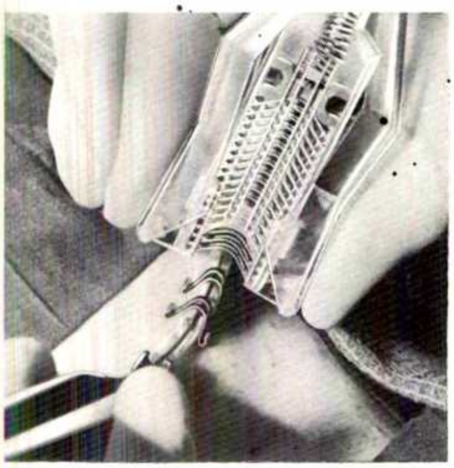

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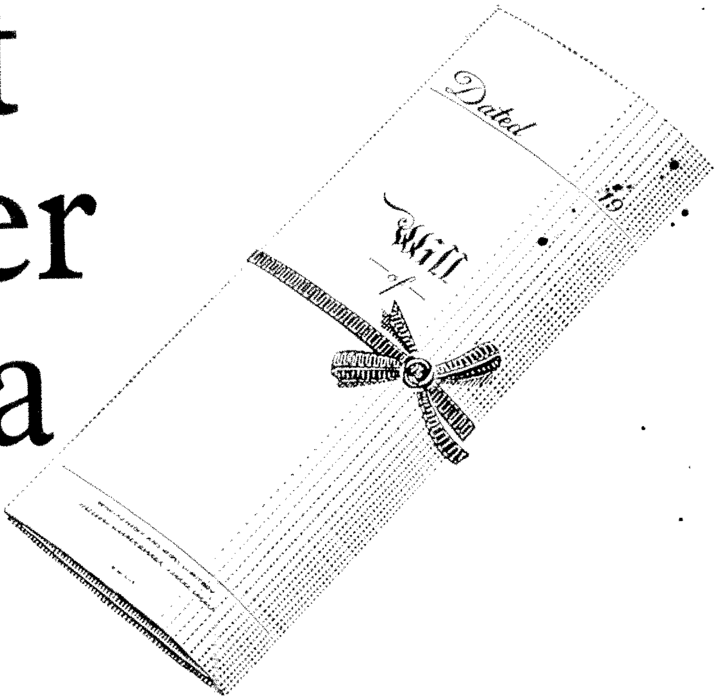

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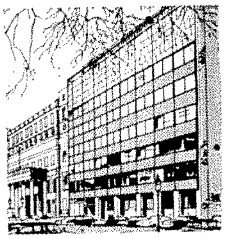

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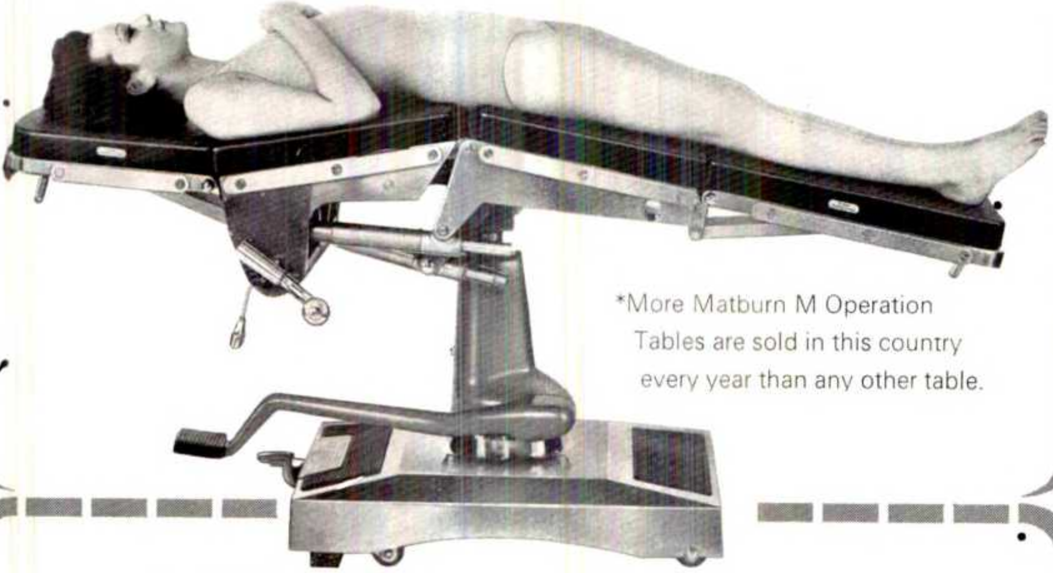

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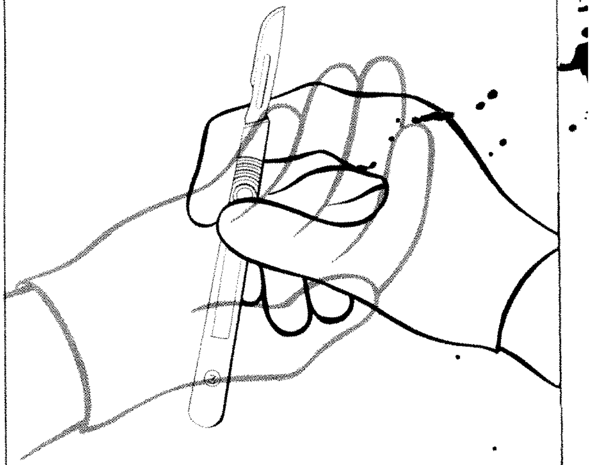

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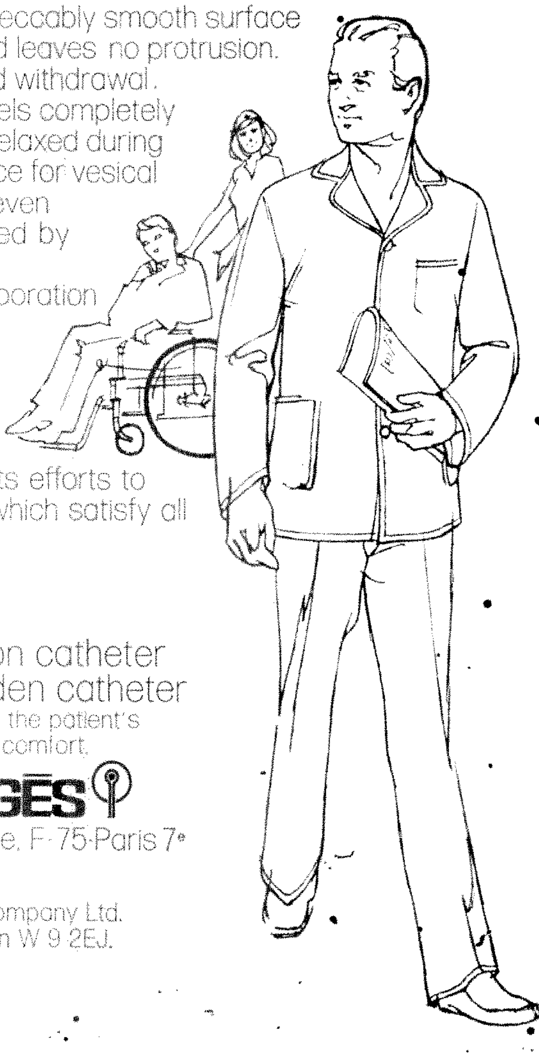

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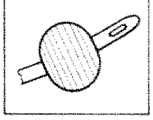

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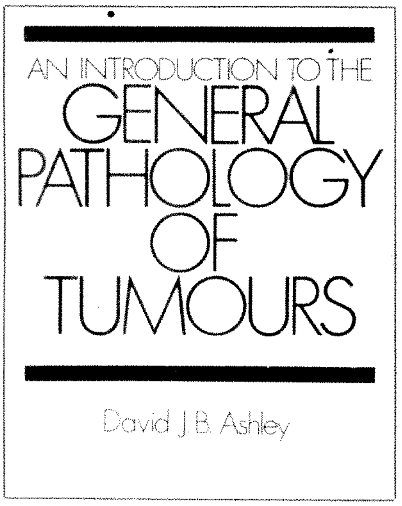

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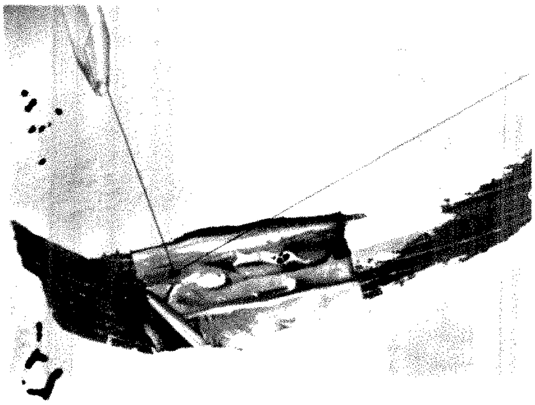

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